HIV Immunology and HIV/SIV Vaccine Databases 2003

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HIV Molecular Immunology 2003

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Contents

Preface

Scope and purpose of the HIV molecular immunology database and the nonhuman primate HIV/SIV vaccine trials databases

HIV Immunology and HIV/SIV Vaccine Databases 2003 is a companion volume to *Human Retroviruses and AIDS Genetic Sequence Compendium*. Parts I–V of this publication, the 2003 issue, is the printed version of the web-based HIV Immunology Database (`http://www.hiv.lanl.gov/content/immunology/`). The web interface for this relational database has many search options, as well as interactive tools to help immunologists design reagents and interpret their results. We summarize through the previous year's literature, which is why the 2003 database is published in 2004.

This year we have produced our first hard copy of the SIV/HIV nonhuman primate vaccine database, and we are sending it as the final part of a two volume set together with the immunology database. Like the data included in the immunology databases, these data are extracted from the HIV/SIV nonhuman primate vaccine literature. Like the HIV sequence and immunology databases, the vaccine database is available in a searchable form on line (`http://www.hiv.lanl.gov/cgi-bin/vaccine/public/index.cgi`). A more comprehensive introduction to this database and its contents can be found at the beginning of Part VI.

In the HIV Immunology Database, HIV-specific B-cell and T-cell responses are summarized and annotated. Immunological responses are divided into three parts, CTL, T helper, and antibody. Within these parts, defined epitopes are organized by protein and binding sites within each protein, moving from left to right through the coding regions spanning the HIV genome. We include human responses to natural HIV infections, as well as vaccine studies in a range of animal models and human trials. Responses that are not specifically defined, such as responses to whole proteins or monoclonal antibody responses to discontinuous epitopes, are summarized at the end of each protein section. Studies describing general HIV responses to the virus, but not to any specific protein, are included at the end of each part.

The annotation includes information such as cross-reactivity, escape mutations, antibody sequence, TCR usage, functional domains that overlap with an epitope, immune response associations with rates of progression and therapy, and how specific epitopes were experimentally defined. Basic information such as HLA specificities for T-cell epitopes, isotypes of monoclonal antibodies, and epitope sequences are included whenever possible. All studies that we can find that incorporate the use of a specific monoclonal antibody are included in the entry for that antibody. A single T-cell epitope can have multiple entries, generally one entry per study.

Finally, maps of all defined linear epitopes relative to the HXB2 reference proteins are provided. Alignments of CTL, helper T-cell, and antibody epitopes are available through the search interface on our web site at `http://www.hiv.lanl.gov/content/immunology`.

Only responses to HIV-1 and HIV-2 are included in the database. CTL responses to SIVs have been periodically summarized in our review section by Dr. Dave Watkins and colleagues. (For their most recent review, please see: Where Have All The Monkeys Gone? Evaluating SIV-Specific CTL in the Post-Mamu-A*01 Era, David H. O'Connor, Todd M. Allen, and David I. Watkins, in the 2001 HIV Immunology compendium). Dr. Christian Brander and colleagues annually provide a concise listing of optimal CTL epitopes. Additional reviews that our editorial board deems of general interest to the HIV research immunology community are solicited each year. This year's reviews are printed in the first part of this database; reviews from previous years can be found at: `http://www.hiv.lanl.gov/content/hiv-db/REVIEWS/reviews.html`.

Comments on the database or requests for the hard copy can be sent via email to `immuno@t10.lanl.gov`.

Citing the database

This publication may be cited as

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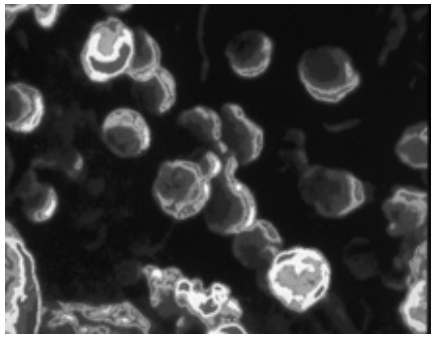
About the cover



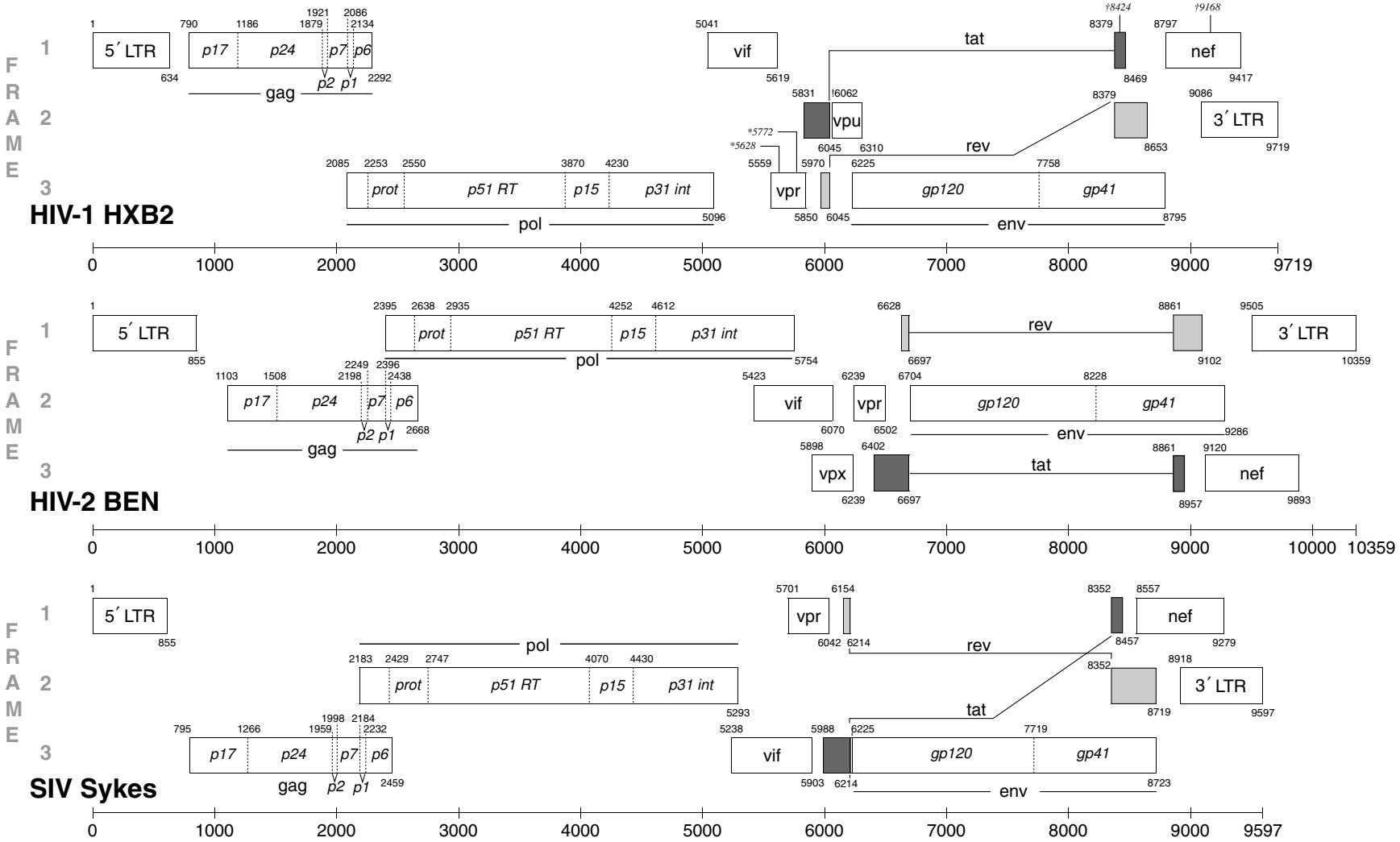
This year's cover is a photograph of several HIV particles located on the surface of a T lymphocyte as seen through a scanning electron microscope. The virus particles have been tinted by a special coloring technique. The capsids of the individual viruses can be seen, and the outgrowth on the virus in center of the picture is probably an aggregate of antibodies against HIV, marked by ferritin. The photo was taken by Dr. h.c. Lennart Nilsson, Karolinska University Hospital, Stockholm, Sweden. Lennart Nilsson has developed new photographic methods and technical improvements, including electron microscopy, opening new dimensions to scientific photography. His work on medical subjects have become world known through publications such as "Behold Man" and "A Child is Born".

About the PDF

The complete *HIV Immunology and HIV/SIV Vaccine Databases 2003* is available in Adobe Portable Document Format (PDF) from our website, `http://www.hiv.lanl.gov/content/immunology`. The PDF version is hypertext enabled and features 'clickable' table-of-contents, indexes, references and links to external web sites.

This volume is typeset using LaTeX. The immunology data tables and epitope maps are produced automatically from the SQL database by a series of Perl programs.

Genome maps



Landmarks of the HIV-1, HIV-2, and SIV genomes. The gene start, indicated by the small number in the upper left corner of each rectangle, normally records the position of the a in the atg start codon for that gene while the number in the lower right records the last position of the stop codon. For *pol*, the start is taken to be the first t in the sequence ttttttag which forms part of the stem loop that potentiates ribosomal slippage on the RNA and a resulting −1 frameshift and the translation of the Gag-Pol polyprotein. The *tat* and *rev* spliced exons are shown as shaded rectangles. In HXB2, *5628 and *5772 mark positions of frameshifts in the *vpr* gene; !6062 indicates a defective acg start codon in *vpu*; †8424 and †9168 mark premature stop codons in *tat* and *nef*. See Korber *et al.*, Numbering Positions in HIV Relative to HXB2CG, in *Human Retroviruses and AIDS*, 1998, p. 102. Available from http://www.hiv.lanl.gov/HTML/reviews/HXB2.html.

HIV/SIV proteins

Name	Size	Function	Localization
Gag MA	p17	membrane anchoring; env interaction; nuclear transport of viral core. (myristylated protein)	virion
CA	p24	core capsid	virion
NC	p7	nucleocapsid, binds RNA	virion
	p6	binds Vpr	virion
Protease (PR)	p15	gag/pol cleavage and maturation	virion
Reverse Transcriptase (RT)	p66, p51	reverse transcription	virion
RNase H	(heterodimer)	RNAse H activity	virion
Integrase (IN)		DNA provirus integration	virion
Env	gp120/gp41	external viral glycoproteins bind to CD4 and chemokine co-receptors	plasma membrane, virion envelope
Tat	p16/p14	viral transcriptional transactivator	primarily in nucleolus/nucleus
Rev	p19	RNA transport, stability and utilization factor (phosphoprotein)	primarily in nuleolus/nucleus shuttling between nucleolus and cytoplasm
Vif	p23	viral infectivity factor, inhibits minus-strand viral DNA hypermutation	cytoplasm (cytosol, membranes), virion
Vpr	p10-15	promotes nuclear localization of preintegration complex, inhibits cell division, arrests infected cells at G2/M	virion nucleus (nuclear membrane?)
Vpu	p16	promotes extracellular release of viral particles; degrades CD4 in the ER; (phosphoprotein only in HIV-1 and SIVcpz)	integral membrane protein
Nef	p27-p25	CD4 and class I downregulation (myristylated protein)	plasma membrane, cytoplasm, (virion?)
Vpx	p12-16	Vpr homolog present in HIV-2 and some SIVs absent in HIV-1	virion (nucleus?)
Tev	p28	tripartite tat-env-rev protein (also named Tnv)	primarily in nucleolus/nucleus

Abbreviations

Common abbreviations used in this database.

Abbrev.	Meaning
Ab	Antibody
ADCC	Antibody-Dependent Cell-medicated Cytotoxicity
ADE	Antibody-Dependent Enhancement
APC	Antigen Presenting Cell
AZT	Azidothymidine
CD4BS	CD4 Binding Site
CD4i	Antibody that has enhanced binding to gp120 in the presence of SCD4 (CD4 induced)
CSF	Cerebrospinal Fluid
CTL	Cytotoxic T Lymphocyte
CTLp	CTL precursor
DTT	Dithiothrietol
EIA	Enzyme Immuno Assay
ELISA	Enzyme Linked ImmunoSorbent Assay
ER	Endoplasmic Reticulum
Fabs	Fragment Antigen Binding-univalent antibody fragment
FIV	Feline Immunodeficiency Virus
gp	glycoprotein
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigens
HLA-MHC	Human Leukocyte Antigens-Major Histocompatibility Complex
IFN	Interferon
IL	Interleukin
IN	Integrase
Ig	Immunoglobulin
MAb	Monoclonal Antibody
MHC	Major Histocompatibility Complex
MRC	Medical Research Council, UK
NAb	Neutralizing Antibody
NIBSC	National Institute for Biological Standards and Control, UK
NIH	National Institutes of Health
PBLs	Peripheral Blood Lymphocytes
PBMC	Peripheral Blood Mononuclear Cell
PR	Protease
RAC	Ricin A Chain
rec/r	recombinant
RIP	Recombinant Identification Program
RIPA	Radio Immuno Precipitation Assay
rsgp160	recombinant soluble gp160
RT	Reverse Transcriptase
sCD4	soluble CD4
SDS	Sodium Duodecyl Sulfate
SIV	Simian Immunodeficiency Virus
Th	T-helper cell
TNF	Tumor Necrosis Factor
VLP	Virus Like Particle, assembled from p55 gag
VV	Vaccinia Virus
WB	Western Blot

Part I

Review Articles

I-A

Broad HIV-1 Specific CTL Responses Reveal Extensive HLA Class I Binding Promiscuity of HIV-Derived, Optimally Defined CTL Epitopes

Nicole Frahm[a], Philip J.R. Goulder[a,b], Christian Brander[a]

I-A-1 Cytotoxic T lymphocyte (CTL) in HIV infection

Together with neutralizing antibodies and virus specific T-helper cells, HIV specific cytotoxic T lymphocytes (CTL) remain at the center of many vaccine development efforts despite the ongoing debate regarding their *in vivo* induction and function and their potential ability to provide effective protection from infection in vaccines. However, numerous reports support the important role that virus specific CTL responses may have in HIV infection and that their detailed characterization needs to continue. As in past years, we again have compiled an updated list of all optimal HIV derived CTL epitopes that have been described over the last 12 months. The total number of optimal CTL epitopes has now exceeded 200 and increasingly also includes epitopes identified in non-clade B infection and in individuals of non-Caucasian descent. Thus, the collective information on the specificity of these HIV directed responses is of growing relevance for vaccine development in populations most affected by the HIV epidemic and should facilitate further immune analyses in these mostly non-Caucasians ethnicities.

[a]Partners AIDS Research Center, Massachusetts General Hospital, Boston, USA
[b]The Peter Medawar Building for Pathogen Research, Oxford, UK

In *HIV Immunology and HIV/SIV Vaccine Databases 2003.* Bette T. M. Korber, Christian Brander, Barton F. Haynes, Richard Koup, John P. Moore, Bruce D. Walker, and David I. Watkins, editors. Publisher: Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico. LA-UR 04-8162. pp. 3–24.

I-A-2 Broad CTL responses are not associated with HIV control

A number of laboratories, including ours, have in the past described the results from comprehensive CTL screening studies, in which overlapping peptide sets spanning the entire HIV genome are used in IFN-γ ELISpot assays [Addo2003, Cao2003a, Draenert2004d, Feeney2003, Frahm2004, Novitsky2002, Sabbaj2003, Kiepiela2004]. While several reports show either a positive or a negative correlation between viral loads and the breadth or magnitude of these CTL responses, none of these recent studies have found any strong significant associations. Importantly, studies describing correlations have often been based on the analysis of CTL responses against a restricted number of proteins or even single epitopes using tetramer stainings and were often restricted to a relatively low number of subjects enrolled [Betts2001, Buseyne2002a, Buseyne2002b, Edwards2002, Ogg1998]. The larger, more comprehensive studies including individuals at different stages of disease fail to see associations between CTL activity and viral loads [Addo2003, Cao2003a, Draenert2004d, Feeney2003, Frahm2004]. Thus, it appears that either total CTL responses are not a correlate of immune protection, or the assays most widely applied do not reflect the number of CTL responses that actually do mediate effective *in vivo* control of viral replication. The latter may indeed play an important role as some of the most widely used approaches clearly have their limitations. Overcoming them may help to obtain a more accurate picture of the HIV specific CTL activity. For instance, recent studies from our laboratory show that the use of autologous test sequences yields more and stronger CTL responses to variable proteins compared to the use of consensus sequence based peptide sets [Altfeld2003]. Thus, most studies may underestimate the true breadth of responses and may hide a

potential association between CTL activity, viral loads and disease progression. This limitation could be overcome by testing an extensive number of individuals using autologous test sequences; an undertaking that, however, will be limited by the exuberant costs for autologous sequence peptide synthesis.

A further concern regards the use of overlapping peptide panels that span the entire expressed HIV genome. In most cases, these utilize peptides that are 15–18 amino acids in length and which overlap by either 10 or 11 amino acids. Recent studies by Draenert [Draenert2004b] indicate that the precise location of the optimal epitope within the overlapping peptide (OLP) significantly affects recognition of the OLP: if the epitope is located precisely at the C-terminal end of the OLP, it will be significantly better recognized than if located in the middle of the OLP. Recent studies in the SIV macaque model, where peptides can be synthesized that correspond exactly to the autologous virus sequence, indicate that even 15-mers overlapping by 11 amino acids fail to pick up a substantial proportion of the responses (Watkins *et al.*, unpublished). The ultimate and ideal situation would be to use a panel of 11-mers overlapping by 10 amino acids, based on autologous virus sequence. The cost of such an enterprise is prohibitive, but for a limited number of subjects this exercise should perhaps be undertaken, as one becomes increasingly aware of the fact that the immunodominant CTL responses may not necessarily be the ones that are critical for immune control.

In addition, only a few different assays are currently being employed for the detection of virus specific CTL. To our knowledge, all optimal CTL epitopes listed in the present database have been identified either by assessing cytotoxic activity in a Cr^{51} release assay or by the induction of IFN-γ in Elispot or intracellular cytokine staining (ICS) assays. While cytolytic function may be an important aspect of effective CTL, IFN-γ release may well be a surrogate for other functions but not occur in all HIV-specific cells. A number of laboratories have tackled these problems and established other assays, such as CD107 degranulation and perforin/granzyme release assays as alternative ways to assess CTL responses. Also, replication inhibition assays of the type first described by Yang *et al.* [Yang1997], in which CTL clones are co-cultured with HLA-matched CD4+ T cells infected with autologous virus clones, may provide a means to come closer to the situation *in vivo*. Such assays will help to address qualitative differences in the viral replication inhibition efficacy of CTL of different specificity and will also help to identify processing mutations that are hard to detect in other, non-replication based assays. The frequency of processing escape mutations is unknown but a recent number of descriptions of mutational processing escape mutations in HIV suggests that this is a mechanism of escape that has been much under-recognized [Draenert2004c, Allen2004, Yokomaku2004]. Overall, these assays still need further adaptation and simplification until comprehensive responses can be measured on a single peptide level in a larger population of HIV infected individuals.

Finally, assessing total CTL responses by comprehensive screening may detect too many immunologically irrelevant responses and thus obscure a possible association between CTL activity and viral control. Indeed, there is compelling evidence that some single epitope-specific responses can control viral replication as viral escape in such epitopes is associated with increased viral loads and acceleration of disease progression [Draenert2004c, Goulder1997c, Cao2003b, Kelleher2001, Allen2000, Barouch2002, Klenerman2002, Leslie2004, Friedrich2004]. Thus, besides single responses that appear to have the capacity to provide strong immune surveillance, the current assays may also detect many less efficient responses and thus hide a possible association between CTL activity and viral load. On the other hand, individuals with high viral loads and fast disease progression can well maintain strong CTL responses without evidence of affecting viral replication [Draenert2004d]. In this study, the lack of control over viral replication could not be explained by sequence variation in the targeted regions of the autologous virus, indicating functional deficiencies specific to these individuals or responses. New data from our lab and other investigators suggest that the ability of HIV-epitope specific CTL to proliferate in response to antigen is lost in the course of infection, and that this defect could be associated with the loss of effective control over viral replication [Migueles2002] (and Lichterfeld *et al.*, unpublished). Together, these studies suggest that at least some HIV specific CTL can exert effective replication control and that the often generalized description of "functional deficiency of HIV specific CTL" is likely an over-simplification.

I-A-3 Extensive HLA class I binding promiscuity of HIV derived optimal epitopes

Regardless of possible associations between CTL activity and viral loads, knowing the precise targets of these CTL is still a prerequisite for many other questions to be asked, such as viral evolution, genetic imprinting and their potential use in epitope-based vaccines. Furthermore, the well-defined epitope landscape can be used to address questions of antigen processing and epitope presentation. In a recent study, we have used the optimally defined CTL epitopes to address the degree of HLA class I binding promiscuity. Briefly, 100 HIV infected individuals of mainly non-Caucasian background were tested for CTL responses against almost 200 described, optimal HIV derived CTL epitopes, regardless of the individual's HLA type. Interestingly, only about 40% of all responses were

detected in individuals who expressed the appropriate HLA class I allele. Another 20% of the responses were attributed to the presence of an allele that fell into the same HLA-supertype as the originally described restricting allele (for instance, an HLA-A3+ individual showing a positive response against an HLA-A11 restricted epitope). This left 40% of all responses to be restricted by alleles that do not share obvious similarities to the originally described allele or were, thus far at least, not grouped into the same HLA-supertype as the original allele. Although more detailed analyses will be required to confirm the precise length and anchor residues for the epitopes presented on alternative alleles, the data strongly suggest the presence of epitopes with wide HLA-class I binding promiscuity. This is supported by some of the epitopes included in the present update, for which presentation and *ex vivo* recognition was documented for up to four different HLA class I alleles (TL9 on B7, B42, B81 and Cw08). Furthermore, strong support for extensive epitope binding promiscuity is derived from the observation that CTL responses to certain regions of the viral genome, such as Gag and Nef, show strong clustering of responses [Frahm2004, Frahm2002a]. In data now publicly available at the Los Alamos database (`http://www.hiv.lanl.gov/content/immunology/hlatem/`), we show that 72 of 150 individuals tested reacted to the very same overlapping 18-mer peptide in Nef. Since these individuals expressed widely diverse HLA types and the number of potential epitopes in a single 18-mer is limited, the data strongly suggest that at least some epitopes must be presented by multiple HLA class I alleles.

I-A-4 Implications for vaccine development and viral evolution studies

Clearly, the identification of CTL epitopes that can bind multiple HLA class I alleles will facilitate the selection of epitopes with an increased population coverage. However, it will also be important to assess potential functional differences between responses to the same epitopes presented on different alleles. This may be of special interest in cases where the epitopes are shared between HLA class I alleles differentially associated with slow or fast HIV disease progression. An example of this is the TL9 response restricted by HLA-B42 and B81. HLA-B81 is associated with low viral loads in the Durban population, whereas B42 is not (Goulder *et al.*, unpublished). Sequencing of the virus indicates that escape mutations are selected in the B81-positive subjects in the region of the virus encoding the TL9 epitope, whereas this does not occur in the B42-positive subjects (Leslie *et al.*, unpublished). Other examples include the epitope QW9, shared by HLA-B57 (slow) and HLA-B53 (fast disease progression). Using these epitopes, one may be able to address the role that the HLA class I molecule or the presented CTL epitope, respectively, play in determining the rate of disease progression. Finally, cross-binding epitopes may also impact the analyses of CTL escape patterns as allele-associated footprints may need to take into consideration other alleles with the ability to share CTL epitopes. Similarly, the assessment of a "functional HLA homozygosity" in which alleles that frequently share CTL epitopes are considered "functionally homozygous" may reveal additional insight into the mechanism by which genetically homozygous individuals show a faster disease progression compared to HLA heterozygous subjects [Carrington1999].

I-A-5 Acknowledgments

As every year, we would like to express our gratitude to the large number of researchers in the field who continuously contribute to this database. The mostly unpublished data added to this years update stemming from the AIDS Research Center at Mass. General Hospital have been largely funded by an NIH contract (#NO1-A1–15442) supporting HLA typing and HIV CTL epitope definition in non-Caucasian populations and non clade B HIV infection.

We very much welcome any criticism, comments and additions to this list since we are sure that some epitopes will unintentionally escape our attention, despite close monitoring of the literature. Please write or call us with any comments you may have at:

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I-A-6 Table of optimal HIV-1 CTL epitopes

Table I-A.1: Best defined HIV CTL epitopes.

HLA	Protein	AA	Sequence	Reference
A*0101 (A1)	gp160	787–795	RRGWEVLKY	Cao2002
A*02 (A2)	RT	127–135	YTAFTIPSV	Draenert2004a
A*0201 (A2)			2 6 C	Falk1991, Barouch1995
		1° anchor	**L** **L**	
			M **V**	
		2° anchor	V	
A*0201 (A2)	p17	77–85	SLYNTVATL	Johnson1991, Parker1992, Parker1994
A*0201 (A2)	p1	1–10	FLGKIWPSYK	Yu2002b
A*0201 (A2)	RT	33–41	ALVEICTEM	Haas1998, Haas1999
A*0201 (A2)	RT	179–187	VIYQYMDDL	Harrer1996a
A*0201 (A2)	RT	309–317	ILKEPVHGV	Walker1989, Tsomides1991
A*0201 (A2)	Vpr	59–67	AIIRILQQL	Altfeld2001a, Altfeld2001b
A*0201 (A2)	gp160	311–320	RGPGRAFVTI	Alexander-Miller1996
A*0201 (A2)	gp160	813–822	SLLNATDIAV	Dupuis1995
A*0201 (A2)	Nef	136–145	PLTFGWCYKL	Haas1996, Maier1999
A*0201 (A2)	Nef	180–189	VLEWRFDSRL	Haas1996, Maier1999
A*0202 (A2)			2 C	Barouch1995
			L **L**	
			V	
A*0202 (A2)	p17	77–85	SLYNTVATL	Goulder1999
A*0205 (A2)	p17	77–85	SLYNTVATL	Goulder1999
A*0205 (A2)	gp41	335–343	RIRQGLERA	Sabbaj2003
A*0207 (A2)	p24	164–172	YVDRFYKTL	Currier2002

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
A*0301 (A3)	p17	18–26	KIRLRPGGK	Harrer1996b
A*0301 (A3)	p17	20–28	RLRPGGKKK	Goulder1997b, Culmann1999, Lewinsohn1999b, Wilkes1999b
A*0301 (A3)	p17	20–29	RLRPGGKKKY	Goulder2000b
A*0301 (A3)	RT	33–43	ALVEICTEMEK	Haas1998, Haas1999
A*0301 (A3)	RT	73–82	KLVDFRELNK	Yu2002a
A*0301 (A3)	RT	93–101	GIPHPAGLK	Yu2002a
A*0301 (A3)	RT	158–166	AIFQSSMTK	Threlkeld1997
A*0301 (A3)	RT	269–277	QIYPGIKVR	Yu2002a
A*0301 (A3)	RT	356–366	RMRGAHTNDVK	Yu2002a
A*0301 (A3)	Integrase	179–188	AVFIHNFKRK	Yu2002a
A*0301 (A3)	Vif	17–26	RIRTWKSLVK	Altfeld2001a, Yu2002a
A*0301 (A3)	Vif	28–36	HMYISKKAK	Yu2002a
A*0301 (A3)	Vif	158–168	KTKPPLPSVKK	Yu2002a
A*0301 (A3)	Rev	57–66	ERILSTYLGR	Addo2002a, Yu2002a
A*0301 (A3)	gp160	37–46	TVYYGVPVWK	Johnson1994a
A*0301 (A3)	gp160	770–780	RLRDLLLIVTR	Takahashi1991
A*0301 (A3)	Nef	73–82	QVPLRPMTYK	Koenig1990, Culmann1991
A*0301 (A3)	Nef	84–92	AVDLSHFLK	Yu2002a
A*1101 (A11)			2 C **K** V I F Y	Zhang1993, Rammensee1995
A*1101 (A11)	p17	84–92	TLYCVHQRI	Harrer1998
A*1101 (A11)	p24	217–227	ACQGVGGPGHK	Sipsas1997
A*1101 (A11)	RT	158–166	AIFQSSMTK	Johnson1994b, Zhang1993, Threlkeld1997
A*1101 (A11)	RT	341–350	IYQEPFKNLK	Culmann1999
A*1101 (A11)	RNase	80–88	QIIEQLIKK	Fukada1999
A*1101 (A11)	Integrase	179–188	AVFIHNFKRK	Fukada1999
A*1101 (A11)	gp160	199–207	SVITQACPK	Fukada1999
A*1101 (A11)	Nef	73–82	QVPLRPMTYK	Buseyne1999
A*1101 (A11)	Nef	75–82	PLRPMTYK	Culmann1991
A*1101 (A11)	Nef	84–92	AVDLSHFLK	Culmann1991

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
A*23 (A23)	gp41	74–82	RYLKDQQLL	Cao2003a
A*2402 (A24)			2 C **Y** **I** **L** **F**	Maier1994
A*2402 (A24)	p17	28–36	KYKLKHIVW	Ikeda-Moore1998, Lewinsohn1999a
A*2402 (A24)	p24	162–172	RDYVDRFFKTL	Dorrell1999, Rowland-Jones1999
A*2402 (A24)	gp160	52–61	LFCASDAKAY	Lieberman1992, Shankar1996
A*2402 (A24)	gp160	585–593	RYLKDQQLL	Dai1992
A*2402 (A24)	Nef	134–141	RYPLTFGW	Goulder1997a, Ikeda-Moore1998
A*2501 (A25)	p24	13–23	QAISPRTLNAW	Kurane1999
A*2501 (A25)	p24	71–80	ETINEEAAEW	Klenerman1996, vanBaalen1996
A*2601 (A26)			12 6 C **V** **Y** **T** **F** **I** **L** **F** D I E L V	Dumrese1998
A*2601 (A26)	p24	35–43	EVIPMFSAL	Goulder1996a
A*2601 (A26)	Pol	604–612	ETKLGKAGY	Sabbaj2003
A*29 (A29)	Nef	120–128	YFPDWQNYT	Draenert2004b
A*2902 (A29)	gp160	209–217	SFEPIPIHY	Altfeld2000a

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
A*3002 (A30)			12 C **Y** **Y** **F** **L** **V** R	Rammensee1999
A*3002 (A30)	p17	76–86	RSLYNTVATLY	Goulder2001
A*3002 (A30)	RT	173–181	KQNPDIVIY	Goulder2001
A*3002 (A30)	RT	263–271	KLNWASQIY	Goulder2001
A*3002 (A30)	RT	356–365	RMRGAHTNDV	Sabbaj2003
A*3002 (A30)	Integrase	219–227	KIQNFRVYY	Sabbaj2003, Rodriguez2004
A*3002 (A30)	gp160	704–712	IVNRNRQGY	Goulder2001
A*3002 (A30)	gp120	310–318	HIGPGRAFY	Sabbaj2003
A*3002 (A30)	gp41	283–291	KYCWNLLQY	Goulder2001
A*3101 (A31)			2 C **R** L V Y F	Falk1994, Rammensee1999
A*3101 (A31)	gp160	770–780	RLRDLLLIVTR	Safrit1994a, Safrit1994b
A*3201 (A32)	RT	392–401	PIQKETWETW	Harrer1996b
A*3201 (A32)	gp160	419–427	RIKQIINMW	Harrer1996b
A*3303 (A33)	gp41	187–196	VFAVLSIVNR	Hossain2001
A*3303 (A33)	gp41	320–327	EVAQRAYR	Hossain2001
A*3303 (A33)	Vpu	29–37	EYRKILRQR	Addo2002b
A*3303 (A33)	Nef	133–141	TRYPLTFGW	Cao2002
A*6801 (A68)	Tat	39–49	ITKGLGISYGR	Oxenius2002
A*6801 (A68)	Vpr	52–62	DTWAGVEAIIR	Sabbaj2004
A*6802 (A68)	Protease	3–11	ITLWQRPLV	Rowland-Jones1999
A*6802 (A68)	Protease	30–38	DTVLEEWNL	Rowland-Jones1999
A*6802 (A68)	gp160	777–785	IVTRIVELL	Wilkes1999a
A*7401 (A19)	Protease	3–11	ITLWQRPLV	Rowland-Jones1999

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*07 (B7)	p24	84–92	HPVHAGPIA	Yu2002a
B*0702 (B7)			123 C **P** **L** A R **F** R K	Englehard1993, Rammensee1999
B*0702 (B7)	p24	16–24	SPRTLNAWV	Lewinsohn1999a
B*0702 (B7)	p24	48–56	TPQDLNTML	Wilson1999a, Wilkes1999c, Jin2000, Wilson1997
B*0702 (B7)	p24	223–231	GPGHKARVL	Goulder1999
B*0702 (B7)	Vpr	34–42	FPRIWLHGL	Altfeld2001a
B*0702 (B7)	Vif	48–57	HPRVSSEVHI	Altfeld2001a
B*0702 (B7)	gp160	298–307	RPNNNTRKSI	Safrit1994b
B*0702 (B7)	gp160	843–851	IPRRIRQGL	Wilkes1999b
B*0702 (B7)	Nef	68–77	FPVTPQVPLR	Haas1996, Maier1999
B*0702 (B7)	Nef	68–76	FPVTPQVPL	Bauer1997, Frahm2002b
B*0702 (B7)	Nef	71–79	TPQVPLRPM	Goulder1999
B*0702 (B7)	Nef	77–85	RPMTYKAAL	Bauer1997
B*0702 (B7)	Nef	106–115	RQDILDLWIY	Goulder1999
B*0702 (B7)	Nef	128–137	TPGPGVRYPL	Culmann-Penciolelli1994, Haas1996
B*0801 (B8)			23 5 C **K K** **L** **R** PR L	Hill1992, Sutton1993, DiBrino1994b
B*0801 (B8)	p17	24–32	GGKKKYKLK	Rowland-Jones1993, Goulder1997d
B*0801 (B8)	p17	74–82	ELRSLYNTV	Goulder1997d
B*0801 (B8)	p24	128–135	EIYKRWII	Sutton1993, Goulder1997d
B*0801 (B8)	p24	197–205	DCKTILKAL	Sutton1993
B*0801 (B8)	RT	18–26	GPKVKQWPL	Walker1989, Sutton1993
B*0801 (B8)	gp160	2–10	RVKEKYQHL	Sipsas1997
B*0801 (B8)	gp160	586–593	YLKDQQLL	Johnson1992, Shankar1996
B*0801 (B8)	Nef	13–20	WPTVRERM	Goulder1997d
B*0801 (B8)	Nef	90–97	FLKEKGGL	Culmann-Penciolelli1994, Price1997

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*14 (B14)	p15	42–50	CRAPRKKGC	Yu2002b
B*1402 (B14)			23 5 C	DiBrino1994a
			R R L	
			K H	
			L	
			Y	
			F	
B*1402 (B14)	p24	166–174	DRFYKTLRA	Harrer1996b
B*1402 (B14)	gp160	584–592	ERYLKDQQL	Johnson1992
B*1501 (B62)			2 C	
			Q Y	Barber1997
			L F	Barber1997
			M	Barber1997
B*1501 (B62)	p24	137–145	GLNKIVRMY	Johnson1991, Goulder1999
B*1501 (B62)	RT	260–271	LVGKLNWASQIY	Johnson1999
B*1501 (B62)	RT	309–318	ILKEPVHGVY	Johnson1991, Johnson1999
B*1501 (B62)	Nef	19–27	RMRRAEPAA	Cao2002
B*1501 (B62)	Nef	117–127	TQGYFPDWQNY	Culmann1999
B*1503 (B72)	Integrase	185–194	FKRKGGIGGY	Honeyborne2003
B*1503 (B72)	Integrase	263–271	RKAKIIRDY	Cao2003a
B*1503 (B72)	Tat	38–47	FQTKGLGISY	Novitsky2001
B*1503 (B72)	Pol	651–660	VTDSQYALGI	Sabbaj2003
B*1503 (B72)	Nef	183–191	WRFDSRLAF	Cao2002
B*1510 (B71)	Gag p24	61–69	GHQAAMQML	Day2003
B*1510 (B71)	Vif	79–87	WHLGHVSI	Honeyborne2003
B*1516 (B63)			2 9	Barber1997, Seeger1998
			T Y	
			S I	
			V	
			F	
B*1516 (B63)	gp160	375–383	SFNCGGEFF	Wilson1997, Wilson1999a

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*1801 (B18)	p24	161–170	FRDYVDRFYK	Ogg1998
B*1801 (B18)	Vif	102–111	LADQLIHLHY	Altfeld2001a
B*1801 (B18)	Nef	135–143	YPLTFGWCY	Culmann1991, Culmann-Penciolelli1994
B*27 (B27)	Vpr	31–39	VRHFPRIWL	Addo2004
B*2703 (B27)	p24	131–140	RRWIQLGLQK	Rowland-Jones1998, Rowland-Jones1999
B*2705 (B27)			12 C **R** **L** **F** K K R R G I A	Jardetzky1991, Rammensee1995
B*2705 (B27)	p17	19–27	IRLRPGGKK	McKinney1999, Lewinsohn1999a
B*2705 (B27)	p24	131–140	KRWIILGLNK	Nixon1988, Buseyne1993, Goulder1997c
B*2705 (B27)	gp160	786–795	GRRGWEALKY	Lieberman1992, Lieberman1999
B*2705 (B27)	Nef	105–114	RRQDILDLWI	Goulder1997b
B*3501 (B35)			2 C **P** **Y** A F V M S L I	Hill1992, Rammensee1999
B*3501 (B35)	p17	36–44	WASRELERF	Goulder1997a
B*3501 (B35)	p17	124–132	NSSKVSQNY	Rowland-Jones1995
B*3501 (B35)	p24	122–130	PPIPVGDIY	Rowland-Jones1995
B*3501 (B35)	p24	122–130	NPVPVGNIY	Rowland-Jones1995
B*3501 (B35)	RT	107–115	TVLDVGDAY	Wilkes1999b, Wilson1999b
B*3501 (B35)	RT	118–127	VPLDEDFRKY	Sipsas1997, Shiga1996
B*3501 (B35)	RT	175–183	NPDIVIYQY	Sipsas1997, Shiga1996
B*3501 (B35)	RT	175–183	HPDIVIYQY	Rowland-Jones1995
B*3501 (B35)	gp160	42–52	VPVWKEATTTL	Wilkes1999b
B*3501 (B35)	gp160	78–86	DPNPQEVVL	Shiga1996
B*3501 (B35)	gp160	606–614	TAVPWNASW	Johnson1994a
B*3501 (B35)	Nef	74–81	VPLRPMTY	Culmann1991, Culmann-Penciolelli1994

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*3701 (B37)			2 C **D F** **E M** **L** **I**	Falk1993
B*3701 (B37)	Nef	120–128	YFPDWQNYT	Culmann1991, Culmann1999
B*3801 (B38)	Vif	79–87	WHLGQGVSI	Sabbaj2004
B*3801 (B38)	gp160	104–112	MHEDIISLW	Cao2002
B*3901 (B39)			2 C **R L** **H**	Falk1995a
B*3901 (B39)	p24	61–69	GHQAAMQML	Kurane1999
B*4001 (B60)			2 C **E L**	Falk1995b
B*4001 (B60)	p17	92–101	IEIKDTKEAL	Altfeld2000b
B*4001 (B60)	p24	44–52	SEGATPQDL	Altfeld2000b
B*4001 (B60)	p6	33–41	KELYPLTSL	Yu2002b
B*4001 (B60)	RT	5–12	IETVPVKL	Draenert2004a
B*4001 (B60)	RT	202–210	IEELRQHLL	Altfeld2000b
B*4001 (B60)	gp160	805–814	QELKNSAVSL	Altfeld2000b
B*4001 (B60)	Nef	37–45	LEKHGAITS	Draenert2004a
B*4001 (B60)	Nef	92–100	KEKGGLEGL	Altfeld2000b
B*4002 (B61)	p17	11–19	GELDRWEKI	Sabbaj2003
B*4002 (B61)	p24	70–78	KETINEEAA	Sabbaj2003
B*4002 (B61)	p24	78–86	AEWDRVHPV	Sabbaj2003
B*4002 (B61)	p15	64–71	TERQANFL	Sabbaj2003
B*4002 (B61)	Nef	92–100	KEKGGLEGL	Sabbaj2003, Altfeld2000b
B*42 (B42)	Integrase	260–268	VPRRKAKII	Kiepiela2002
B*4201 (B42)	p24	48–56	TPQDLNTML	Goulder2000a
B*4201 (B42)	RT	271–279	YPGIKVRQL	Wilkes1999b
B*4201 (B42)	Nef	128–137	TPGPGVRYPL	Goulder1999

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*44 (B44)	Protease	34–42	EEMNLPGRW	Rodriguez2004
B*4402 (B44)			2 C **E** **F** **Y**	Rammensee1999
B*4402 (B44)	p24	162–172	RDYVDRFYKTL	Ogg1998
B*4402 (B44)	p24	174–184	AEQASQDVKNW	Lewinsohn1999a
B*4402 (B44)	gp160	31–40	AENLWVTVYY	Borrow1997
B*4415 (B12)	p24	28–36	EEKAFSPEV	Bird2002
B*4501 (B45)	Gag-p2	1–10	AEAMSQVTNS	Sabbaj2004
B*50 (B50)	Nef	37–45	LEKHGAITS	Draenert2004a
B*51 (B51)	Vif	57–66	IPLGDAKLII	Bansal2004
B*51 (B51)	Vpr	29–37	EAVRHFPRI	Cao2003a
B*5101 (B51)			2 C **A** **F** **P** **I** **G**	Falk1995a
B*5101 (B51)	RT	42–50	EKEGKISKI	Haas1998, Haas1999
B*5101 (B51)	RT	128–135	TAFTIPSI	Sipsas1997
B*5101 (B51)	gp160	416–424	LPCRIKQII	Tomiyama1999
B*5201 (B52)			2 C **I** **V** Q	Rammensee1999
B*5201 (B52)	p24	143–150	RMYSPTSI	Wilkes1999b, Wilson1997
B*53 (B53)	Nef	135–143	YPLTFGWCF	Kiepiela2002

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*5301 (B53)			2 C	
			P **L**	Hill1992
B*5301 (B53)	p24	48–56	TPYDINQML	Gotch1993
B*5301 (B53)	p24	176–184	QASQEVKNW	Buseyne1996, Buseyne1997, Buseyne1999
B*5301 (B53)	Tat	2–11	EPVDPRLEPW	Addo2001
B*5301 (B53)	Nef	135–143	YPLTFGWCY	Sabbaj2003
B*5501 (B55)			2 C	Barber1995
			P	
			A	
B*5501 (B55)	gp160	42–51	VPVWKEATTT	Shankar1996, Lieberman1999
B*57 (B57)	Integrase	123–132	STTVKAACWW	Rodriguez2004, Addo2004
B*57 (B57)	Nef	116–124	HTQGYFPDW	Draenert2002
B*5701 (B57)			12 C	Barber1997
			A **F**	
			T **W**	
			S	
			K Y	
B*5701 (B57)	p24	15–23	ISPRTLNAW	Johnson1991, Goulder1996b
B*5701 (B57)	p24	30–40	KAFSPEVIPMF	Goulder1996b
B*5701 (B57)	p24	108–118	TSTLQEQIGWF	Goulder1996b
B*5701 (B57)	p24	176–184	QASQEVKNW	Goulder1996b
B*5701 (B57)	RT	244–252	IVLPEKDSW	vanderBurg1997, Hay1999
B*5701 (B57)	Integrase	173–181	KTAVQMAVF	Goulder1996b, Hay1999
B*5701 (B57)	Vpr	30–38	AVRHFPRIW	Altfeld2001a
B*5701 (B57)	Vif	31–39	ISKKAKGWF	Altfeld2001a
B*5701 (B57)	Rev	14–23	KAVRLIKFLY	Addo2001
B*5701 (B57)	Nef	116–125	HTQGYFPDWQ	Culmann1991
B*5701 (B57)	Nef	120–128	YFPDWQNYT	Culmann1991
B57 (B57)	Nef	116–124	HTQGYFPDW	Draenert2002
B*5703 (B57)	p24	30–37	KAFSPEVI	Goulder2000b
B*5703 (B57)	p24	30–40	KAFSPEVIPMF	Goulder2000b

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
B*5801 (B58)			12 C **A F** **T W** **S** K V I	Barber1997, Falk1995b
B*5801 (B58)	p24	108–117	TSTVEEQQIW	Bertoletti1998
B*5801 (B58)	p24	108–117	TSTLQEQIGW	Goulder1996b
B*5801 (B58)	RT	375–383	IAMESIVIW	Kiepiela2002
B*5801 (B58)	Rev	14–23	KAVRLIKFLY	Addo2001
B*81 (B81)	Pol	715–723	LFLDGIDKA	Addo2002a
B*8101 (B81)	p24	48–56	TPQDLNTML	Goulder2000a
B*8101 (B81)	Vpr	34–42	FPRIWLHGL	Altfeld2001a
Cw*0102 (Cw1)			23 C **A L** **L** P	Barber1997
Cw*0102 (Cw1)	p24	36–43	VIPMFSAL	Goulder1997a
Cw*03 (Cw03)	Nef	83–91	AALDLSHFL	Draenert2004a
Cw*0303 (Cw9)	Gag p24	164–172	YVDRFFKTL	Honeyborne2003
Cw*0304 (Cw10)	Gag p24	164–172	YVDRFFKTL	Honeyborne2003
Cw*0304 (Cw10)	gp41	46–54	RAIEAQQHL	Currier2002, Trocha2002
Cw*0401 (Cw4)			2 6 C **Y L** **P F** **F M** V I L	Falk1994
Cw*0401 (Cw4)	gp160	375–383	SFNCGGEFF	Wilson1997, Johnson1993

Table I-A.1: Best defined HIV CTL epitopes (cont.).

HLA	Protein	AA	Sequence	Reference
Cw*05 (Cw05)	Gag p24	174–185	AEQASQEVKNWM	Draenert2004a
Cw*07 (Cw7)	Nef	105–115	KRQEILDLWVY	Kiepiela2002
Cw*07 (Cw7)	Nef	105–115	RRQDILDLWIY	Yu2002a
Cw*0802 (Cw8)	p24	48–56	TPQDLNTML	Goulder2000a
Cw*0802 (Cw8)	Nef	83–91	AAVDLSHFL	Cao2003a
Cw*12 (Cw12)	Tat	30–37	CCFHCQVC	Cao2003a, Nixon1999
Cw*15 (Cw15)	gp41	46–54	RAIEAQQHL	Trocha2002

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I-B

Enhanced Motif Scan: A Tool to Scan for HLA Anchor Residues in Proteins

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I-B-1 Introduction

The HIV Immunology Database at `http://www.hiv.lanl.gov/` is a repository of information about HIV T-cell and antibody epitopes, integrated with the sequence variability data from the HIV Sequence Database [Kuiken2003]. The immunology database includes tables, maps and alignments of HIV-specific cytotoxic T lymphocyte (CTL) epitopes that are updated through annual summaries of the literature. We also develop simple web-based tools with the goal of assisting immunologists in experimental design and interpretation of their results. While these tools emphasize ease of application for HIV studies, many are also useful for studies of other pathogens and immune responses.

Several tools in the immunology database that rely on HLA anchor motif assignments are available to help identify potential CTL epitopes in HIV proteins[Calef2001, Calef2002, Thakallapally2001]. HLA anchor motifs are the conserved elements in epitopes that allow binding with specific HLA class I or class II proteins for presentation on the cells surface and recognition by T-cells. The peptide binding groove is divided into six pockets (A, B, C, D, E and F). Only 2 to 4 of these are generally occupied, although most of the residues within a peptide contribute to some degree to MHC binding. There are usually two dominant binding anchors for an epitope bound to an MHC class I molecule. These are usually the second position residue and the carboxy-terminus (C-terminus), and these residues bind to the B and F pockets, respectively, of the MHC class I peptide-binding groove. Class I epitopes are typically 9 amino acids long, ranging between 8-12 amino acids long. The optimal length of class II presented epitopes is often higher, and the spacing of the anchor residues relative to each other within the epitope tends to be more variable.

Anchor motif patterns are relatively, although not perfectly, preserved in peptides that are presented by specific HLA molecules. Only a fraction of the peptides that retain an anchor motif will actually bind to the appropriate HLA molecule (for an example, see Altfeld2001), and only a small fraction of those peptides that bind to HLA molecules will actually be properly processed and presented and stimulate specific T-cells responses. So the presence of an anchor motif only suggests the possibility of an epitope that could be presented by a specific HLA molecule. Knowledge of the peptide-binding motif can be very useful, however, for example in fine mapping of novel epitopes when one has identified a CTL response against a longer peptide that contains an epitope.

We have updated our HLA binding motif scanner tool [Thakallapally2001] (Motif Scan) to include a more comprehensive list of known anchor motifs. The interface has been improved, and now includes the ability to track anchor motifs in alignments of proteins, not just single proteins; and to differentiate between C-terminal and interior anchor motif residues. Also, we are working on the feature that would allow to identify all available motifs within protein fragments of up to 100 amino acids in length. Some basic reference sets of HIV proteins can be automatically entered for searches. The general purpose of this tool is to help users to identify known anchor residue motifs for epitopes presented by class I and class II HLA molecules, and then use these motifs to highlight potential epitopes within a protein sequence. Although the automated search capabilities of Motif

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Scan are based on HIV proteins, it can be applied to any protein. The tool could also be applied to look for general functionally important motifs of amino acid or nucleotides in sequences that have characteristic spacing. As the program is searching sequences of letters for motifs of interest, it would work equally well for identifying repeated patterns in proteins and in DNA. For example, if one put the restriction enzyme BamHI site `[G]-[G]-[A]-[T]-[C]-[C]` in as a custom motif and searched a DNA alignment, BamHi sites would be highlighted within the alignment.

I-B-2 HLA anchor motif sources

Primary anchor motif sources

The main data source for Motif Scan is a database of HLA binding motifs stored on our website. The HLA binding motif database has been recently updated to include two major motif libraries from *The HLA Facts Book* [Marsh2000] (`http://www.anthonynolan.com/HIG/`) and *MHC Ligands and Peptides Motifs* [Rammensee1997] (`http://syfpeithi.bmi-heidelberg.com`). We also searched the literature for the new motifs, not yet listed in these two major sources. What we found in the primary literature is presented as an additional source. Because motifs presented in different sources sometimes differ, in our tool the motifs presented are listed along with their sources, and the user can choose which ones to use for scanning the protein sequences for specific motif patterns. A number of HLA class I and class II alleles have not been characterized with respect to their peptide binding motif, and so we will continue to periodically update the database as new motifs are defined.

Table I-B.1: HLA motifs that are predicted based on conserved patterns found in a minimum of two optimal HIV epitopes in positions P2 or C-term (see Frahm2004, page 3 this volume, for lists of well defined epitopes presented by these HLA's).

Allele	Anchor motif	Number of epitopes that share this pattern
A*2501	`xxxxxxxxx[W]`	2
A*3201	`x[I]xxxxxxx[W]`	2
A*6802	`x[TV]xxxxxx[VL]`	3
B*4002	`x[E]xxxxxx[IAVL]`	5
B*4201	`x[P]xxxxxx[L]`	3
B*8101	`x[P]xxxxxx[L]`	2

Additional proposed anchor motifs

We have added several additional possible motifs, listed in Table I-B.1, based on conserved patterns in known optimal epitopes in HIV proteins [Frahm2004]. These motifs are not well established, and we will update the suggested motifs as they become better characterized.

Predicting HLA-C motifs by genetic similarities in HLA molecules

Although many of the A and B alleles have had their motif described, very few of the anchor motifs for HLA-C alleles have been characterized to date. As an increasing number of HLA-C-restricted CTL responses are being characterized, we have sought to predict the peptide-binding motif of the currently uncharacterized HLA-C alleles by comparing them to pockets with similar residues. Table I-B.2 shows the positions of amino acids lining the pockets of MHC class I molecules. Predicting the motif is straightforward if there is an identical or similar molecule that has been previously described, because a pocket having the same amino acid side chains can be expected to bind similar residues. Previously described F pockets of Cw*0102 and Cw*0304, for example, are identical, except for a leucine to isoleucine change at amino acid 95 and their motifs have both been found to bind small hydrophobic residues. Characteristics such as size, polarity and hydrophobicity (Table I-B.3) of the amino acid side-chains that line the pocket directly influence the motif. For example, a pocket with an overall strong positive charge will be expected to bind residues with negatively charged side chains, whereas a strongly hydrophobic pocket, where the constituent residues have bulky aromatic side chains, may often bind a small hydrophobic residue in that pocket. Based on this rationale, we have made predictions regarding potential anchor motifs for HLA-C subtype proteins that do not otherwise have a defined anchor motif. For the purposes of prediction we have focused on the principal pockets, B and F, although occasionally alleles have dominant anchor residues in other pockets. Elucidation of Cw*0102 has shown, for example, that residue 3 is an important anchor in the D pocket, and the anchor motif for Cw*0102 includes a proline at residue 3.

Tables I-B.4 and I-B.5 compare the variation in key binding residues along the B and F pockets of HLA-C alleles respectively, and, on the basis of similarity and known anchor motifs, make predictions regarding additional motifs. Table I-B.6 provides the predicted HLA-C summary motifs for B and F pockets.

Here is an example of our approach for motif prediction. The motif for the molecule Cw*0304 has previously been described. In pocket B (Table I-B.4) the residues have canceling charges and several large hydrophobic aromatic

Table I-B.2: The positions of the amino acids lining the HLA-C class I peptide binding site.

Pocket	Constituent residues	Peptide position accomodated
A	5, 7, 59, 63, 66, 99, 159, 163, 167, 171	1
B	7, 9, 24, 25, 34, 45, 63, 66, 67, 70, 99	2
C	9, 70, 73, 74, 97	6
D	99, 113, 114, 155, 156, 159, 160	3
E	97, 114, 147, 152, 156	7
F	77, 80, 81, 84, 95, 116, 123, 143, 146, 147	Carboxy terminus

Table I-B.3: Amino acid categories.

Category of amino acid	Members in group
Non-polar, hydrophobic	A, V, I, L, M
Non-polar, hydrophobic, large aromatic ring structure	F, W, Y
Non-polar, hydrophobic, small	P
Non-polar, hydrophilic	G, S, T, C, N
Positively charged, hydrophilic	R, H, K
Negatively charged, hydrophilic	D, E

residues. This pocket has been found in Cw*0304 to prefer the small hydrophobic residue alanine, and based on the B pocket similarity, we predicted alanine to be the B pocket anchor residue for Cw*0302 and Cw*0303.

The F pocket (Table I-B.5) for these alleles is likely to differ, however, since at position 116 there is a change from tyrosine to serine in Cw*0302 compared to Cw*0304 and Cw*0303. This substantial change would be expected to result in a more spacious F pocket for Cw*0302 than for Cw*0303 and Cw*0304. Thus, since for Cw*0304, the published motif at the F pocket is a medium-sized hydrophobic residue (`L` or `M`), for Cw*0302 we would predict a larger hydrophobic residue such as `F`, `W` or `Y`.

We are currently testing the validity of these predictions. For example, we have identified six HIV-1 relevant HLA-Cw*18 restricted responses toward 18-mer peptides. Using the motifs predicted above we can now compare the predicted optimal epitopes with actual epitopes.

Table I-B.4: Anchor motif predictions for the HLA-C locus B pocket. For each allele, the amino acids lining the pocked are shown along with the published or predicted motif. Amino acids at positions 9, 45, 63 and 67, shown in bold, are believed to be particularly important in determining the resulting motif.

Allele	Binding pocket residues											Published Motif	Predicted Motif	Comments
	7	**9**	24	25	34	**45**	**63**	66	**67**	70	99			
Cw*0102	Y	**F**	S	V	V	**G**	**E**	K	**Y**	Y	C	A,L		
Cw*0103	Y	**F**	S	V	V	**G**	**E**	K	**Y**	Y	C		A,L	Pocket is identical to Cw*0103
Cw*0202	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0203	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0302	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0303	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0304	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y	A		Strong preference for small hydrophobic residues
Cw*0305	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0306	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0307	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0308	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0309	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0401	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F	Y,P		
Cw*0402	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F		Y,P	Pocket is identical to Cw*0401
Cw*0403	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	F		P	Pocket is similar to Cw*0401 but smaller S to Y change
Cw*0404	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F		Y,P	Pocket is identical to Cw*0401
Cw*0405	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F		Y,P	Pocket is identical to Cw*0401
Cw*0406	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	F		P	Pocket is similar to Cw*0401but smaller S to Y change
Cw*0501	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0502	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0602	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	Y		R,Q	Pocket is negatively charged predict positive residues
Cw*0603	Y	**Y**	S	V	V	**G**	**E**	K	**Y**	Q	Y		A,L,P	Pocket is similar to Cw*0602 but less negatively charged
Cw*0604	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	Y		R,Q	Pocket is identical to Cw*0602
Cw*0701	Y	**D**	S	V	V	**G**	**E**	N	**Y**	Q	Y		R,H,K	Pocket is similar to Cw*0602 but more negatively charged
Cw*0702	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	S	Y,P		
Cw*0703	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	S		Y,P	Pocket is identical to Cw*0702
Cw*0704	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	Y		R,Q	Pocket is identical to Cw*0602
Cw*0705	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	Y		R Q	Pocket is identical to Cw*0602
Cw*0706	Y	**D**	S	V	V	**G**	**E**	N	**Y**	Q	Y		R,H,K	Pocket is similar to Cw*0602 but more negatively charged
Cw*0707	Y	**D**	S	V	V	**G**	**E**	N	**Y**	Q	Y		R,H,K	Pocket is similar to Cw*0602 but more negatively charged
Cw*0708	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	F		R,Q	Pocket is almost identical to Cw*0602
Cw*0709	Y	**D**	S	V	V	**G**	**E**	N	**Y**	Q	Y		R,H,K	Pocket is similar to Cw*0602 but more negatively charged

Table I-B.4: Anchor motif predictions for the HLA-C locus B pocket (cont.)

Allele	Binding pocket residues											Published	Predicted	Comments
	7	**9**	24	25	34	**45**	**63**	66	**67**	70	99	**Motif**	**Motif**	
Cw*0710	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	S		Y,P	Pocket is identical to Cw*0702
Cw*0711	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	Y		R,Q	Pocket is identical to Cw*0602
Cw*0712	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	Y		R,Q	Pocket is identical to Cw*0602
Cw*0801	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0802	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0803	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0804	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0805	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*0806	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1202	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1203	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1204	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1205	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1206	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1402	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F		Y,P	Pocket is identical to Cw*0401
Cw*1403	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F		Y,P	Pocket is identical to Cw*0401
Cw*1404	Y	**S**	A	V	V	**G**	**E**	K	**Y**	Q	F		Y,P	Pocket is identical to Cw*0401
Cw*1502	Y	**Y**	A	V	V	**G**	**E**	N	**Y**	Q	Y		A	Similar to Cw*0304 but less positively charged K to N change
Cw*1503	Y	**Y**	A	V	V	**G**	**E**	N	**Y**	Q	Y		A	Similar to Cw*0304 but less positively charged K to N change
Cw*1504	Y	**Y**	A	V	V	**G**	**E**	N	**Y**	Q	Y		A	Similar to Cw*0304 but less positively charged K to N change
Cw*1505	Y	**Y**	A	V	V	**G**	**E**	N	**Y**	Q	Y		A	Similar to Cw*0304 but less positively charged K to N change
Cw*1506	Y	**Y**	A	V	V	**G**	**E**	N	**Y**	Q	Y		A	Similar to Cw*0304 but less positively charged K to N change
Cw*1507	Y	**Y**	A	V	V	**G**	**E**	N	**Y**	Q	Y		A	Similar to Cw*0304 but less positively charged K to N change
Cw*1601	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1602	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1604	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1701	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1702	Y	**Y**	A	V	V	**G**	**E**	K	**Y**	Q	Y		A	Pocket is identical to Cw*0304
Cw*1801	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	F		R,Q	Pocket is similar to Cw*0602 except Y to F change
Cw*1802	Y	**D**	S	V	V	**G**	**E**	K	**Y**	Q	F		R,Q	Pocket is similar to Cw*0602 except Y to F change

Table I-B.5: Anchor motif predictions for the HLA-C locus F pocket. For each allele, the amino acids lining the pocked are shown along with the published or predicted motif. Amino acids at positions 77, 80, 81, 95 and 116, shown in bold, are believed to be particularly important in determining the resulting motif.

Allele	Binding pocket residues										Published	Predicted	Comments
	77	**80**	**81**	84	**95**	**116**	123	143	146	147	Motif	Motif	
Cw*0102	**S**	**N**	**L**	Y	**L**	**Y**	Y	T	K	W	L		Strong preference for small hydrophobic residues
Cw*0103	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L	Pocket almost identical to Cw*0102 except Y to F change
Cw*0202	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*0203	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*0302	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket similar to Cw*0304 except Y to S change
Cw*0303	**Y**	**N**	**L**	Y	**I**	**Y**	Y	T	K	W		L,M	Pocket is identical to Cw*0304
Cw*0304	**S**	**N**	**L**	Y	**I**	**Y**	Y	T	K	W	L,M		Strong preference for hydrophobic residues
Cw*0305	**S**	**N**	**L**	Y	**I**	**Y**	Y	T	K	W		L,M	Pocket is identical to Cw*0304
Cw*0306	**S**	**N**	**L**	Y	**I**	**Y**	Y	T	K	W		L,M	Pocket is identical to Cw*0304
Cw*0307	**N**	**K**	**L**	Y	**I**	**Y**	Y	T	K	W		L,F	Pocket is similar to Cw*0401
Cw*0308	**S**	**N**	**L**	Y	**I**	**Y**	Y	T	K	W		L,M	Pocket is identical to Cw*0304
Cw*0309	**S**	**N**	**L**	Y	**I**	**Y**	Y	T	K	W		L,M	Pocket is identical to Cw*0304
Cw*0401	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W	L	F	Strong preference for hydrophobic residues
Cw*0402	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0403	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0404	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0405	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0406	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0501	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0502	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,F	Pocket is identical to Cw*0401
Cw*0602	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W	L		
Cw*0603	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*0604	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*0701	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	L		Y	Pocket is identical to Cw*0702
Cw*0702	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	L	Y		
Cw*0703	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		Y,L	Pocket is similar to Cw*0702 but smaller L to W change
Cw*0704	**S**	**N**	**L**	Y	**F**	**F**	Y	T	K	L		L,M	Pocket is similar to Cw*0304
Cw*0705	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	L		Y	Pocket is identical to Cw*0702
Cw*0706	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	L		Y	Pocket is identical to Cw*0702
Cw*0707	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	L		Y,L	Pocket is similar to Cw*0602 but larger
Cw*0708	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	L		Y,L	Pocket is identical to Cw*0702
Cw*0709	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	L		Y,L	Pocket is similar to Cw*0602 but larger

Table I-B.5: Anchor motif predictions for the HLA-C locus F pocket (cont.)

Allele	Binding pocket residues										Published Motif	Predicted Motif	Comments
	77	**80**	**81**	84	**95**	**116**	123	143	146	147			
Cw*0710	**S**	**N**	**L**	Y	**I**	**S**	Y	T	K	L		F,W,Y	Pocket is similar to Cw*0302
Cw*0711	**S**	**N**	**L**	Y	**F**	**F**	Y	T	K	L		L,M	Pocket is similar to Cw*0304 but smaller I to F change
Cw*0712	**S**	**N**	**L**	Y	**F**	**F**	Y	T	K	W		L,M	Pocket is similar to Cw*0304 but smaller I to F change
Cw*0801	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L,M	Pocket is almost identical to Cw*0304
Cw*0802	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L,M	Pocket is almost identical to Cw*0304
Cw*0803	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L,M	Pocket is almost identical to Cw*0304
Cw*0804	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L,M	Pocket is almost identical to Cw*0304
Cw*0805	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L,M	Pocket is almost identical to Cw*0304
Cw*0806	**S**	**N**	**L**	Y	**L**	**F**	Y	T	K	W		L,M	Pocket is almost identical to Cw*0304
Cw*1202	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1203	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1204	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*1205	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*1206	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1402	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1403	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1404	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1502	**N**	**K**	**L**	Y	**I**	**L**	Y	T	K	W		L,M,Y,F	Pocket is similar to Cw*0401 except L to I change and F to L change
Cw*1503	**N**	**K**	**L**	Y	**I**	**L**	Y	T	K	W		L,M,Y	Pocket is similar to Cw*0401 except L to I change and F to L change
Cw*1504	**N**	**K**	**L**	Y	**I**	**S**	Y	T	K	W		L	Pocket is almost identical Cw*0602 but smaller L to I change
Cw*1505	**N**	**K**	**L**	Y	**I**	**F**	Y	T	K	W		L	Pocket is similar to Cw*0202 but smaller S to F change
Cw*1506	**N**	**K**	**L**	Y	**I**	**Y**	Y	T	K	W		L,M	Pocket is similar to Cw*0602 but smaller S to Y change
Cw*1507	**S**	**N**	**L**	Y	**I**	**L**	Y	T	K	W		L,M,Y	Pocket is similar to Cw*0304 but larger Y to L change
Cw*1601	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		F,W,Y	Pocket is identical to Cw*0302
Cw*1602	**N**	**K**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0602
Cw*1604	**S**	**N**	**L**	Y	**L**	**S**	Y	T	K	W		L	Pocket is identical to Cw*0302
Cw*1701	**N**	**K**	**L**	Y	**I**	**F**	Y	S	K	L		L	Pocket similar to Cw*0602
Cw*1702	**N**	**K**	**L**	Y	**I**	**F**	Y	S	K	L		L	Pocket similar to Cw*0602
Cw*1801	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,Y	Pocket is identical to Cw*0401
Cw*1802	**N**	**K**	**L**	Y	**L**	**F**	Y	T	K	W		L,Y	Pocket is identical to Cw*0401

Table I-B.6: Anchor motif predictions for the HLA-C locus. The motifs for Cw*0102, Cw*0304, Cw*0401, Cw*0602 and Cw*0702 are previously published and are shown in bold.

Allele	Anchor motif
Cw*0102	x[**AL**]xxxxxx[**L**]
Cw*0103	x[AL]xxxxxx[L]
Cw*0202	x[A]xxxxxx[L]
Cw*0203	x[A]xxxxxx[L]
Cw*0302	x[A]xxxxxx[FWY]
Cw*0303	x[A]xxxxxx[LM]
Cw*0304	x[**A**]xxxxxx[**LM**]
Cw*0305	x[A]xxxxxx[LM]
Cw*0306	x[A]xxxxxx[LM]
Cw*0307	x[A]xxxxxx[LF]
Cw*0308	x[A]xxxxxx[LM]
Cw*0309	x[A]xxxxxx[LM]
Cw*0401	x[**YP**]xxxxxx[**LF**]
Cw*0402	x[YP]xxxxxx[LF]
Cw*0403	x[P]xxxxxx[LF]
Cw*0404	x[YP]xxxxxx[LF]
Cw*0405	x[YP]xxxxxx[LF]
Cw*0406	x[P]xxxxxx[LF]
Cw*0501	x[A]xxxxxx[LF]
Cw*0502	x[A]xxxxxx[LF]

Allele	Anchor motif
Cw*0602[1]	x[**RQ**]xxxxxx[**L**]
Cw*0603	x[ALP]xxxxxx[L]
Cw*0604	x[RQ]xxxxxx[L]
Cw*0701	x[RHK]xxxxxx[Y]
Cw*0702	x[**YP**]xxxxxx[**Y**]
Cw*0703	x[YP]xxxxxx[YL]
Cw*0704	x[RQ]xxxxxx[LM]
Cw*0705	x[RQ]xxxxxx[Y]
Cw*0706	x[RHK]xxxxxx[Y]
Cw*0707	x[RHK]xxxxxx[YL]
Cw*0708	x[RQ]xxxxxx[YL]
Cw*0709	x[RHK]xxxxxx[YL]
Cw*0710	x[YP]xxxxxx[FWY]
Cw*0711	x[R]xxxxxx[LM]
Cw*0712	x[R]xxxxxx[LM]
Cw*0801	x[A]xxxxxx[LM]
Cw*0802	x[A]xxxxxx[LM]
Cw*0803	x[A]xxxxxx[LM]
Cw*0804	x[A]xxxxxx[LM]
Cw*0805	x[A]xxxxxx[LM]
Cw*0806	x[A]xxxxxx[LM]

Allele	Anchor motif
Cw*1202	x[A]xxxxxx[FWY]
Cw*1203	x[A]xxxxxx[FWY]
Cw*1204	x[A]xxxxxx[L]
Cw*1205	x[A]xxxxxx[L]
Cw*1206	x[A]xxxxxx[FWY]
Cw*1402	x[YP]xxxxxx[FWY]
Cw*1403	x[YP]xxxxxx[FWY]
Cw*1404	x[YP]xxxxxx[FWY]
Cw*1502	x[A]xxxxxx[LMYF]
Cw*1503	x[A]xxxxxx[LMYF]
Cw*1504	x[A]xxxxxx[L]
Cw*1505	x[A]xxxxxx[L]
Cw*1506	x[A]xxxxxx[LM]
Cw*1507	x[A]xxxxxx[LMY]
Cw*1601	x[A]xxxxxx[FWY]
Cw*1602	x[A]xxxxxx[L]
Cw*1604	x[A]xxxxxx[L]
Cw*1701	x[A]xxxxxx[L]
Cw*1702	x[A]xxxxxx[L]
Cw*1801	x[RQ]xxxxxx[LY]
Cw*1802	x[RQ]xxxxxx[LY]

[1]The published motif for Cw*0602 is xxxxxxxx[L].

I-B-3 Using Motif Scan

Data dictionaries

The HLA genotype/serotype classification used in the tool was based on the *The HLA Facts Book* [Marsh2000] and checked against more recent sources [Marsh2002, Schreuder2001]. Motif Scan can also be used as a quick web-based reference to look up associated HLA genotype/serotype nomenclature. Also, we added class I supertype classification and binding supermotifs from work of Sette and Sidney [Sette1999].

Search fields

The main web page of Motif Scan contains links to the downloadable lists of HLA genotypes, serotypes and supertypes, choice for motif length, window for the custom motif and motif sources. Here are detailed explanations for these search fields

HLAs The user can select multiple HLA class I or class II alleles to search the database for known or predicted motifs. (To find motifs for more than one allele, use the mouse to click on the first choice, and then hold down the control key while clicking on additional alleles for the search). HLA alleles may be specified by genotype, serotype or supertype.

- **Genotype** HLA genotypes are in general specified by four digit number, for example A*0201.
- **Serotype** If a user selects a serotype as a search field, anchor residues that have been defined for all related genotypes will be returned. For example, A2 will return motifs for the set of A2 related genotypes, including: A*0201, A*0202, etc. If a user knew only the serotype of the individual, it might be useful to have the anchor residues for all related genotypes displayed; if the specific HLA genotype was defined, then the specific anchor residues would be of greater interest. Because of the way HLA nomenclature has evolved, occasionally a two-digit HLA specification will be related to a genotype in a non-intuitive manner. For example, the genotype B*1513 might be specified by the serotype B15 or B77, where B15 is inclusive of many B*15 genotypes, and B77 is specifically B*1511. The serotype-genotype dictionary link on the main page provides a quick reminder of the naming conventions and relationships.
- **Supertype** Supermotifs will be provided for a given supertype, as defined by Sette and Sidney [Sette1999].

Motif Source Multiple sources (see above) may be selected to search for the variants of the suggested binding motif.

Motif Syntax The anchor residues are shown in the square brackets. The preferred but not dominant amino acids in the anchor positions are shown in parentheses. For example, motif for A*2602 taken from SYFPEITHY library is `x-[VTILF]-x-x-x-x-x-x-[YF(ML)]`. This means that second and C-terminal positions are anchor positions. The dominant amino acids at the second position are `V`, `T`, `I`, `L`, and `F`. At the C-terminal anchor position the dominant amino acids are `Y` and `F`, while `M` and `L` are also found, but not as commonly, among A*2602 epitopes. Note that as a default, Motif Scan will search on all possible anchor position amino acids, both dominant and preferred. It is possible to restrict a search to the dominant amino acids only, by composing a custom motif excluding the amino acids in parentheses (see below).

Supermotif Syntax For the supermotifs, residues within brackets are residues predicted to be tolerated and sometimes cross-presented by multiple Class I molecules within the putative supertype.

Motif Length Motifs are stored in the database with a length of 9 amino acids and the motifs for other lengths (8, 10 or 11 amino acids) are computed on-the-fly by adding or removing amino acids in front of the C terminus. Lengths are adjusted only for motifs from HLA class I genotypes, serotypes and supertypes. Anchor motifs for class II HLAs and custom motifs are not adjusted in length, and often for class II epitopes the last anchor residue of the motif will be embedded within the epitope, and not be the C-terminal amino acid.

Custom Motif A helpful feature of Motif Scan is the ability for users to define custom motifs. The syntax for the custom motif is the same as for the database motifs. Positions where several amino acids may be possible include all amino acids listed within square brackets [], and an `x` denotes arbitrary residues that specify the spacing in a motif. One can optionally use a dash (−) to separate the residues. For example, `x[LM]xxx[K]xx[V]` or `x-[LM]-x-x-x-[K]-x-x-[V]` are equivalent. With regard to defining epitopes, this feature, for example, allows the user to restrict a search to dominant anchor residues, or to add in auxiliary residues that are available in the listings of Marsh2000 and Rammensee1997. Auxiliary residues in epitopes do not bind directly in the pockets of HLA proteins that hold the anchor residues, but still influence the ability of a peptide to bind; auxiliary residues are not included in the Motif Scan database. The custom motif feature is useful also for the purposes other than scanning sequences for the HLA binding motifs. One can scan query sequences for any pattern of

interest, for example, studying motifs with characteristic functions found in functional domains.

Sequences and sequence alignments

To scan for a binding motif, a user can select from our predefined HIV protein sequences or upload or copy and paste their own sequences.

Predefined Sequences The predefined sequences include either all proteins from the HIV-1 HXB2 reference strain, or alignments of consensus and ancestral protein sequences for M group (subtypes A-D, F-H, J, K and circulating recombinant forms CRF01, CRF02) and O Group of HIV-1, from Los Alamos HIV Sequence Database, 2002 [Kuiken2003]. The alignments can give a rapid assessment of how well the search motif is preserved among the diverse forms in the epidemic. This will be updated periodically, as consensus and ancestral sequences are updated.

User's Own Sequences The user can upload or cut and paste either an individual protein sequence, or a set of individual sequences, or an alignment of sequences. User sequences should be input as simple text files in FASTA or TABLE format. Examples of sequence formatting can be obtained by clicking on the links provided on the web page. Individual sequences are stripped of gaps before processing. Gaps inserted to maintain the alignment are specified with a dash (−). If the sequences are aligned and the user wants to preserve the alignment, the user should check "Yes" in the box "Are the input sequences aligned"? In this case the gaps will be maintained and the alignment will be preserved, but they will not be counted as characters in terms of motif spacing.

Output

The results of the program are presented in several stages. First, the motifs corresponding to the input HLA types are presented. Then, the user chooses which motifs or set of motifs to scan with, chooses motif length (between 8-11 amino acids, one can select all possible lengths to be comprehensive), uploads query sequences or chooses predefined sequences, and initiates the scanning of these sequences for the respective motifs.

The final output is organized by search pattern, and all motifs with identical search patterns are grouped together. The matching motifs are presented on the input sequences in two colors: C-terminal anchor amino acids are shown in magenta and anchor amino acids in the other positions are shown in cyan. If a given amino acid is matched by more than one motif, then it is highlighted as a C-terminal anchor amino acid if any of the motifs are matched at the C-terminal anchor. All motif amino acids are shown in uppercase and non-anchors are lowercase. Following the sequences is a list of potential epitopes showing their positions in the input sequences.

The output can be viewed and downloaded in a format convenient for further coding and analysis: sequences can be downloaded in the FASTA format where the anchor amino acids are presented in uppercase and all the remaining ones in lowercase, but the colors are omitted. Alternatively, the color-highlighted motifs can be retained and copied and pasted from the web page directly into a word processor file. The list of potential epitopes and their positions in the protein can be downloaded in CSV (comma-separated value) format, which can be read into a spreadsheet.

Example

The motif search on all motif libraries for HLA A*0214 reveals the following table of motifs:

Genotype	Serotype	Motif	Source	Scan?
A*0214	A2	x-[QV]-x-x-[K]-x-x-[VL]	Luscher2001	☑
A*0214	A2	x-[VQ(L)]-x-x-x-x-x-[L]	Marsh2000	☑
A*0214	A2	x-[VQL(A)]-x-x-x-x-x-x-[L(VM)]	SYFPEITHI	☑

(`x` can be any amino acid). Here the three sources listed give slightly different information. In Luscher2001, either `Q` or `V` is favored in the second position, `K` in the sixth position, and either `V` or `L` is favored in the C-terminal position. In the Marsh2000 and SYFPEITHI sources, only the second and C-terminal positions are listed as anchor positions. In Marsh2000, the second position favors either `V` or `Q`, or less frequently `L`, and the C-terminal position favors `L`. In SYFPEITHI, the second position favors either `V` or `Q` or `L`, or less frequently `A`, and the C-terminal position favors `L`, or less frequently `V` or `M`. We do not address this different sources motif discrepancy in Motif Scan, rather, we display all existing views and let the user decide which one (or more) to use for scanning the protein sequences. Additionally, the user can compose a custom motif that would combine or summarize the information we present.

Once the motif is chosen, the user can either use our predefined consensus and ancestral sequence alignments, or copy-paste or upload their own sequences. For example, we scanned the following two aligned test sequences to search for the Marsh2000 A*0214 motif `x-[VQ(L)]-x-x-x-x-x-x-[L]`:

```
>Test.1
KTIIFKVSSQGDPLIVLHSQN--LEFLYCNLTKLFNSTW
>Test.2
KTI--KKSSQGDPEIVLHSQNCGGEFLHCNSTQFFNSTW
```

The resulting output contains query sequences in lowercase letters, where the anchor residues are uppercase and colored: C-terminal anchor is magenta and the other anchor is cyan[2], and the list of potential epitopes based on these anchor motifs:

```
Test.1    ktiifkVssQ gdpLivLhsq n--LefLycn LtkLfnstw
Test.2    kti--kkssQ gdpeivLhsQ ncggefLhcn stqffnstw
```

Protein	Seq. Pos.	Aln. Pos.	Sequence	Anchors
Test.1	6-14	6-14	KVSSQGDPL	.V.....L
Test.1	9-17	9-17	SQGDPLIVL	.Q.....L
Test.1	21-29	21-31	NLEFLYCNL	.L.....L
Test.1	24-32	26-34	FLYCNLTKL	.L.....L
Test.2	7-15	9-17	SQGDPEIVL	.Q.....L
Test.2	17-25	19-27	SQNCGGEFL	.Q.....L

I-B-4 Summary and future directions

We envision several applications for Motif Scan. It is particularly useful for the situations when a CTL response is partially characterized from an individual with a known HLA type, and already localized to a protein or protein region. The presence of HLA appropriate anchor residues could help focus the search for potential epitopes in known reactive protein regions. These anchor residues have to be considered with caution however, as anchor residues are frequently present in regions with no reactive epitopes, and there are many true epitopes that do not contain the anchor residue motifs. This simple tool is useful, however, as an initial indication for potential epitopes. Many external tools for HLA binding predictions are also available. These include methods based on "extended" motifs including secondary anchors and disfavored residues and statistical matrices representing the weight of every amino acid in every position [De Groot1997, Parker1995, Rammensee1997] and relatively new methods based on artificial neural networks (ANNs) [Buus2003, Milik1998, Schönbach2002], which, in contrast to motif based methods, are well suited to recognize complex nonlinear sequence-dependent correlated effects.

We are working on adding several more features to Motif Scan in the near future. One useful feature would be to identify all possible HLA motifs listed in our database for a peptide. Currently it is possible to do so by scanning the protein sequence for all HLA motifs. However the current output then contains results for both positive matches (those HLAs that have anchor residues in the query peptide) and negative ones (those HLAs that do not), and is a little cumbersome to navigate. We plan in the future to have a special field for this kind of search and have output showing only positive matches in a convenient form.

Motif Scan is useful not only for HIV sequences, but for any protein or DNA sequence; the only feature of the tool that is specifically tailored for HIV is the ready availability of predefined HIV sequences. We are in the process of adapting this tool for the hepatitis C database website (`http://hcv.lanl.gov/`), where we will link Motif Scan with the hepatitis C consensus sequences as the predefined sequences.

[2]For better visibility in print, the example shows the C-terminal anchors in a black box (X) and shows the other anchors in a gray box (X).

I-B-5 References

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I-C

Human Monoclonal Antibodies that Neutralize HIV-1

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Abstract

The HIV Immunology Database provides continuously updated information on monoclonal antibodies (mAbs) against HIV-1 produced by various techniques, including cellular methods utilizing Epstein-Barr transformation, phage display technology, antigen stimulation of lymphoid cells *in vitro*, and preparation of hybridomas from cells of transgenic mice. In this review, particular attention is focused on those human mAbs that are able to inhibit the infectivity of HIV virions. These mAbs target several clusters of neutralizing epitopes in the HIV-1 envelope proteins, including V1, V2, V3, CD4bs, CD4i in gp120, and cluster I, cluster II, and a region adjacent to cluster II in gp41. Only five of the 174 mAbs listed here can be classified as broadly and potently neutralizing for HIV-1 primary isolates; these include mAbs 2G12, IgG1b12, and 447-52D (specific for gp120) and 2F5 and 4E10 (specific for gp41). Certain other monoclonal reagents are capable of broad neutralization as Fab fragments but not as IgG molecules. The existence of human mAbs with neutralizing activity against diverse HIV-1 isolates demonstrates the ability of the human immune response to recognize B cell epitopes on the HIV-1 envelope that are shared and that, when complexed with antibody, prevent virus infectivity. The paucity of such broadly neutralizing mAbs highlights the challenge faced by designers of HIV-1 vaccines: to design a vaccine that will induce that small proportion of antibodies with broad neutralizing activity.

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I-C-1 Introduction

The HIV Immunology Database catalogues existing rodent and human monoclonal antibodies (mAbs) that are specific for various proteins of HIV-1. The human mAbs, which are reviewed herein, were produced by a variety of different techniques, although the two techniques that have given rise to the majority of useful mAbs are based on hybridoma and recombinant technologies. Both techniques have resulted in extremely valuable mAbs that have provided important information about the antigenic structure of neutralizing epitopes. Hybridoma techniques are based on the transformation of B cells from the cells of infected individuals [Gorny1989], and the mAbs derived from these cells represent antibodies that are part of the normal human B cell repertoire. In contrast, while the recombinant technology has several advantages over the cellular technology [Barbas1992], given the random recombination of heavy and light chains that takes place in vitro during this process, the resulting Fab fragments and IgG molecules may not actually represent antibodies that exist in human hosts [Huang2004].

The 174 mAbs summarized in this review are grouped on the basis of the epitopes that they recognize in gp120 and gp41. Among these mAbs and Fab fragments, 11 regions are recognized, however, only five human mAbs specific for four regions of gp120 and gp41 have been established as capable of broad and potent neutralization of HIV-1; these include mAbs 2G12, IgG1b12, and 447-52D (specific for various epitopes in gp120) and 2F5 and 4E10 (specific for gp41). Thus, while the existence of these latter mAbs demonstrates that the human immune system has the capacity to recognize shared neutralizing epitopes on the HIV-1 envelope glycoproteins, the paucity of broadly neutralizing mAbs highlights the limited immunogenicity and/or restricted availability of the regions in the native virions that are critical for virus infectivity.

Several phenomena may explain the rarity of functional antibodies against regions of the virus that are indispensable for its infectivity. These include, but are not limited to, the following: (a) the ability of the virus to continually vary its sequence in critical regions while maintaining function [Zolla-Pazner2004a];

(b) carbohydrate masking of critical epitopes [Back1994, Wei2003]; (c) conformational masking of receptor-binding sites [Kwong2002]; (d) poor immunogenicity of some neutralizing epitopes [Trkola1996b]; and (e) inaccessibility or transient exposure of neutralizing epitopes on the intact virus and on the virus as it binds to cell receptors.

Despite these phenomena, which form the basis for virus escape from the neutralizing potential of antibodies, the human humoral immune response is able to produce antibodies that neutralize HIV-1. The characterization of neutralizing epitopes recognized by human mAbs provides the basic data for the rational design of effective vaccine immunogens. In addition, the identification and characterization of neutralizing human mAbs may provide reagents for passive immunization to prevent infection, as in the setting of maternal-fetal transmission. These mAbs should also provide important information about mechanisms of virus neutralization, the antigenic structure of the virus, and the nature of the B-cell repertoire that can be tapped to provide protective humoral immune responses against the virus.

The characteristics of 174 human mAbs that target the envelope glycoproteins of HIV-1 are reviewed below. The epitopes within gp120 and gp41 that are recognized by these mAbs have been mapped and are catalogued in the HIV Immunology Database. For the convenience of the reader, we have linked the mAbs discussed in this review with each antibody's web page in the HIV Immunology Database (`http://www.hiv.lanl.gov/`).

I-C-2 Anti-V1 mAbs

No anti-V1 mAbs have been derived from the cells of infected humans. However, the HIV Immunology Database provides information on ten human anti-V1 mAbs (Table I-C.1) that were generated from transgenic mice carrying the genes coding for fully human IgGκ. These "xeno-mAbs" were derived from transgenic mice that had been immunized with native recombinant gp120 from HIV-1_{SF162}; the Ab-producing cells were selected with recombinant $gp120_{SF162}$ [He2002]. All of these anti-V1 xeno-mAbs display potent type-specific neutralizing activity against the autologous strain SF162 with 50% neutralizing doses (ND50) in the range of 0.3 to 4.5 µg/ml, as determined in a luciferase assay. Ten out of the 35 xeno-mAbs selected with $rgp20_{SF162}$ were specific for V1, suggesting that in this transgenic model, V1 is an immunodominant epitope [He2002]. The dearth of human anti-V1 mAbs derived from the cells of infected humans is probably related to the very high diversity of the V1 domain; this would render the selection of anti-V1 mAbs with heterologous gp120 reagents a difficult task. However, the lower immunogenicity of this region in the setting of natural infection cannot be excluded.

I-C-3 Anti-V2 mAbs

Anti-V2 antibodies have the capacity to neutralize HIV, but their activity is generally weak and their cross-reactivity is usually limited, suggesting that the antibodies with this specificity may have limited utility in mediating vaccine-induced, broad-based protection. The HIV Immunology Database contains a list of five anti-V2 human mAbs, two Fab fragments generated from HIV-infected individuals, and one xeno-mAb (Table I-C.2). The most thoroughly analyzed of the anti-V2 mAbs, mAb 697-D, could only weakly neutralize three of four primary isolates when a relatively high dose of mAb was used against a low virus input [Gorny1994]; this mAb displayed no neutralizing activity against four TCLA strains [Gorny1994, Nyambi1998]. mAb 697-D recognizes a conformational epitope, showing only weak reactivity with a V2 peptide; it binds weakly and only sporadically to intact virions from clades A, B and D [Nyambi2000]; similarly, other human anti-V2 mAbs, such as mAbs 830A, 1357, 1362 and 1393A, could bind to soluble gp120 but showed only weak and sporadic binding to virions of primary isolates, with the most frequent binding to B, C and D clades [Nyambi1998, Nyambi2000]. mAb 697-D could not inhibit the ability of gp120 to block the binding of MIP-1 beta to CCR5, suggesting that the V2 region does not block envelope/coreceptor interaction [Trkola1996a].

Two Fab fragments, L15 and L17, are specific for the V2 domain (Table I-C.2) and four Fab fragments, L25, L39, L40 and L78, are directed to complex epitopes that include the V2 loop and the CD4 binding site (CD4bs) (Table I-C.3) [Ditzel1995, Ditzel1997]. These latter Fab fragments were retrieved after epitope masking of gp120 with CD4bs Fab fragments during the screening stage. They were characterized by their V2 region-dependence, indicated by their sensitivity to amino acid changes in the V2 loop and by competition with murine anti-V2 mAbs. In addition, they are sensitive to amino acid changes usually associated with CD4 binding, and their binding to gp120 can be inhibited by soluble CD4. Among these several Fab molecules, only L25 and L78 mediate weak neutralization of T cell line-adapted (TCLA) viruses; neutralizing activity against primary isolates was not reported. The poor performance of these anti-V2 and anti-V2/CD4bs Fab fragments in neutralization assays does not exclude the possibility that, as whole IgG molecules, they could display neutralizing activity since Fab fragments usually display affinities that are lower by two to three orders of magnitude than intact IgG molecules. However, no studies of these

Table I-C.1: Anti-V1 mAbs

mAbs	Ab type	Neutralization	Reference
35D10/D2, 40H2/C7, 43A3/E4, 43C7/B9, 45D1/B7, 46E3/E6, 58E1/B3, 64B9/A6, 69D2/A1, 82D3/C3	Xeno-mAb	psSF162	He2002

Table I-C.2: Anti-V2 mAbs

mAbs	Ab type	Neutralization	Reference
697-D	mAb	PI (weakly)	Gorny1994
830A	mAb	psSF162	Pinter2004
1357, 1361, 1393A	mAb	non-neutralizing	Nyambi1998
8.22.2	Xeno-mAb	psSF162 (weakly)	He2002
L15, L17	Fab	non-neutralizing	Parren1998

Table I-C.3: Anti-V2-CD4bs mAbs

mAbs	Ab type	Neutralization	Reference
L25, L78	Fab	TCLA (weakly)	Ditzel1995
L39, L40	Fab	non-neutralizing	Ditzel1995

fragments as whole IgG molecules have been published, and the lack of potent neutralizing activity by anti-V2 IgG mAbs (see above) is not an encouraging indicator.

In summary, the information about anti-V1 and anti-V2 mAbs is incomplete because the number of mAbs, Fab fragments and xeno-mAbs is still relatively small. The results utilizing these mAbs suggest that anti-V1 mAbs are rather type-specific but can be quite potent, while anti-V2 are more broadly neutralizing but of low activity. A notable exception is the chimp mAb C108G, which is directed against a glycan-dependent epitope localized in V2 and was shown to neutralize primary HIV-1BaL isolate and TCLA strain IIIB [Vijh-Warrier1996].

I-C-4 Anti-V3 mAbs

Human antibodies directed to the V3 loop of gp120 constitute the major group of human mAbs in the database. There are currently 33 IgG mAbs, two Fab fragments generated from HIV-infected individuals, four xeno-mAbs produced by transgenic mice, and three IgM mAbs produced by in vitro stimulation of peripheral blood mononuclear cells (PBMC) with V3 peptides (Table I-C.4). These numbers reflect both the strong immunogenicity of the V3 region and the early interest in anti-V3 Abs generated when it was shown that they could neutralize TCLA virus strains [Rusche1988]; subsequent studies have documented the ability of anti-V3 antibodies to also neutralize primary isolates [Conley1994, Gorny2004, Gorny2002, Scott1990] and to mediate protection as demonstrated

Table I-C.4: Anti-V3 mAbs

mAbs	Ab type	Neutralization	Reference
N70-1.9b	mAb	TCLA	Robinson1990
19b	mAb	TCLA	Moore1994
257-D, 268-D, 311-11-D, 386-D, 391/95-D, 412-D, 418-D, 419-D, 453-D 504-D, 694/98-D, 782-D, 838-D, 908-D, 1006-15D, 1027-15D, 1108, 1324-E, 1334-D	mAb	TCLA	Karwowska1992, Gorny1993
447-52D, 2182, 2191, 2219, 2412, 2442, 2456	mAb	PI	Gorny1993, Gorny2002
4117C, 41148D	mAb	TCLA	Tilley1992, Pinter1993
M77	mAb	TCLA	diMarzo Veronese1992
MN215	mAb	TCLA	Schutten1995
TH1	mAb	TCLA	D'Souza1995
loop 2, DO142-10	Fab	TCLA	Barbas1993, Seligman1996
8E11/A8, 8.27.3	Xeno-mAb	TCLA	He2002
6.1, 6.7	Xeno-mAb	non-neutralizing	He2002
MO96/V3, MO97/V3, MO99/V3	IgM mAb, in vitro stimulation	non-neutralizing	Ohlin1992

in passive immunization experiments in various animal models [Andrus1998, Emini1992].

Many of the human anti-V3 mAbs were produced from cells of HIV-infected individuals who had been infected for several years; these were shown to neutralize TCLA and/or primary isolates [Gorny2004, Gorny1997, Gorny2002, Gorny1993, Moore1995, Scott1990]. In contrast, the IgG anti-V3 xeno-mAbs displayed neutralizing activity that appeared to be specific for the immunizing SF162 virus strain [He2002], while the IgM mAbs that were induced *in vitro* by antigenic stimulation of cells from HIV-uninfected individuals displayed no neutralizing activity [Ohlin1992]. These results suggest that the induction of broadly reactive and potent anti-V3 antibodies may require prolonged antigenic stimulation, resulting in mature and broadly reactive anti-V3 antibodies. This is consistent with the slow appearance of broadly reactive antibodies in the sera of infected individuals [Pilgrim1997], a factor that could have profound implications for the development of vaccine regimens.

Another important element in the generation of broadly reactive and potent human anti-V3 mAbs is the method used to select for cells producing the appropriate mAbs. Although the most broadly reactive of the neutralizing anti-V3 mAbs, 447-52D, was selected using a V3 peptide, the majority of mAbs selected with V3 peptides do not efficiently neutralize primary isolates [Gorny1993]. This is most probably due to the fact that peptides are highly flexible and may assume a myriad of conformations. Thus, most of the V3 mAbs selected with peptides are directed to structures which are irrelevant in the context of primary isolate infectivity; by chance, the structure of the $V3_{MN}$ peptide that captured mAb 447 bore a relevant conformation. In contrast, the use of a V3 fusion protein for mAb selection in which the V3 region retains a structure which approximates that of the native V3 loop [Kayman1994] resulted in the identification of mAbs that recognize conformation-sensitive V3 epitopes; the majority of these latter anti-V3 mAbs neutralize many primary isolates [Gorny2002]. Thus, within the repertoire of anti-V3 antibodies elicited in HIV-infected subjects, there are broadly reactive neutralizing antibodies, and these can be rescued if appropriate selection methods are employed.

The conformation-sensitive anti-V3 mAbs can neutralize primary isolates, and most can cross-neutralize a variety of isolates from clade B and, to a lesser extent, those from other clades [Gorny2004, Gorny2002]. The mAb 447-52D, though selected with a peptide, recognizes a conformational determinant [Gorny2002, Sharon2003, Stanfield2004], and it is the most broadly neutralizing of all the currently existing anti-V3 mAbs. This mAb interacts with the 14 residues at the crown of the V3 loop; its "core epitope" is defined by the sequence GPxR, a motif that is highly conserved among clade B viruses and which exists in a minority of other HIV subtypes [Gorny1992]. The presence and recognition of the arginine (R) residue in the core epitope is required for mAb 447-52D to exercise its activity [Zolla-Pazner2004b]), a fact that is explained by structural studies of this mAb in complex with a V3 peptide showing salt bridge and cation-pi interactions formed between the R residues in the core epitope and residues in the heavy chain of the mAb [Stanfield2004]. Other anti-V3 mAbs, such as mAbs 2182, 2191, 2219, 2412, 2442 and 2456 (Table I-C.4), do not recognize the same epitope as 447-52D, yet also display the ability to cross-neutralize primary isolates [Gorny2004, Gorny2002]. This cross-reactivity reveals the presence of features within the V3 loop which are conserved despite the sequence variation in this region. This structural conservation is also reflected in the role of the V3 loop in binding to the chemokine receptors which act as coreceptors for the virus [Cormier2002, Hill1997, Suphaphiphat2003, Trkola1996a].

I-C-5 Anti-CD4-binding site (CD4bs) mAbs

The HIV Immunology Database provides information about 30 anti-CD4bs human mAbs and 15 recombinant Fab fragments generated from PBMCs or bone marrow of HIV-1-infected individuals. In addition, there are six human anti-CD4bs mAbs listed which were produced from the cells of transgenic mice (Table I-C.5). Antibodies specific to the CD4bs inhibit the binding of sCD4 to gp120 and, as a consequence, interfere with virus attachment to the target cells. The CD4bs is made up of residues from C2, C3 and C4, conferring the conserved character of this domain and explaining the cross-reactivity of anti-CD4bs mAbs when tested for their ability to bind to gp120 molecules from viruses of diverse subtypes [Jeffs2001]. This immunochemical cross-reactivity is reflected in the ability of these mAbs to neutralize a broad array of TCLA strains; surprisingly, however, most anti-CD4bs mAbs cannot neutralize primary isolates [D'Souza1997, McDougal1996, Sullivan1995]. Since the CD4bs is a key feature of both TCLA and primary isolates, the selective neutralization of TCLA strains as opposed to primary isolates by most anti-CD4bs mAbs is surprising and still not fully explained. MAb IgG1b12 is a striking exception to the generalization that anti-CD4bs do not neutralize primary isolates [Burton1994]. Indeed, this mAb neutralized half of 90 primary isolates from diverse subtypes, and when tested against 30 primary isolates of subtype B, it neutralized 73% [Binley2004, Burton2004].

The differential activity of IgG1b12 vs. other anti-CD4bs mAbs has not been fully explained. It is possible that IgG1b12, which was produced using recombinant technology [Barbas1992], possesses a paratope that does not exist in na-

Table I-C.5: Anti-CD4bs mAbs

mAbs	Ab type	Neutralization	Reference
F105	mAb	TCLA	Posner1991
IgG1b12	mAb	PI	Burton1991
15e, 21h, F91	mAb	TCLA	Ho1991, Moore1993, Thali1992
1125H, 5145A	mAb	TCLA	Tilley1991
448-D, 559/64-D, 588-D, 654-D, 729-D, 830D, 9CL, 1027-30D, 1202-D, 1331E, 1570, 1595, 1599	mAb	TCLA	Karwowska1992
GP13, GP44, GP68	mAb	TCLA	Schutten1993
S1-1	mAb	TCLA	Moran1993
120-1B1	mAb	TCLA	Watkins1993
50-61A	mAb	TCLA	Fevrier1995
48-16	mAb	non-neutralizing	Fevrier1995
TH9	mAb	TCLA	D'Souza1995
205-43-1(HT5), 205-46-9(HT7), 205-42-15(HT6)	mAb	TCLA	Fouts1997
L28, L33, L41, L42, L52	Fab	TCLA	Ditzel1995
DA48, DO8i, b3, b6, b11, b13, b14, 2G6	Fab	TCLA	Parren1998
MTW61D	Fab	TCLA	Fouts1998
28A11/B1, 35F3/E2, 38G3/A9	Xeno-mAb	TCLA	He2002
55D5/F9, 46D2/D5, 67G6/C4	Xeno-mAb	non-neutralizing	He2002

ture. There is, however, nothing notably unusual about the structure of this mAb [Saphire2001]. Other explanations for its broad and potent activity may lie in its unusual dependence on regions within the V2 domain in order for binding to occur. Thus, it was shown that the Fab fragment of b12, as opposed to that of other anti-CD4bs mAbs, has reduced binding activity to V2-deleted gp120, and that deletion of V2 from isolate SF162, but not of V1, diminished the neutralizing activity of IgG1b12 for this virus; this distinguished IgG1b12 from another anti-CD4bs mAb, 654-D, and from IgG-CD4 [Stamatatos1998]. Additional evidence that the IgG1b12 epitope includes a portion of V2 comes from data showing that escape mutants generated when JR-FL was cultured in the presence of IgG1b12 displayed two substitutions in V2 as well as one in C3 [Mo1997]. The specificity of IgG1b12 for the CD4bs and V2 is reminiscent of the "V2/CD4bs" Fab fragments described by Dietzl *et al.* [Ditzel1995, Ditzel1997] (see above); however, no primary isolate neutralizing activity has been described for these latter Fab fragments, nor have they been compared to IgG1b12 in any published experiments.

A notable feature of mAb IgG1b12 is its long CDR H3 region, consisting of 18 amino acids. The CDR H3 projects above the rest of the antigen-binding site of the mAb, fitting into the pocket of the CD4bs of gp120 [Saphire2001]. Interestingly, several other broadly reactive and potent neutralizing human mAbs, such as anti-V3 mAb447-52D (see above), anti-CD4i mAbX5 (see below) and anti-gp41 mAb 2F5 (see below), also have long CDR H3 regions consisting of 20 to 22 residues [Darbha2004, Kunert1998, Stanfield2004], a characteristic that is shared by many human anti-viral Abs [Stanfield2004].

I-C-6 Anti-CD4-induced (CD4i) epitopes

This is a small group of human mAbs (Table I-C.6) which binds to the gp120 bridging sheet, a beta-sheet consisting of four anti-parallel beta-strands contributed by the C4 region and the V1/V2 stem [Kwong1998].

Several anti-CD4i mAbs were derived by Epstein-Barr virus transformation of B cells from the PBMCs of HIV-infected subjects [Thali1991, Xiang2002], while Fab X5 was selected from a phage display library derived from an HIV-1 infected donor whose serum displayed strong neutralizing activity [Moulard2002]. The phage library was screened with gp120-CD4-CCR5 complexes which exposed the CD4i epitope. The X5 epitope is near the CD4bs and CCR5 binding site but does not overlap with them; its specificity is slightly different than the 17b epitope which reacts with the CCR5 binding site only [Darbha2004, Moulard2002]. Immunochemical analyses show that the CD4i epitope only becomes accessible after the binding of gp120 to CD4. For example, anti-CD4i mAbs have little or no ability to bind to gp120 in ELISA until the envelope protein is preincubated with sCD4, which, by definition, induces the conformational changes that expose the CD4-induced epitope.

Since the bridging sheet interacts with the chemokine receptors, the mechanism of neutralization of the anti-CD4i mAbs is thought to be through the inhibition of gp120 binding to CCR5 and CXCR4 [Trkola1996a]. However, the anti-CD4i mAbs display no neutralizing activity against primary isolates. Only the Fab or single chain forms of antibodies with specificity for the CD4i epitope display neutralizing activity [Labrijn2003]. Thus, the scFv and Fab fragments of mAbs 17b and 48d displayed more potent neutralizing activity against JR-CSF, JR-FL and ADA than did the intact IgG forms of these mAbs, and, similarly, the scFv and Fab fragments of X5 potently neutralized these viruses but lost this activity when converted into a whole IgG molecule [Labrijn2003]. These data suggest that the size of the neutralizing molecule is a critical factor, and models juxtaposing the gp120 molecule on the virus particle and the chemokine receptor on the surface of the target cell indicate that the bulk of an intact IgG molecule prevents its insertion between gp120 and the coreceptor [Dey2003, Labrijn2003, Moulard2002]. Thus, steric hindrance precludes the ability of anti-CD4i IgGs from effectively neutralizing virus infectivity. Nevertheless, the X5 Fab neutralizes primary isolates from clades A, B, C, D, E, F and G, and neutralizes R5, X4 and R5X4 isolates, showing the exceptionally conserved character of CD4i epitopes [Moulard2002].

I-C-7 Anti-carbohydrate mAbs

There is only one neutralizing human mAb, 2G12, which recognizes an epitope composed of carbohydrates (Table I-C.7); this mAb is specific for high-mannose and/or hybrid glycans at residues 295, 332 and 392 with peripheral glycans from 386 and 448 on either flank [Sanders2002, Scanlan2002]. These carbohydrate moieties are located on an exposed surface of the gp120 trimer that does not interact with CD4 or the chemokine receptors. Nonetheless, mAb 2G12 inhibits gp120 interaction with CCR5 as shown in MIP-1beta-CCR5 competition studies [Sanders2002, Trkola1996a]. These data led to the hypothesis that the neutralizing activity of mAb 2G12 is an indirect, steric effect manifested by a binding site that is physically close to the receptor-binding sites of gp120 [Scanlan2002]. mAb 2G12 potently neutralizes TCLA and was recently shown to neutralize 41% of primary isolates representing various subtypes [Binley2004, Burton2004, Scanlan2002, Trkola1996b].

Table I-C.6: Anti-CD4i mAbs

mAbs	Ab type	Neutralization	Reference
17b, 21c, 23e, 48d, 49e	mAb	TCLA	Thali1993, Xiang2002
X5	Fab	PI	Moulard2002

Table I-C.7: Anti-Carbohydrate mAbs

mAbs	Ab type	Neutralization	Reference
2G12	mAb	PI	Buchacher1994

Despite the standard cellular technique used in the generation of mAb 2G12 and the commonly employed approach for selection of the mAb by measuring binding to gp160 [Buchacher1994], mAb 2G12 is unique both in terms of structure as well as specificity. Recent crystallographic studies revealed that two Fabs of mAb 2G12 assemble into an interlocked VH domain-exchanged dimer forming an extended binding site which targets the aforementioned conserved cluster of oligomannose moieties on the surface of gp120 [Calarese2003].

The 2G12 epitope is poorly immunogenic as reflected by competitive binding assays that demonstrated that 2G12-like antibodies were absent from all of 16 sera from HIV-infected long-term survivors and AIDS patients [Trkola1996b]. These factors—the unusual structure of mAb 2G12, its unusual epitope, and the poor immunogenicity of this epitope—suggest that, despite the undeniable potency and breadth of activity of mAb 2G12, the probability of inducing similar Abs with a vaccine may be quite low.

I-C-8 Anti-gp41 mAbs

As shown in Table I-C.8, there are 28 human mAbs and 24 Fab fragments directed to the highly immunogenic regions of gp4 [Binley1996, Xu1991]. Twenty-four mAbs and Fab fragments are directed to the most immunodominant region, cluster I (aa 579–604), 19 mAbs and Fab fragments are specific for cluster II (aa 644–663), three are specific for an epitope adjacent to cluster II, and six Fab fragments are specific for cluster III (a conformational epitope involving aa 619–648). Only four out of these 52 mAbs and Fab fragments have documented neutralizing activity: mAbs 2F5, 4E10, clone 3 and Fab fragment Z13.

MAb 2F5 is one of the best studied of the human mAbs. It has broad and potent activity, neutralizing 67% of 90 isolates from various virus subtypes [Binley2004, Burton2004, Trkola1995]. The linear 2F5 epitope is located near the transmembrane domain at aa 662–667, a region which is adjacent to cluster II and is not well exposed on the virus or on virus-infected cells [Nyambi1998, Ofek2004, Sattentau1995]. Immunochemical data show that 2F5 reacts strongly with peptide C43 representing a portion of the C-heptad repeat region of gp41, while there is no reactivity with peptide N51, the N-heptad repeat region of gp41. While mAb 2F5 reacts with the N51:C43 complex, which forms a coiled-coil complex, it reacts with the complex less strongly than it does with C43 alone [deRosny2004, Gorny2000]. While this might suggest that 2F5 interferes with the formation of the gp41 coiled-coil, this was not borne out by recent studies [deRosny2004]. Thus, the mechanism of neutralization by mAb 2F5 is still unknown, although interference with the late fusion process has been suggested [deRosny2004].

MAb 4E10 and Fab Z13 are also specific for a region that is adjacent to cluster II. They recognize the same epitope, and both are specific for a predominantly linear and relatively conserved epitope at aa 671–677 that is proximal to that of 2F5 [Zwick2001]. mAbs 4E10 and Z13 neutralize primary isolates of diverse clades, including A, B, C, D and E [Zwick2001]. While mAb 4E10 is the most broadly neutralizing mAb currently described, it is less potent than the other well-described, broadly neutralizing mAbs [Binley2004, Burton2004, Zwick2001].

MAb clone 3 binds to a linear epitope between aa 597 and 606 at the C-terminal end of cluster I, the most immunodominant region of gp41 [Cotropia1996]. The epitope is quite conserved, a fact reflected by its ability to neutralize three diverse TCLA viruses from clade B and three primary isolates

Table I-C.8: Anti-gp41 mAbs

mAbs	Ab type	Neutralization	Reference
Cluster I*			
1B8	mAb	non-neutralizing	Banapour1987
86	mAb	non-neutralizing	Sugano1988
50-69, 181-D, 240-D, 246-D, 1367	mAb	non-neutralizing	Gorny1989, Nyambi1998
V10-9	mAb	non-neutralizing	Robinson1990
3D6	mAb	non-neutralizing	Felgenhauer1990
2F11	mAb	non-neutralizing	Eaton1994
1F11, 1H5, 3D9, 4B3, 4D4, 4G2	mAb	non-neutralizing	Buchacher1994
clone 3	mAb	TCLA, PI	Cotropia1996
F240	mAb	non-neutralizing	Cavacini1998
A1, A4, M8B, M12B, M26B, T2	Fab	non-neutralizing	Binley1996
Cluster II*			
98-6, 126-6, 167, 1281, 1342, 1379	mAb	non-neutralizing	Gorny1989, Xu1991
ND-15GI	mAb	non-neutralizing	Eddleston1993
Md-1	mAb	non-neutralizing	Chen1995
D5, D11, G1, M10, M12, M15, S6, S8, S9, S10, T3	Fab	non-neutralizing	Binley1996
Adjacent to Cluster II*			
2F5	mAb	PI	Buchacher1994
4E10	mAb	PI	Buchacher1994
Z13	Fab	PI	Zwick2001
Cluster III*			
A9, G5, G15, L1, L2, L11	Fab	non-neutralizing	Binley1996

* Cluster I: aa 596–613; Cluster II: aa 644–663; Adjacent to Cluster II: aa 662–676; Cluster III: conformational epitope involving aa 619–648.

from group O [Cotropia1996, Ferrantelli2004]. Beyond the activity of clone 3 against these viruses, few details are known about its functional breadth. The clone 3 epitope overlaps with the epitope of mAbs 246 and 240 (aa 590–597 and 592–600, respectively). Interestingly, these latter mAbs bind to cluster I but have little or no neutralizing activity [Hioe1997] despite their ability to bind to intact virus particles [Nyambi1998].

As noted above, the mechanism(s) of neutralization of all four neutralizing anti-gp41 mAbs is still unknown. An indication that at least some anti-gp41 mAbs may interfere with virus/cell fusion was provided by studies of the fusion process at a suboptimal temperature (31.5°C), which prolongs the time during which fusion intermediates are exposed to mAbs [Golding2002]. These experiments showed that human mAbs against cluster II (mAbs 98-6, 1281 and 167-D) strongly inhibited fusion between HIV envelope-expressing effector cells and target cells expressing appropriate receptors [Golding2002].

I-C-9 Concluding remarks

Among the 174 human mAbs summarized in Tables I-C.1–I-C.8, only five mAbs (2G12, IgGb12, 447-52D, 2F5 and 4E10) and two Fab fragments (X5 and Z13) can be classified as broadly and potently neutralizing for HIV-1 primary isolates. Presently, the epitopes targeted by some of these mAbs do not appear to be practical targets for vaccine development due to their weak immunogenicity (2G12, 2F5) or their inaccessibility to antibody molecules (17b, X5, etc.). The CD4bs, which would appear to be an ideal target for neutralizing antibodies, induces antibodies which, for the most part, have little or no activity against primary isolates. And, while the epitopes recognized by neutralizing V3 mAbs are accessible and immunogenic, they induce a spectrum of antibodies ranging from narrowly to broadly cross-reactive, but the latter apparently require prolonged antigenic stimulation to emerge.

While the search for and design of effective immunogens continues, the most efficacious of the mAbs described to date may serve as beacons to illuminate the effort. Meanwhile, continuing work is needed, using new screening techniques, to identify neutralizing mAbs to additional classes of epitopes in order to provide the maximum number of viral determinants to target with a vaccine.

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I-C-11 References

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Part II

HIV CTL Epitopes

II-A

Summary

Part II includes tables, maps, and associated references of HIV-specific CTL epitopes arranged sequentially according to the location of the proteins in the HIV-1 genome. We attempted to make this part as comprehensive as possible, requiring that the epitope be contained within a defined region of a maximum of 30 amino acids, but not that the optimal boundaries be defined. Studies that were based on the analysis of whole proteins are described at the end of each protein section. The same epitope can have multiple entries, and each entry represents a single publication in this part of the database. For more recent updates and useful searching capabilities, please see our web site: `http://www.hiv.lanl.gov/content/immunology`. For a concise listing of the best defined CTL epitopes, see the summary by Nicole Frahm, Christian Brander and Philip Goulder on page 3 in Part I of this compendium. CTL protein reactions with no well-defined epitopes are listed at the end of each protein section.

Recent studies utilize multiple functions attributed to T cells to define responses, and the simple distinctions of cytotoxic T-cell and helper T-cells have become blurred as more is learned about the range of responses triggered in CD4 and CD8 positive T-cells responding to antigenic stimulus. When adding the most recent studies, we have tried to place T cell responses in a reasonable manner into our traditional helper T cell and CTL parts, and to specify the assay used to measure the response in each study.

II-A-1 CTL epitope tables

Each CTL reference has a multi-part basic entry:

HXB2 Location: The viral strain HXB2 (GenBank Accession Number K03455) is used as a reference strain throughout this publication. The position of the defined epitope location relative to the sequence of the HXB2 protein is indicated. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2, rather the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://www.hiv.lanl.gov/content/hiv-db/LOCATE/locate.html`.

Author Location: The amino acid positions of the epitope boundaries and the reference sequence are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases the reference sequence identification was not provided, and in such cases it is not possible to use these numbers to specify precise locations.

Epitope Sequence: The amino acid sequence of the epitope of interest as defined in the reference, based on the reference strain used in the study defining the epitope. On occasions when only the position numbers and not the actual peptide sequence were specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Immunogen: The original stimulus of the CTL response. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(HLA): The species responding and HLA or MHC specificity of the epitope.

Reference: The primary reference (sometimes two or more directly related studies are included). Details for some of the earlier references are in Part V.

Keywords: Keywords are a searchable field for the web interface that is included in the T-cell sections of the printed version to help identify entries of particular interest.

Following the entry for a given CTL epitope are brief comments explaining the context in which the epitope was studied and what was learned about the epitope in a given study.

II-A-2 HIV protein epitope maps

All HIV CTL epitopes mapped to within a region of 21 amino acids or less are indicated on the HIV protein epitope maps. The location and HLA restriction elements of CTL epitopes are indicated on protein sequences of HXB2. These maps are meant to provide the relative location of defined epitopes on a given protein, but the HXB2 sequence may not actually carry the epitope of interest, as it may vary relative to the sequence for which the epitope was defined. Epitopes with identical boundaries and HLA fields are included in the maps only once. If one laboratory determines HLA presenting molecules at the serotype level (example: A2) and another at the genotype level (example: A*0201) both will be included in the map. MHC specificities are indicative of the host species; when no MHC presenting molecule is defined, the host species is noted.

II-A-3 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the CTL epitope search tool at `http://www.hiv.lanl.gov/content/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site (`http://www.hiv.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html`). The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

II-B

HIV CTL Epitope Tables

All HIV CTL epitopes arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location and finally by HLA presenting molecule. CTL reactions against proteins with undefined epitopes are listed at the end of the protein that stimulated the response.

II-B-1 p17 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (11–19)		GELDRWEKI	HIV-1 infection	human (B*4002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-GI9. **Donor HLA** A*0201 A*0217 B*0801 B*4002 Cw*0303 Cw*070. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized KETINEEAA p24(70-78), HLA B*4002, and TAFTIPSI, RT(128-135), HLA A*0217. • Among HIV+ individuals who carried HLA B40, 2/5 (40%) recognized this epitope.			
p17 (11–19)	p17 (11–19)	GELDRWEKI	HIV-1 infection	human (B*4002)	Frahm2004
p17 (11–30)	Gag (11–30)	GELDRWEKIRLRPGGKKKYK	HIV-1 infection	human (B62)	Musey2003
	Keywords genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A2, A32, B27, B62. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood and semen.			
p17 (16–30)	p17 (16–30 HXB2)	WEKIRLRPGGKKKYK	HIV-1 infection	human	Addo2003
	Keywords immunodominance, early treatment. **Assay type** T-cell Elispot.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p17 (18–26)	p17 (18–26 IIIB) • C. Brander notes that this is an A*0301 epitope.	KIRLRPGGK		human (A*0301)	Frahm2004
p17 (18–26)	p17 (18–26 SF2) • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301.	KIRLRPGGK	HIV-1 infection	human (A*0301)	Altfeld2001a
p17 (18–26)	p17 (18–26 IIIB) **Keywords** responses in children, mother-to-infant transmission, escape. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • KIRLRPGGR and RIRLRPGGR, naturally occurring variants, were found in mother, and are escape mutants.	KIRLRPGGK	HIV-1 infection	human (A3)	Wilson1996
p17 (18–26)	p17 (18–26) **Keywords** dendritic cells. • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses. • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA. • A weak response to KLTPLCVSL was stimulated using macrophages as the APC. • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.	KIRLRPGGK	in vitro stimulation or selectio	human (A3)	Zarling1999
p17 (18–26)	Gag (18–26) • The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptive transfer. • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively-infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects.	KIRLRPGGK	HIV-1 infection	human (A3)	Brodie1999
p17 (18–26)	(18–26) • Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL. • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication. • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism.	KIRLRPGGK	HIV-1 infection	human (A3)	Brodie2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p17 (18–26)	p17 (18–26 IIIB)	KIRLRPGGK	HIV-1 infection	transgenic mouse (A3)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • KIRLRPGGR and RIRLRPGGR were escape mutants. • This epitope was recognized and many escape mutants were detected in an HLA A3 transmitting mother, and was recognized but invariant in an HLA A3 non-transmitting mother.				
p17 (18–26)	p17 (18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human (A3)	Goulder1997e, Goulder1997a
	Keywords review, escape. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. One had a response to this epitope, the other did not. [Goulder1997e] is a review of immune escape that summarizes this study.				
p17 (18–26)	p17 (subtype B)	KIRLRPGGK	HIV-1 exposed seronegative	human (A3)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
p17 (18–26)	p17 (SF2)	KIRLRPGGK	HIV-1 infection	human (A3)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (18–26)	p17	KIRLRPGGK	HIV-1 infection	human (A3)	Seth2001
	Keywords HAART. • CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.				
p17 (18–26)	p17 (18–26 SF2)	KIRLRPGGK	HIV-1 infection	human (A3)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 0/4 group 2, and 2/2 group 3.				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	HIV-1 infection, HIV-1 exposed seronegative	human (A3)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • KIRLRPGGK is cross-reactive for A, B, and D clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p17 (18–26)	p17 (JRCSF)	KIRLRPGGK	HIV-1 infection	human (A3)	Severino2000
	• Primary HLA-A3+ CD4+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the A3-restricted CTL clone 11504/A7 specific for KIRLRPGGK, and viral inhibition was MHC-restricted. • Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL. • DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture.				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	HIV-1 infection	human (A3)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.				
p17 (18–26)	p17	KIRLRPGGK	HIV-1 infection	human (A3)	Ostrowski2000
	Keywords dendritic cells. • The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients. • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes. • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
p17 (18–26)	Gag (p17) (18–26)	KIRLRPGGK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** A3-KK9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 8/14 HLA-A3 positive individuals had detectable A3-restricted responses during acute infection. Only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 7/8 individuals with acute responses had specific responses for this epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• KIRLRPGGK and RLRPGGKKK were the most commonly recognized HLA-A3 epitopes during acute infection, after 1 year of treatment, and after STI. RLRPGGKKK was immunodominant.				
p17 (18–26)	p17 (18–26)	KIRLRPGGK	HIV-1 infection	human (A3, A3.1, B27)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p17 (18–26)		KIRLRPGGK	HIV-1 infection	human (B*0301)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
p17 (18–27)	p17 (18–27 LAI)	KIRLRPGGKK		human (B27)	Brander1996b
	• D. Lewinsohn, pers. comm.				
p17 (18–27)	p17 (18–27)	KIRLRPGGKK	HIV-1 infection	human (B27)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (18–31)	p17 (18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human (A3)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (18–31)	p17 (18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human (B62)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of CTL response. • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response. • A subject who was HLA-B62+ had CTL that recognized this peptide, and p24 LGLNKIVRMYS, and one additional unknown epitope.				
p17 (18–42)	p17 (18–42 IIIB)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (A3)	Jassoy1992
	• Epitope recognized by CTL clone derived from CSF.				
p17 (18–42)	p17 (18–42 PV22)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (A3)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (18–42)	p17 (18–42 BH10)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (Bw62)	Johnson1991
	• Gag CTL response was studied in three individuals.				
p17 (19–27)	p17 (19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse (B*2705)	Frahm2004
	• Noted by Brander to be B*2705.				
p17 (19–27)	p17 (19–27 LAI)	IRLRPGGKK		human (B27)	Brander1996b
p17 (19–27)	p17 (19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse (B27)	McKinney1999
	Keywords escape. • Epitope-specific CTL were infused in infected human PBL-SCID mice, and transient decreases in viral load were observed, however virus was not eradicated and the HIV-specific CTL rapidly disappeared. • No escape mutants were observed. • Control CTL were long lived in both infected and uninfected mice, showing the rapid loss of CTL was due to target interaction.				
p17 (19–27)	p17 (SF2)	IRLRPGGKK	HIV-1 infection	human (B27)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 2/3 individuals that were B27+ had a dominant response to this epitope. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (19–27)	p17 (19–27)	IRLRPGGKK	HIV-1 infection	human (B27)	Day2001
p17 (19–27)	p17 (19–27)	IRLRPGGKK	HIV-1 infection	human (B27)	Goulder2001b
	Keywords immunodominance, escape. **Epitope name** IK9. • This B27 epitope is generally recognized only if there is escape in the B27 dominant epitope, p24 KRWIILGLNK.				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • Three of the four individuals that responded to SLYNTVATL recognized HIV epitopes, and one individual who was A*0201, A31 and B51 and B58w4 recognized this epitope (previously described as HLA A3.1), as well as one other.				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A*03)	Goulder1997e, Goulder1997a
	Keywords review, escape. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. • One had a response to gag A3 epitope RLRPGGKKK, the other non-responder carried the sequence RLRPGGKKC. • [Goulder1997a] is a review of immune escape that summarizes this study.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A*0301)	Frahm2004
	• C. Brander notes that this is an A*0301.				
p17 (20–28)	p17	RLRPGGKKK	HIV-1 infection	human (A*0301)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
p17 (20–28)	p17 (20–28 SF2)	RLRPGGKKK	HIV-1 infection	human (A*0301)	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301.				
p17 (20–28)	Gag (p17) (20–28)	RLRPGGKKK	HIV-1 infection	human (A*0301)	Sabbaj2002a
	Keywords mother-to-infant transmission. **Epitope name** RK9. **Donor HLA** A3, A11, B35, B51. • IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • Tetramer analysis of breast milk and peripheral blood samples of one volunteer showed responses to RLRPGGKKK in both compartments, 0.65% of CD3+/CD8+ cells in breast milk, and 0.22% of CD3+/CD8+ cells in peripheral blood cells. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
p17 (20–28)		RLRPGGKKK	HIV-1 infection	human (A03)	Sabbaj2002b
	Epitope name Gag-RK9. • Among HIV+ individuals who carried HLA A03, 7/20 (35%) recognized this epitope.				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder2000c
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten. • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder1997f
	• A control CTL line that reacts with this peptide was included in the study.				
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Cao1997a
	Keywords inter-clade comparisons. • The consensus peptide of A, B, and D clade viruses is RLRPGGKKK. • The consensus peptide of C clade viruses is RLRPGGKKH and is equally reactive.				
p17 (20–28)	p17 (SF2)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.			
p17 (20–28)	p17 (20–28 SF2)	RLRPGGKKK	HIV-1 infection	human (A3)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 5/7 group 1, 2/4 group 2, and 2/2 group 3.			
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.			
p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Goulder2001b
	Keywords acute infection. **Epitope name** RK9. • Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection. • Mutations in this epitope were observed in autologous clones of subjects who were A3-positive with a higher frequency than those who were A3-negative (P = 0.0002) • These mutations are being sexually transmitted in adult infections.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–28)	Gag (p17) (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Yu2002a

Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection.
Epitope name A3-RK9.
Donor HLA A3, B7, Cw7.

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 8/14 HLA-A3 positive individuals had detectable A3-restricted responses during acute infection. Only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 7/8 individuals with acute responses had specific responses for this epitope.
- KIRLRPGGK and RLRPGGKKK were the most commonly recognized HLA-A3 epitopes during acute infection, after 1 year of treatment, and after STI. RLRPGGKKK was immunodominant during acute infection and throughout the study period in the 5/6 individuals who targeted it.

p17 (20–28)	Gag (LAI)	RLRPGGKKK	HIV-1 infection	human (A3)	Lewinsohn2002

Keywords class I down-regulation by Nef.

- CTL kill targets through releasing perforin, that forms pore in the plasma membrane, and granzymes, that induce apoptosis.
- Vpr is capable of arresting infected cells in the G2 phase, and it was hypothesized that Vpr may inhibit CTL-mediated apoptosis because it interacts with the granzyme B molecular complex.
- Vpr expression in the target cell did not inhibit epitope specific lysis – neither perforin or granzyme mediated events were inhibited, as measured by a Chromium release assay and a TUNEL assay.
- In contrast, deletion of Nef, which is thought to protect primary HIV infected cells by down-regulating cell-surface expression of MHC class I complexes, increased the susceptibility of HIV-1 infected cells to CTL mediated killing 2-fold using the TUNEL assay.

p17 (20–28)	p17	RLRPGGKKK	HIV-1 infection	human (A3)	Sabbaj2002a

Keywords mother-to-infant transmission.
Donor HLA A3, A11, B35, B51.

- IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release.
- T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known A3 epitope RLRPGGKKK.
- The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.

p17 (20–28)	p17 (20–28)	RLRPGGKKK	HIV-1 infection	human (A3)	Cao2003

Keywords acute infection, early-expressed proteins.
Assay type CD8 T-cell Elispot - IFNγ.
Donor HLA A*0201, A3, B44, B57, Cw5, Cw6; A1, A3, B7, B14, Cw*0702, Cw*0802; A1, A3, B8, B35; A1, A3, B8, B62, Cw3, Cw7.

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was recognized in four individuals during early infection, each time presented by A3. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
p17 (20–29)	p17 (20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human (A*0301)	Frahm2004
	• C. Brander notes this is an A*0301 epitope.				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (A3)	Goulder2000c
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten. • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC.				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (A3.1)	Brander1995b
	• Unpublished, C. Jassoy and Beatrice Culman, pers. comm.				
p17 (20–29)	p17 (20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human (A3.1)	Wilkens1999
	• Pers. comm., B. Wilkens and D. Ruhl.				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (A30, A3.1)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was A30, and one was A3, and both responded to RLRPGGKKKY. • The A2+ A3 individual also reacted with two other A3.1 epitopes.				
p17 (20–29)	p17 (20–29 IIIB)	RLRPGGKKKY	HIV-1 infection	human (B42)	Wilson1996
	Keywords responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • RLRPGGKKRY, a naturally occurring variant, was found in non-transmitting mother and is recognized. • Binds HLA-A3 and Bw62 as well.				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (B42, Bw62)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p17 (20–29)	p17 (20–29)	RLRPGGKKKY	HIV-1 infection	human (B62)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL. • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication. • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism. • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (20–29)	p17 (20–29 LAI)	RLRPGGKKKY		human (Bw62)	McMichael1994
	Keywords review.				
	• Review of HIV CTL epitopes.				
	• Also P. Johnson, pers. comm.				
p17 (20–30)	p17 (SF2)	RLRPGGKKKYK	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance.				
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – the dominant response in a Haitian immigrant living in Boston who was HLA A24/29 B7/B44 Cw6/7 was to this epitope, although the restricting element was not determined.				
	• Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.				
	• Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (20–35)	p17 (90–105 SF2)	CLRPGGKKKYKLKHIV	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.				
	• Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.				
	• One of these 12 had CTL response to this peptide.				
	• The responding subject was HLA A-2, A-24, B-13, B-35.				
p17 (21–35)	Gag	LRPGGKKKYKLKHIV	HIV-1 infection	human	Weekes1999a
	• Peptide 703.3: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.				
p17 (21–35)	p17 (91–105 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.				
	• Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.				
	• One of these 12 had CTL response to this peptide.				
	• The responding subject was HLA-A1, A2, B50, B57.				
p17 (21–35)	Gag	LRPGGKKKYKLKHIV	HIV-1 infection	human (A3)	Weekes1999b
	Keywords TCR usage.				
	• Peptide 703.3: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population.				
	• HIV CTL responses to 3 Env and 2 Gag peptides were studied.				
	• The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.1 and Vβ5.2.				
p17 (21–35)	p17 (21–35)	LRPGGKKKYKLKHIV		human (B8)	Nixon1991
	• Two CTL epitopes defined (see also p24(191-205))				
p17 (21–35)	p17 (21–35)	LRPGGKKKYKLKHIV	HIV-1 infection	human (not B8)	vanBaalen1996
	• Unknown HLA specificity, but not B8.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (21–40)	p17 (21–40 subtype A)	LRPGGKKKYRLKHLVWASRE	HIV-1 infection	human (Cw4)	Dorrell1999
	Keywords inter-clade comparisons. • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa. • This epitope was defined in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTL from this patient were not A-B cross-reactive.				
p17 (22–31)	Gag (22–31)	RPGGKKRYKL	HIV-1 infection	human (B7)	Jin2000b
	• This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor. • A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing.				
p17 (24–31)	p17 (24–31)	GGKKKYKL		human (B8)	Goulder1997g
	• The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation. • The predictions were experimentally confirmed. • The anchors for HLA-B8 epitopes, as defined by peptide elution data, are P3 (K), P5 (K/R), and P8 (L) • Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe. • Small hydrophobic residues at P2 may be favorable for binding. • A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor.				
p17 (24–31)	p17 (24–31 SF2)	GGKKKYKL	HIV-1 infection	human (B8)	McAdam1998
	Keywords inter-clade comparisons. • CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope.				
p17 (24–31)	p17 (24–31 LAI)	GGKKKYKL	HIV-1 infection	human (B8)	Reid1996
	Keywords TCR usage. • The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied. • Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined. • 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement. • 7Q and 7R alter the TCR exposed surface, and retain some recognition. • Reactivity of 5R depends on the T cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound. • Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues.				
p17 (24–31)	p17 (24–31 LAI)	GGKKKYKL	HIV-1 infection	human (B8)	Price1997
	• A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual. • Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present.				
p17 (24–31)	p17 (24–31 SF2)	GGKKKYKL	HIV-1 infection	human (B8)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 1/3 group 2, and 2/2 group 3.				
p17 (24–31)	p17 (24–31)	GGKKKYRL	HIV-1 infection, HIV-1 exposed seronegative	human (B8)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p17 (24–31)	p17 (24–31)	GGKKKYKL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
p17 (24–31)	p17	GGKKKYKL	HIV-1 infection	human (B8)	McMichael2002
	Keywords binding affinity, review, inter-clade comparisons, epitope processing, escape. • CTL response-eliciting vaccines are reviewed. The natural epitope interactions with the HLA class I presenting molecules and T-cell receptors are described, using the structure of this epitope, taken from [Reid1996], as an example.				
p17 (24–32)	p17 (24–32 LAI)	GGKKKYKLK	HIV-1 infection	human (B*0801)	Frahm2004
	• C. Brander notes epitope to be presented by B*0801.				
p17 (24–32)	p17 (24–32 LAI)	GGKKKYKLK	HIV-1 infection	human (B8)	Sutton1993
	• Exploration of HLA-B8 binding motif through peptide elution.				
p17 (24–32)	p17 (24–32 LAI)	GGKKKYKLK	HIV-1 infection	human (B8)	Rowland-Jones1993
	Keywords epitope processing. • Study of an individual with partially defective antigen processing.				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Klenerman1994
	• Naturally occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists.				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Klenerman1995
	• Naturally occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA.				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Nowak1995
	Keywords escape. • Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive.				
p17 (24–32)	p17 (24–32)	GGKKKYKLK	HIV-1 infection	human (B8)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective. • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.				
p17 (24–32)	p17	GGKKKYKLK		human (B8)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: GGKKKYKMK – no cross-reactivity [Phillips1991]				
p17 (24–32)	p17 (24–32) **Keywords** HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** GGK. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • This epitope was recognized by 1/7 study subjects that were HLA-B8+ • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy.	GGKKKKYKLK	HIV-1 infection	human (B8)	Oxenius2000
p17 (24–32)	p17 **Keywords** HAART. • CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.	GGKKKKYKKL	HIV-1 infection	human (B8)	Seth2001
p17 (24–32)	p17 **Keywords** HAART, supervised treatment interruptions (STI). **Epitope name** GGK. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.	GGKKKYKLK	HIV-1 infection	human (B8)	Oxenius2002b
p17 (24–35)	p17 (25–35 SF2) **Keywords** review, immunodominance, escape. • Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time. • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.	GGKKKYKLKHIV	HIV-1 infection	human (B8)	Goulder1997a, Phillips1991
p17 (24–35)	p17 (25–35) • A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.	GGKKKYKLKHIV	HIV-1 infection	human (B8)	Birk1998b
p17 (28–36)	 **Keywords** HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.	KYRLKHLVW	HIV-1 infection	human	Kaul2001c

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls (ML1573)				
p17 (28–36)	p17 (28–36 LAI) • C. Brander notes that this is an A*2402 epitope.	KYKLKHIVW		human (A*2402)	Frahm2004
p17 (28–36)	p17 (28–36 SF2) • Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+ • HLA A24 is very common in Japanese (70% carry it) and is common globally. • This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.	KYKLKHIVW	HIV-1 infection	human (A*2402)	Ikeda-Moore1998
p17 (28–36)	p17 (28–36 LAI) • P. Goulder, pers. comm.	KYKLKHIVW		human (A23)	Goulder1999b
p17 (28–36)	p17 (28–36 LAI) • D. Lewinsohn, pers. comm.	KYKLKHIVW		human (A24)	Brander1996b
p17 (28–36)	p17 (28–36 SF2) **Keywords** HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3.	KYKLKHIVW	HIV-1 infection	human (A24)	Altfeld2001b
p17 (28–36)	p17 (28–36 93TH253 subtype CRF01) **Keywords** inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • The only HLA-A24 FSWs tested did not recognized the E clade version of this epitope KYKMKHLVW, which differs from the previously defined B clade version by two amino acids, KYKLKHIVW.	KYKLKHIVW	HIV-1 infection	human (A24)	Bond2001
p17 (28–36)	Gag (p17) **Keywords** supervised treatment interruptions (STI), acute infection. **Epitope name** KW9. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2, A24 B38, B60, Cw2, Cw12.	KYKLKHIVW	HIV-1 infection	human (A24)	Montefiori2003

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-1+ patient AC10 underwent early HAART treatment, which was discontiuned 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.				
p17 (28–36)	p17 (728–736 subtype A)	KYRLKHLVW	HIV-1 infection, HIV-1 exposed seronegative	human (Cw4)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-Cw4 women, 2/2 HEPS and 7/11 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in both of the 2/2 HEPS cases and in 3 of the 7/11 HIV-1 infected women.				
p17 (28–36)	p17 (28–36)	KYRLKHLVW	HIV-1 infection	human (Cw4)	Appay2000
	• This epitope is newly defined in this study. • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p17 (36–44)	p17 (SF2)	WASRELERF	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The dominant response in an African American who was HLA A3/33 B35/B53 Cw4/7 was to this epitope, although the restricting element was not determined – this epitope fell outside the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (36–44)	p17 (35–43 LAI)	WASRELERF	HIV-1 infection	human (B*3501)	Goulder1997d
	• Optimal epitope defined from within p17(30-44), LKHIVWASRELERFA. • Dominant CTL response in an HIV+ asymptomatic donor was to this epitope. • The Phe in the C-term anchor is distinct from the previously-defined Tyr for B*3501 C-term anchors.				
p17 (36–44)	p17 (36–44 LAI)	WASRELERF		human (B*3501)	Frahm2004, Goulder1997b
	• C. Brander notes this is a B*3501 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (36–44)	p17 (36–44)	WASRELERF	HIV-1 infection	human (B35)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (36–44)	p17 (36–44)	WASRELERF	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p17 (36–44)	p17 (36–44 SF2)	WASRELERF	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3.				
p17 (36–44)		WASRELERF	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Gag-WF9. • Among HIV+ individuals who carried HLA B35, 1/21 (5%) recognized this epitope.				
p17 (69–93)	p17 (69–93 BH10)	QTGSEELRSLYNTVATLYC-VHQRIE	HIV-1 infection	human (A2)	Johnson1991
	• Gag CTL response studied in three individuals.				
p17 (71–79)	p17 (71–79 LAI)	GSEELRSLY		human (A1)	Brander1996b
	• P. Goulder, pers. comm.				
p17 (71–79)	p17 (71–79)	GSEELRSLY	HIV-1 infection	human (A1)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (71–79)	p17 (71–79 HXB2)	GSEELRSLY	HIV-1 infection	human (A1)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** GSE. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • This epitope was not recognized by the 6/8 study subjects that were HLA-A1.				
p17 (71–79)	p17 (71–79)	GSEELRSLY	HIV-1 infection, HIV-1 exposed seronegative	human (A1)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-A1 women, 1/1 HEPS and 3/3 HIV-1 infected women recognized this epitope, and the response was the dominant HLA-A1 response in all cases.				
p17 (71–79)	p17	GSEELRSLY	HIV-1 infection	human (A1)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** GSE. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p17 (71–85)	p17 (71–85 SF2)	GSEELRSLYNTVATL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A1, A11, B8, B27.				
p17 (71–85)	p17 (71–85 HXB2)	GSEELRSLYNTVATL	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p17 (71–90)	Gag (HXB2)	GSEELRSLYNTVATLYCVHQ	HIV-1 infection	human	Chitnis2003
	Keywords assay standardization, HAART. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2. • 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In 10/14 children, addition of exogenous IL-15 induced increased frequencies of SFCs to the Gag peptide. IL-2 and IL-7 did not increase SFCs, however IL-2, IL-7 and IL 15 could all increase the intensity of the spots in some patients. In 4 children, IL-15 addition brought the SFC response up to the level of detection.				
p17 (74–82)	p17	ELRSLYNTV		human (B*0801)	Frahm2004
	• Noted by Brander to be a B*0801 epitope.				
p17 (74–82)	p17	ELRSLYNTV		human (B8)	Goulder1997g
	• Defined in a study of the B8 binding motif.				
p17 (74–82)	p17 (74–82)	ELRSLYNTV	HIV-1 infection	human (B8)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (74–82)	p17 (74–82)	ELRSLYNTV	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p17 (74–82)	p17 (74–82)	ELRSLYNTV	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
p17 (76–86)	p17 (74–86 LAI)	RSLYNTVATLY		human (A*3002)	Frahm2004
	• C. Brander notes this is an A*3002 epitope.				
p17 (76–86)	p17 (SF2)	RSLYNTVATLY	HIV-1 infection	human (A*3002)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a single HIV+ individual from Boston – this epitope fell outside the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (76–86)	Gag (96ZM651.8)	RLSYNTVATLY		human (A*3002)	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • Only 3 of 13 (23.1%) A*3002-positive subjects demonstrated moderate CTL responses to the peptide GTEELRSLYNTVATLYCVHE (residues 71 to 90), which contains the previously described A*3002 epitope RLSYNTVATLY.				
p17 (76–86)	p17 (76–86)	RSLYNTVATLY	HIV-1 infection	human (A*3002)	Goulder2001a
	Epitope name RY11 (p17). • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule. • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood. • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant. • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41) • HLA-A*3001-positive targets do not present RSLYNTVATLY.				
p17 (76–86)		RSLYNTVATLY	HIV-1 infection	human (A*3002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-RY11. **Donor HLA** A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; AETFYVDGA, RT(437-445), HLA B*4501; and HIGPGRAFY, gp160(310-318), HLA A*3002. • Among HIV+ individuals who carried HLA B30, 3/16 (19%) recognized this epitope.				
p17 (76–86)	p17 (74–86 SF2)	RSLYNTVATLY	HIV-1 infection	human (A30)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A30+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/0 group 2, and 1/1 group 3.				
p17 (76–86)	p17	RSLYNTVATLY	HIV-1 infection	human (A30)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** A30-RY11(p17). **Donor HLA** A30,A32,B18,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human	Sewell2000
	Keywords review, escape.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Review of the impact of CTL on viral immunity and escape that notes that SLYNTVATL-tetramer binding cells in individuals that react to this epitope inversely correlate with plasma viral load.				
p17 (77–85)	(SF2, HXBc2/Bal chimeric) **Keywords** rate of progression, escape. **Epitope name** SL9. • Seven HIV-positive subjects tended to make their strongest CD8+ T-cell response against Gag; these responses had varying breadth and magnitude that were unrelated to disease progression. • Patient TX7 primarily recognized SL9 during a three year study period and used six T-cell clonotypes for this recognition. • SLYNTVATL was the only form of the epitope found initially, but three alternate forms eventually appeared: SLYNTVAVL, SLYNTIATL, and most commonly SLYNTIAVL. These distinct forms bind A2, but have distinct abilities to stimulate different T-cell clonotypes. • In subject TX7, the observed mutations of SL9 failed to escape overall CTL recognition, presumably because the six T-cell clonotypes allowed a more flexible response. • The BV17 T-cell clone recognized SL9 but not SLYNTIAVL, and BV17 became undetectable at week 20 when SLYNTIAVL predominated. Subsequently BV17 became the second most common clone. Thus the relative frequency of of the T-cell clonotypes varied with respect to each other and to epitope variation.	SLYNTVATL	HIV-1 infection		Douek2002
p17 (77–85)	Gag p17 (77–85 LAI) **Keywords** HAART, responses in children. **Donor HLA** A*0201. • Longitudinal study of 8 infants with prolonged viral suppression due to combination antiretroviral therapy showed no HIV-1 specific CTL responses in peripheral blood cells. 6/8 were studied using a Chromium release assay and no response was detected using Gag expressed in vaccinia in the target cells. Three HLA-A*0201 children were tested using SLYNTVATL or ILKEPVHGV HLA A*0201 tetramers and again no HIV-specific response was detected, either using PBMC specimens, or PBMC which had been stimulated *in vitro* for a week. • In contrast, one of the children with therapy suppressed HIV viral replication who was co-infected with HIV and EBV, while HIV-tetramer negative, had EBV-tetramer staining cells at a frequency of 0.14% in the PBMC.	SLYNTVATL	HIV-1 infection	human	Luzuriaga2000
p17 (77–85)	p17 (77–85) **Keywords** HAART. • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed. • Increases in gamma IFN producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT. • 4/8 A*02 subjects had a positive response to this epitope indicating that it is a major epitope for CD8+ gamma IFN production. • In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both gamma IFN production and T cell lysis was a B27 epitope, p24(263-272), not the A2 SLYNTVATL epitope.	SLYNTVATL	HIV-1 infection	human (A*02)	Huang2000
p17 (77–85)	p17 (77–85) **Keywords** HAART. **Epitope name** SL9. • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection.	SLYNTVATL	HIV-1 infection	human (A*02)	Rinaldo2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A*02)	Scott-Algara2001

Keywords HAART, immunodominance.
Epitope name SL9.
- This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV.
- 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV)
- There were no differences observed in children that had therapy versus those that did not.
- Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells.

p17 (77–85)	p17 (77–85 HXB2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Brander1999

Keywords epitope processing, immunodominance, escape.
Epitope name SL9.
- Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope.
- The substitution Y79F was an escape mutation in that it interfered with CTL recognition by one CTL clone from an A*0201 infected individual, clone 13010.B17, but it was still recognized by another CTL clone, 115.D4.

p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A*0201)	Wilson2000a

Keywords acute infection.
- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.
- The subject with A*0201 had a moderately strong response to SLYNTVATL.
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.

p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A*0201)	Tan1999

- Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts.

p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Betts2000

Keywords immunodominance.
- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.
- 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.
- Individuals that did not respond to SLYNTVATL recognized other HIV epitopes, and 2/4 SLYNTVATL responders had stronger responses to epitopes restricted by other class I alleles.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• SLYNTVATL was the only response detected in a one individual that was HLA A*0201, B44, B70.				
p17 (77–85)	p17 (77–85) **Keywords** HAART. **Epitope name** SL9. • CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SLYNTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient. • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy. • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days.	SLYNTVATL	HIV-1 infection	human (A*0201)	Ogg1999
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs – HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and quantitate HIV-specific CD8+ cell lines in freshly isolated PBMCs. • Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%)	SLYNTVATL	HIV-1 infection	human (A*0201)	Altman1996
p17 (77–85)	Gag **Keywords** HAART. • Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL.	SLYNTVATL	HIV-1 infection	human (A*0201)	Gray1999
p17 (77–85)	p17 (77–85 SF2) **Keywords** inter-clade comparisons. **Epitope name** SL9. • CTL from a patient infected with clade B virus did not recognize the clade A analog of this epitope.	SLYNTVATL	HIV-1 infection	human (A*0201)	McAdam1998
p17 (77–85)	p17 (77–85) **Keywords** TCR usage. **Epitope name** SL9. • HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo*. • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls. • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases. • An A2-Gag specific line from one patient was found to be BV8, and at its highest level represented 17.5% of the patient's CD8+ T cells.	SLYNTVATL	HIV-1 infection	human (A*0201)	Wilson1998a
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load. • Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity. • No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells.	SLYNTVATL	HIV-1 infection	human (A*0201)	Ogg1998b
p17 (77–85)	p17 (77–85) **Keywords** epitope processing.	SLYNTVATL	in vitro stimulation or selectio	human (A*0201)	Walter1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name SL9. • HLA-A2 heavy chain and β2-microglobulin expressed in E. coli were refolded in the presence of this peptide. • The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2. • Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens.				
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers. • This peptide was one of the test peptides for optimizing the protocol.	SLYNTVATL	HIV-1 infection	human (A*0201)	Lalvani1997
p17 (77–85)	p17 (76–84) **Epitope name** SL9. • Slow dissociation rate is associated with immunogenicity. • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.	SLYNTVATL	in vitro stimulation or selectio	human (A*0201)	vanderBurg1996
p17 (77–85)	p17 (77–85) **Keywords** review, escape. **Epitope name** SL9. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. • One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV. • Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL. • 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL. • Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL. • An additional subject went from SLYNTVATL responder to non-responder coincident with a switch to the variant SLFNTVATL. • [Goulder1997a] is a review of immune escape that summarizes this study.	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder1997e, Goulder1997a
p17 (77–85)	Gag (77–85) **Keywords** HAART. **Epitope name** SL9. • Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells. • 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL. • After HAART, the majority of the epitope-specific CTL were apparently memory cells.	SLYNTVATL	HIV-1 infection	human (A*0201)	Gray1999
p17 (77–85)	p17 (77–85 subtype A) **Keywords** inter-clade comparisons. **Epitope name** SL9. • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa. • This epitope is most commonly SLYNTVATL in B subtype, and CTL from the C subtype infection did not recognize B clade gag or the 3Y form of the epitope, but do recognize the predominant A and C clade form, SLFNTVATL.	SLFNTVATL	HIV-1 infection	human (A*0201)	Dorrell1999
p17 (77–85)	p17 (77–85) **Keywords** immunodominance.	SLYNTVATL	HIV-1 infection	human (A*0201)	Brander1998a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name SL9. • Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope. • Only one subject had CTL against all three epitopes. • There was significant heterogeneity in the CTL response to this immunodominant epitope. • The overall variation in this epitope among the 17 who had a CTL response and 11 non-HLA A*0201 HIV-1+ individuals was similar, suggesting a lack of immune pressure. • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area.				
p17 (77–85)	p17 (77–85 HXB2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Hay1999b
	Keywords rate of progression, immunodominance. **Epitope name** SL9. • CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201. • The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted. • Despite the initial narrow response to two epitopes, no other CTL responses developed. • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak. • A variant of this epitope was observed *in vivo* (–F—-V-), but this mutation is recognized by SLYNTVATL-specific CTL, and in this case the patient's cells could present the peptide to SLYNTVATL-specific CTL.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Kalams1999b
	Keywords HAART. • Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV-specific in-vivo activated CTL such that by day 260 CTL activities were undetectable. • ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant. • Sporadic breakthrough in viremia resulted in transient increases in CTLp. • Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Spiegel2000
	• High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen. • Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Larsson1999
	• ELISPOT was used to assay the CD8 T cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia vectors in 19 HIV+ people. • The highest CTL frequency was directed at epitopes Pol. • In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2.				
p17 (77–85)	p17 (SF2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (77–85)	p17 (77–85 LAI) • C. Brander notes this is an A*0201 epitope.	SLYNTVATL		human (A*0201)	Frahm2004
p17 (77–85)	p17 (77–85 SF2) **Keywords** escape, acute infection. **Epitope name** SL9. • This epitope is targeted by 75% of HLA-A*0201, HIV+ adults, and the magnitude of the response is inversely correlated with viral load. • CTL responses to SL9 and autologous SL9 variants were not detected in 11 HLA-A*0201 positive subjects during acute infection. • Longitudinal studies of two individuals (AC13 and PI004) showed that the initial control of viremia was independent of the SL9 CTL response. • Low Gag expression levels did not correlate with the delayed CTL response to this epitope. • Autologous SL9 variants SLYNTIAVL, SLYNTVAVL, SLFNTVATL, SLFNTVATL, and SLFNTVATL are each capable of inducing a range of CTL responses, sometimes strong, sometimes diminished, and sometimes complete escape relative to the than the wild type variant SLYNTVATL in patients with chronic HIV-1 infection – the ability to cross-react with a particular variant was patient dependent.	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder2001a
p17 (77–85)	p17 **Keywords** inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** p17 SL9. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, including p17 SL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • p17 SL9 was recognized in 12/22 patients with chronic HIV-1 infection. • Only 1/13 patients with acute HIV-1 infection recognized p17 SL9.	SLYNTVATL	HIV-1 infection	human (A*0201)	Altfeld2001c
p17 (77–85)	Gag **Epitope name** (SL9). • This paper describes a comparison of results of different CTL assays, a SL9 tetramer assay and IFN-gamma ELISPOT, using 7 HIV-positive patients. • The IFN-gamma ELISPOT assay was compared using the single SL9, a pool of overlapping 20 mers, and recombinant vaccinia encoding Gag as antigen – pooled peptides gave the highest number of spot forming cells, vaccinia gave high background. • A correlation with results of the tetramer assay was found only for ELISPOT using the Gag epitope as antigen, but the tetramer assay detected a 10-fold higher number of cells than could produce IFN-gamma in the ELISPOT assay – the authors suggest not all tetramer-positive cells may produce IFN-gamma, some may be undergoing apoptosis, some may be producing other cytokines. • The tetramer assay could detect a reaction to SLYNTVATL in most of the HLA-A*0201 chronically HIV-1 infected study subjects.	SLYNTVATL	HIV-1 infection	human (A*0201)	Goepfert2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	Gag (LAI)	SLYNTVATL	in vitro stimulation or selectio	human (A*0201)	Engelmayer2001
	Keywords dendritic cells.				
	• Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors.				
	• Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses.				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	HIV-1 infection	human (A*0201)	Mollet2000
	Keywords HAART.				
	Epitope name G3.				
	• A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNgamma production to measure responses.				
	• In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished.				
	• Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A*0201)	Gea-Banacloche2000
	• In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found.				
	• High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products.				
	• 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope.				
p17 (77–85)	p17 (77–85 SF2)	SLYNTVATL	HIV-1 infection	human (A*0201)	Propato2001
	Keywords supertype, rate of progression.				
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.				
	• Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.				
	• A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.				
	• Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Jin2000a
	Keywords HAART, rate of progression.				
	• The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay.				
	• LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV.				
	• HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.				
	• In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A*0201)	Ostrowski2000
	Keywords dendritic cells. • The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients. • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes. • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
p17 (77–85)		SLYNTVATL	Vaccine	human (A*0201)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol **Keywords** vaccine-specific epitope characteristics. • Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 • Two vaccinees with Gag responses were HLA-A*0201+, but neither made SLYNTVATL responses to the Gag vaccine, in contrast to its frequent recognition in natural infections. No HLA-A*0201 responses were observed to an Env vaccine.				
p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A*0201)	Migueles2001
	Keywords rate of progression, immunodominance. • CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2 and B57.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Sewell2002
	Keywords epitope processing, immunodominance. • Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing. • ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.				
p17 (77–85)	Gag (ADA)	SLYNTVATL	HIV-1 infected monocyte-derived	mouse (A*0201)	Poluektova2002
	Epitope name SL-9. • Nonobese diabetic NOD-C.B-17 SCID mice were reconstituted with HLA-A*0201 positive human PBL and injected with HIV-1 infected monocyte-derived macrophages MDM in the basal ganglia to provide a mouse model of HIV-1 encephalitis. • HLA-A*0201 CTL responses were detected by tetramer staining in the spleen in seven days, increased through day 14, and the numbers of productively infected were reduced >85% in the second week.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85)	SLYNTVATL	computer prediction	(A*0201)	Schönbach2002

Keywords inter-clade comparisons, computational epitope prediction, vaccine-specific epitope characteristics, escape.

- Computational methods (artificial neural networks (ANN), hidden Markov models (HMM), binding matrices based on HLA association rates BIMAS) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.
- The SLYNTVATL epitope received focused discussion. SLYNTVATL, slFntvatl, slyntvaVl, and slyntIaVl are all recognized variants, ANN predicts all four variants would be recognized, while BIMAS only predicts SLYNTVATL and slFntvatl would be recognized. However, [Sewell1997] suggested certain substitutions may be antagonistic, including slFntvatl, and vaccines do not stimulate SLYNTVATL responses as well as natural infections. The authors note these kinds of issues complicate the application of computational predictions of epitopes to vaccine design.

p17 (77–85)	Gag (76–84)	SLYNTVATL	Vaccine	mouse (A*0201)	Singh2002, Sykes1999

Vaccine *Vector/Type:* DNA *HIV component:* HIV-1

Keywords epitope processing, vaccine-specific epitope characteristics, immunodominance.

- C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome.
- A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.
- Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen.
- The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.

p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A*0201)	Imami2002b

Keywords rate of progression, Th1, Th2.

Donor HLA A0202/2501, B1801/62, C10/1203, DRB1 1501, DQB1 8.

- 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. Long term non-progressors had much strong Th responses, particularly to p24 peptides, and they tended to be balanced between Th1, IL-2 producing and Th2, IL-4 producing responses.
- One of the immunologically discordant progressors became symptomatic during the course of the study, and he had a rapid drop in proliferative response to all antigens and also a shift from a Th1 to a Th2 response. To find out if the CD8 response also shifted in cytokine production, the CD8+ T-cell response to SLYNTVATL in this patient was also tested. It to was found to shift, from IFNgamma to IL-4 producing in Elispot, and using a bioassay of indicator lines, from IL-2 to IL-4 production.

p17 (77–85)	Gag p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Cao2003

Keywords binding affinity, acute infection, early-expressed proteins.

Assay type CD8 T-cell Elispot - IFNγ.

Donor HLA A*0201, A11, B51, B61, Cw2, Cw14.

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- Only 1/10 HLA A*02 carrying individuals in this study recognized SLYNTVATL.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A*0201)	Dagarag2003
	Assay type cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay. • Telomer length is short in the CD8+ T-cell compartment of HIV-1 infected people, indicating excessive CTL activation and premature senescense. Here human telomerase RT (hTERT) transduction of HIV-1-specific CTL was used to study the functional impact of telomerase. Telomerase expression enhanced proliferative capacity, as well as cytolytic and antiviral capabilities; cytokine production was unchanged. hTERT transduced CTLs were 10-fold more efficient in controlling HIV-1 replication in culture. Thus telomerase transduction can restore CTL mediated cytolysis, and may have therapeutic potential. • Three polyclonal CD8+ T-cell lines derived from an HIV-1, HLA A*0201 positive patient were used in this study, including one specific for this epitope.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	Vaccine	mouse (A*0201)	Okazaki2003
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag **Keywords** binding affinity, vaccine-induced epitopes. **Assay type** cytokine production, Chromium-release assay. **Donor HLA** A2.1. • Alanine substitutions of VIYQYMDDL were tested for importance of each amino acid for HLA-A2.1 binding. Peptide variant (vLyqymddV) showed an 8 fold higher MHC binding affinity than wild type. YLyqymddV had an even higher binding affinity, but the Y at positions one blocked TCR recognition. The higher affinity form of vLyqymddV induced CTL *in vivo* that could protect against a vaccinia virus expressing RT and the wild type epitope. • SLYNTVATL was included as a control.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A*0201)	Shacklett2003
	Keywords genital and mucosal immunity. **Epitope name** SL9. **Assay type** Tetramer binding. • Lymphocytes from rectal biopsies were used to characterize the CD8+ T cell response to HIV in GALT, Gut-associated lymphoid tissues. Patients were selected on the basis of being HLA-A2+ and having detectable SLYNTVATL and ILKEPVHGV tetramer responses in PBMC. SLYNTVATL frequency was increased in GALT relative to PBMC in 6/7 patients studied, while a control response to a CMV-peptide was diminished in GALT. Only two patients had ILKEPVHGV CD8+ T cell responses, and both had slightly higher frequencies in GALT than PBMC. • HIV may perturb lymphocyte retention in GALT, suggested by an overall reduction of GALT CD8+ cells expressing alphaEbeta7. GALT HIV-specific CD8+ T cells expressed alphaEbeta7, suggesting mucosal priming.				
p17 (77–85)	p17 (77–85)	SLYNTVATL		human (A*0202)	Frahm2004
	• C. Brander notes that this epitope can be presented by A*0201 and A*0202.				
p17 (77–85)	p17 (SF2)	SLYNTVATL	HIV-1 infection	human (A*0202)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL		human (A*0205)	Frahm2004
	• C. Brander notes that this epitope can be presented by A*0201 and A*0202.				
p17 (77–85)	p17 (subtype A)	SLYNTVATL	HIV-1 exposed seronegative	human (A*0214, A*0201)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women. • The epitope variants SLYNTVATL and SLFNTVATL were both recognized.				
p17 (77–85)		SLYNTVATL	HIV-1 infection	human (A02)	Sabbaj2002b
	Epitope name Gag-SL9. • Among HIV+ individuals who carried HLA A02, 17/30 (57%) recognized this epitope.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2. • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice. • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost. • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested. • SLYNTVATL was recognized by 5/16 HLA-A2 patients.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	Vaccine	human (A2)	Carruth1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease **Keywords** immunodominance. • The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease) • CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination. • CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls. • The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Lack of response to SLYNTVATL led the authors to speculate that the immunodominance of this epitope in natural infections may not be recapitulated by vaccine antigen.				
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.	SLYNTVATL	HIV-1 infection	human (A2)	Birk1998b
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • Included as a negative control in a tetramer study of A2-EBV CTL response.	SLYNTVATL	HIV-1 infection	human (A2)	Callan1998
p17 (77–85)	p17 **Epitope name** SL9. • CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.	SLYNTVATL	HIV-1 infection	human (A2)	Wagner1998a
p17 (77–85)	p17 (77–85 HXB2) **Epitope name** SL9. • Two CTL clones recognize this epitope, but not the NL4-3 form of the epitope SLYNTIAVL. • Nef down-regulates MHC class I molecules, which inhibits CTL killing, and this down-regulation can be partially compensated for by adding excess soluble peptide.	SLYNTVATL	HIV-1 infection	human (A2)	Collins1998
p17 (77–85)	p17 (77–85) **Keywords** inter-clade comparisons. **Epitope name** SL9. • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia. • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested. • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag. • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef. • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env. • Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL.	SLYNTVATL	HIV-1 infection	human (A2)	Durali1998
p17 (77–85)	p17 (77–85) **Keywords** dendritic cells. **Epitope name** SL9. • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients. • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated. • SLYNTVATL is a conserved HLA-A2 epitope included in this study – 3/6 patients had this sequence as their HIV direct sequence, one had the form SLYNTVAVL and all four of these had a detectable CTL response – the other two had either the sequence SLFSAVAVL or SLFSAVAAL and no detectable CTL response.	SLYNTVATL	HIV-1 infection	human (A2)	Kundu1998b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85 IIIB)	SLYNTVATL	HIV-1 infection	human (A2)	Sipsas1997
	Epitope name SL9. • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • SLYNTVAVL, a variant found in HIV-1 MANC, was also recognized. • SLFNTVAVL, a variant found in HIV-1 NY5CG, was also recognized.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A2)	Rowland-Jones1998a
	Keywords inter-clade comparisons. **Epitope name** SL9. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is SLfNtvatL. • The D subtype consensus is SLyNTvATL.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A2)	Sewell1997
	Keywords binding affinity. **Epitope name** SL9. • Naturally occurring variants of this epitope escaped killing and acted as antagonists. • The following variants were found in HIV-1 infected patients who mounted a strong response against this epitope: –F——, –F—-V-, –S——, -SF——, –L——, ——I—, ——I-V-, –F–I—, –F–I-V-, –F-A—- • All variants bound to A2 with at least half the affinity of SLYNTVATL except the triple mutant: –F–I-V- • Antagonism could be observed at low concentrations, abrogating lysis at an antagonist:agonist ratio of 1:10 – the antagonism was observed in one SLYNTVATL-specific CTL line but not another.				
p17 (77–85)	p17 (77–85 HXB2)	SLYNTVATL	HIV-1 infection	human (A2)	Yang1997b
	Keywords kinetics. **Epitope name** SL9. • A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transduced into CD8+ cells. • The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency. • A CTL clone specific for this epitope was used for the comparison.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	in vitro stimulation or selectio	human (A2)	Stuhler1997
	Epitope name SL9. • Keyhole limpit hemocyanin or tetanus toxoid Th epitope co-expression with peptide CTL epitopes on the same APC was required for induction of peptide-specific CTL.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Yang1996
	Epitope name SL9. • CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL. • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones. • The distinction was thought to be due to lower expression of RT relative to Env and Gag. • CTL can lyse infected cells early after infection, possibly prior to viral production.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85) **Epitope name** SL9. **Assay type** CTL suppression of replication. • CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*. • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation. • CTL suppress HIV replication more efficiently in HLA-matched cells.	SLYNTVATL	HIV-1 infection	human (A2)	Yang1997a
p17 (77–85)	p17 (77–85 LAI) **Epitope name** SL9. • Examined in the context of motifs important for HLA-A2 binding.	SLYNTVATL	HIV-1 infection	human (A2)	Parker1992, Parker1994
p17 (77–85)	p17 (77–85 LAI) **Keywords** review. **Epitope name** SL9. • Review of HIV CTL epitopes.	SLYNTVATL	HIV-1 infection	human (A2)	McMichael1994
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • CTL clones recognize naturally processed peptide.	SLYNTVATL	HIV-1 infection	human (A2)	Tsomides1994
p17 (77–85)	p17 (77–85) **Epitope name** SL9. • A three cell-type cluster consisting of APCs, Th, and CTLs is the minimal regulatory unit required for Th cell-dependent induction of CTLs.	SLYNTVATL	in vitro stimulation or selectio	human (A2)	Stuhler1997
p17 (77–85)	p17 (77–85) **Keywords** inter-clade comparisons. **Epitope name** SL9. • The consensus peptides of B and D clade viruses and some Cs have the sequence SLYNTVATL. • The consensus peptide of A, and some C strains have SLFNTVATL, a form that is cross-reactive.	SLYNTVATL	HIV-1 infection	human (A2)	Cao1997a
p17 (77–85)	Gag (77–85) **Epitope name** SL9. • CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective. • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.	SLYNTVATL	HIV-1 infection	human (A2)	Dyer1999
p17 (77–85)	p17 (77–85) **Keywords** escape. **Epitope name** SL9. • Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL) • Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape.	SLYNTVATL	HIV-1 infection	human (A2)	Harrer1998
p17 (77–85)	p17 (77–85 SF2) **Keywords** acute infection.	SLYNTVATL	HIV-1 infection	human (A2)	Altfeld2001a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The relative contribution of CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection. • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells. • The A2 epitopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded.				
p17 (77–85)	p17 (BRU)	SLYNTVATL	in vitro stimulation or selectio	human (A2)	Buseyne2001
	Keywords epitope processing, dendritic cells. **Epitope name** SL9. • Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL. • Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in SLYNTVATL specific CTL line EM71-1 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency. • Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion.				
p17 (77–85)	p17	SLYNVATL	HIV-1 infection	human (A2)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load. • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional. • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival. • In one patient with a SLYNVATL response, no SLYNVATL mutations were found among 21 clones despite high viral load (260,000 RNA copies/ml serum), suggesting low *in vivo* efficacy of the SLYNVATL response.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p17 (77–85)	p17	SLYNVATL	HIV-1 infection	human (A2)	Seth2001
	Keywords HAART, immunodominance. • CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized. • 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy. • 4/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope. • Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Islam2001
	Keywords HAART, TCR usage. **Epitope name** SL9. • Transcript frequencies were followed for four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL, and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL. • This epitope sequence from clone p175b uses the Vβ5, CDR3 (FDS), Jβ2.7 TCR beta gene.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responses were stable even through HAART with undetectable viral loads, but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time.				
p17 (77–85)	p17 (77–85 SF2)	SLYNTVATL	HIV-1 infection	human (A2)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 2/4 group 3.				
p17 (77–85)	p17 (77–85)	SLFNTVATL	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS), immunodominance. • Variants SL(F/Y)NTVATL are A/B clade specific. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-A2 women, 1/10 HEPS and 22/26 HIV-1 infected women recognized this epitope, likelihood ratio 18.3, p value < 0.003, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women. • The dominant response to this HLA allele was to this epitope in the 1/10 HEPS case and in 18 of the 22/26 HIV-1 infected women that responded. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort. • Subject ML 1250 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, which switched to SL(F/Y)NTVATL post-seroconversion. • Subjects ML 1575 and ML 1592 had no response to SL(F/Y)NTVATL prior to seroconversion, but made responses post-seroconversion. • Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion.				
p17 (77–85)	p17 (77–85 93TH253 subtype CRF01)	SLYNTIATL	HIV-1 infection	human (A2)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** G77-85. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (77–85)	p17 (77–85 93TH253 subtype CRF01)	SLYNTIATL	HIV-1 infection	human (A2)	Bond2001
	Keywords inter-clade comparisons.				
	• More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.				
	• 2/4 tested FSWs recognized the E clade version of this epitope, SLYNTIATL, the B clade version is SLYNTVATL.				
	• This epitope was only conserved in CRF01 and subtypes B and D, and exact matches were uncommon.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Day2001
	Keywords rate of progression, acute infection.				
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)				
	• 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
	• SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes.				
	• Three subjects had an A2 response only to SLYNTVATL.				
	• The two subjects with acute infection did not respond to SLYNTVATL.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Goulder2001c
	Keywords mother-to-infant transmission, escape.				
	Epitope name SL9.				
	• Immune escape variants in this epitope where transmitted both horizontally and vertically in two families.				
	• Eight transmitting mothers and 14 non-transmitters mothers were studied and variation within the SL9 epitope was associated carrying HLA-A2 (P=0.04), but no link between variation from the SL9 consensus and vertical transmission was established.				
p17 (77–85)	p17 (SF2)	SLYNTVATL	HIV-1 infection	human (A2)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
	• The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	HIV-1 infection	human (A2)	Kelleher2001a
	Keywords HAART, epitope processing, immunodominance.				
	• Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in in an intracellular context.				
	• RTV did not reduce antigen presentation and concentration of the two immunodominant Gag CTL epitopes (KRWIIMGLNK (B27) and SLYNTVATL (A2)).				
	• RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 infection	human (A2)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS).				
	• Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
p17 (77–85)	Gag (p17) (77–85 NL43)	SLYNTVATL	HIV-1 infection	human (A2)	Yang2002
	Keywords class I down-regulation by Nef. • Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL-43. The CTL clone 18030D23, specific for the class I A2 presented SLYNTVATL epitope, was one of four used in this study.				
p17 (77–85)	p17 (77–85 BRU)	SLYNTVATL	HIV-1 infection	human (A2)	Cohen2002
	Keywords epitope processing. • The antigen presentation of two A2-restricted epitopes was compared, SLYNTVATL (p17) and ILKEPVHGV (RT). HIV-1 infected cells were more sensitive to lysis by SLYNTVATL-specific CTL than by ILKEPVHGV-specific CTL, because of a higher density of SLYNTVATL-A2 resulting from differences in processing. • Incubation with a T1-cell proteolytic extract showed that by four hours, 25% of a p17 peptide had a C-term Leu-85 and were SLYNTVATL-precursors, while ILKEPVHGV-precursors were far less frequent (6.8%) even with four times more proteolytic extract after 30 hours. • p17 was preferentially cleaved between Leu85 and Tyr86, while appropriate Val484 and Tyr485 cleavage was minor for RT. • In a competition experiment, RSLYNTVATL bound TAP 3.7-fold more efficiently than RT peptides. • No difference in CTL avidity was detected in six patients with HLA-A2-restricted responses to these epitopes. • No significant difference in HLA-A2 binding of to p17 or RT epitopes was observed.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	Vaccine	mouse (A2)	Kmieciak2001
	Vaccine *Strain:* B clade IIIB *HIV component:* Gag, Pol *Adjuvant:* IL-12 • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with either a p17-p24-p51 fusion protein (vG/P-92) or the Gag-Pol precursor protein (vVK1). • Compared to vVK1, vG/P-92 induced a significant increase in Gag and Pol induced IFNgamma production and CTL responses, and to the epitopes SLYNTVATL and ILKEPVHGV, as determined by Elispot and 51Cr-release assays.				
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	human (A2)	Appay2002
	Keywords HAART. **Donor HLA** A2,A3,B7,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
p17 (77–85)	p17 (77–85 NL-43)	SLYNTVATL	HIV-1 infection	human (A2)	Ali2003
	Keywords class I down-regulation by Nef, escape. • NL43 was passaged in the presencNL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days. • Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNVATL in p17 Gag.				
p17 (77–85)	Gag	SLYNTVATL	HIV-1 infection	human (A2)	Bobbitt2003
	Keywords class I down-regulation by Nef. **Epitope name** SL9. **Assay type** Chromium-release assay, Flow cytometric CTL assay. • Nef, through Nef-mediated MHC-1 down-regulation, is not the only viral protein to influence levels of HIV-specific CTL recognition. The Rev L60F mutation, a common natural variant, can decrease CTL recognition of late gene products. The Rev mutation impacts the early to late gene switch, reducing late gene product production (Gag, Pol, Env, Vpu, Vpr and Vif), while increasing Nef production, both of which reduce the impact CTL recognition of late gene products. As expected, Rev L60F rendered HIV infected cells more resistant to CTL that recognized epitopes from the late proteins Env and Gag. Gag expression is more profoundly reduced than Env, and Gag-specific CTL were more profoundly affected. Conversely CTL against an epitope in an early gene product, Tat, were more effeciently recognized when infected with viruses carrying the Rev L60F mutation. • Patients in the asymptomic phase with active immune responses had more CTL resistant viruses, with lower Rev activity, lower Gag expression and greater resistance to Gag-specific CTL killing, while viruses isolated from people with AIDS were more sensitive to CTL killing.				
p17 (77–85)	Gag (77–)	SLYNTVATL	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag77. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • 10/17 HIV-infected HLA-A2+ people in this study recognized this epitope, and CTL and CD8+ T cells responses were elicted by immunization of transgenic mice with this peptide.				
p17 (77–85)	Gag (p17)	SLYNTVATL	HIV-1 infection	human (A2)	Kaul2003
	Keywords immunodominance, genital and mucosal immunity. **Assay type** Intracellular cytokine staining. • Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher. • The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).				
p17 (77–85)	Gag (p17)	SLYNTVATL	HIV-1 infection	human (A2)	Montefiori2003
	Keywords supervised treatment interruptions (STI), early treatment. **Epitope name** SL9. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2, A24, B38, B60, Cw2, Cw12.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-1+ patient AC10 underwent early HAART treatment, which was discontiuned 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.				
p17 (77–85)	Gag (77–85)	SLYNTAVTL	HIV-1 infection	human (A2)	Sandberg2003
	Keywords responses in children. **Assay type** CD8 T-cell Elispot - IFNγ, Tetramer binding, Flow cytometric CTL assay. • 65 vertically HIV-1 infected children, ages 1-16, the majority undergoing ART, were analyzed in regard to their plasma viremia and CD4+ and CD8+ T cell counts, and CD8+ T cell responses. • Using vaccina expressed Gag, Pol, Env, Rev, Nef in target cells in an Elispot assay, 85% of the children recognized at least one HIV antigen. Strong CD8+ T cell responses were directed against Pol, followed by Gag and Nef. Children younger than 4 had significantly weaker responses (7/14 had no reponse) than older children (only 1/32 had no response, and responses were greater in magnitude). • SLYNTVATL and ILKEPVHGV tetramers were used to quantitate specific responses. 49 chlidren in an expanded cohort carried HLA-A2. 1/11 children under 3 years of age had detectable CD8+ T-cell responses to SLYNTVATL, 2/11 to ILKEPVHGV. Among children over 3, 11/38 recognized SLYNTVATL and 9/38 recognized ILKEPVHGV. • Older children that maintained a CD4 count greater than 400 cells/ul tended to have stronger CTL reponses.			
p17 (77–85)	Gag (77–85)	SLYNTVATL	HIV-1 infection	(A2)	Sun2003
	Keywords assay standardization, memory cells. **Assay type** cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding, Intracellular cytokine staining. **Donor HLA** A2, A3, B27, B51; A2, A3, B27, B57; A2, A23, B57. • This study compares assay methods for testing CTL responses using samples from 20 HIV+ patients. The study compares ELISpot, tetramer-binding, and intracellular IFNγ. Tetramer-bidning analysis was performed with Gag (SLYNTVATL) or Pol (ILKEPVHGV) tetramers. Antigen presentation using recombinant vaccinia viruses (rVVs) encoding HIV-LAI Gag, Pol, Env, Nef, Tat and Vif proteins was compared to peptide panels. HIV antigen recognition in memory CTLs was measured by chronium release assay and compared to effector/memory CD8+ T cells in an IFN-γ ELISpot assay. • Results: IFNγ Elispot and flow cytometry gave similar frequencies of HIV specific CD8+ Tcells. Tetramer-binding analysis was most sensitive. Pools of peptides and the sum of frequencies of individual peptides were comparable. Elispot assays using peptides were more sensitive than assays using vaccinia expressed proteins. Cr release and Elispot against rVVs gave comparable memory cell responses 2/3s of the time. • 3/7 HLA-A2+ patients recognized this epitope.			
p17 (77–85)	p17 (77–85 NL43)	SLYNTVATL	HIV-1 infection	human (A2)	Yang2003
	Keywords escape, TCR usage. **Epitope name** SL9. **Assay type** Chromium-release assay, CTL suppression of replication. • Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts. • Three CTL clones were studied that recognized SLYNTVATL, 161JxA14, 18030D23, and 115DEC4. The different TCR usage on the CTL clones resulted in different patterns of recognition and escape. 161JxA14 suppressed the variant slFntvatl, 18030D23 did not; conversely the variants slfntIaVl and slFntIatl were suppressed by 18030D23, but not 161JxA14.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• After two weeks of passage the predominant escape mutant from 161JxA14 was slyntIatl. Amino acid residues flanking SL9 were unchanged. Escape mutations did not occur within two weeks for the two additional SL9-specific CTL clones 18030D23 and 115DEC4.				
p17 (77–85)	p17	SLYNTVATL	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	Keywords inter-clade comparisons. **Epitope name** SL9. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among B and D clade viruses. • The Clade A version of the epitope, SLFNTVATL, was preferentially recognized by CTL. • This epitope was recognized by two different exposed seronegative prostitutes.				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR23. • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
p17 (77–85)	p17 (77–85 LAI)	SLYNTVATL	Vaccine	mouse (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30 **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR23. • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
p17 (77–85)	p17 (77–85)	SLYNTVATL	HIV-1 infection	human (B62)	Goulder1997a
	Keywords review. **Epitope name** SL9. • This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form.				
p17 (77–85)	Gag (77–85)	SLYNTVATL		human (HLA-A201)	Sandberg2000
	Keywords binding affinity. • This epitope served as a positive control in a study comparing peptide binding affinity to HLA-A201 to CTL responses upon vaccination with a nef DNA vaccine.				
p17 (80–88)	Gag (80–)	NTVATLYCV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* p17 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag80. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.				
p17 (82–91)	p17 (82–91 93TH253 subtype CRF01)	IATLWCVHQR	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** G82-91. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11. • This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11.				
p17 (82–91)	p17 (82–91 93TH253 subtype CRF01)	IATLWCVHQR	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined. • 3/8 tested FSWs recognized this epitope. • This epitope was not conserved in other subtypes, and exact matches were uncommon.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (84–91)	Gag (83–90)	TLYCVHQR	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons, TCR usage.				
	• Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals.				
	• TLYCVHQR was found to elicit clade-specific responses in clade B (TLYCVHQR is most common, and is also common in clade A – the variant tlycvhqK is common in clade B) and clade E (tlWcvhqr is most common). TLYCVHQR was not recognized by any CTL, tlycvhqK was recognized by CTL from 1/5 B clade infected Japanese subjects, and tlWcvhqr was not recognized by CTL from infected Thai subjects, so this seems to be a B clade exclusive epitope.				
	• The binding of the variant peptides to HLA A*1101 was comparable, but CTL that recognized tlycvhqK did not cross-recognize the other forms, implicating TCR interaction differences.				
p17 (84–91)	p17 (83–91)	TLYCVHQR	HIV-1 infection	human (A11)	Harrer1998
	Keywords escape.				
	• Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL)				
	• Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape.				
	• A Q90E substitution resulted in a loss of the ability of the peptide to induce lysis, a R91K substitution was still reactive, and a R91Q substitution show a reduced ability to stimulate lysis.				
p17 (84–92)	p17 (84–92)	TLYCVHQRI	HIV-1 infection	human (A*1101)	Frahm2004
	• C. Brander notes that this is an A*1101 epitope.				
p17 (84–92)	p17 (84–92)	TLYCVHQRI	HIV-1 infection	human (A11)	Brander1995b
	Keywords responses in children, mother-to-infant transmission.				
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.				
p17 (84–92)	p17 (84–92)	TLYCVHQRI	HIV-1 infection	human (A11)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (84–92)	p17 (84–92)	TLYCVHQRI	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p17 (84–92)	p17 (84–92 SF2)	TLYCVHQRI	HIV-1 infection	human (A11)	Altfeld2001b
	Keywords HAART, acute infection.				
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.				
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.				
	• Previously described and newly defined optimal epitopes were tested for CTL response.				
	• Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (84–92)	p17 (84–92)	TLYCVHQRI	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p17 (86–101)	p17 (SF2)	YCVHQRIEIKDTKEAL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual. • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
p17 (86–101)	p17 (SF2)	YCVHQRIEIKDTKEAL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual. • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
p17 (87–105)	p17 (91–105 SF2)	CRIDVKDTKEALEKIE	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
p17 (88–115)	p17 (88–115 ARV)	VHQRIEIKDTKEALDKIEE-EQNKSKKKA	HIV-1 infection	human (A2)	Achour1990
	• B cell epitope HGP-30 also serves as a CTL epitope.				
p17 (88–115)	p17 (88–115 ARV)	VHQRIEIKDTKEALDKIEE-EQNKSKKKA	Vaccine	mouse (H-2^d)	Hamajima1997
	Vaccine *Vector/Type:* peptide *HIV component:* CD4BS, HPG30, V3 *Adjuvant:* IL-12 • B cell epitope HGP-30 also serves as a CTL epitope. • Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide. • IL-12 expression plasmid included with the vaccination enhanced the CTL response.				
p17 (91–101)	p17 (SF2)	RIDVKDTKEAL	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A23/68 B45/72 Cw2/16 – this epitope fell outside the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (91–105)	p17 (91–105 SF2)	RIDVKDTKEALEKIE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A3, A24, B8, B55.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (92–101)	p17 (92–101)	IEIKDTKEAL	HIV-1 infection	human (B*4001)	Frahm2004
	• C. Brander notes this is a B*4001 epitope.				
p17 (92–101)	p17	IEIKDTKEAL	HIV-1 infection	human (B60)	Wagner1998a
	• CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.				
p17 (92–101)	p17 (92–101 SF2)	IEIKDTKEAL	HIV-1 infection	human (B60)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3.				
p17 (92–101)	Gag (92–101)	IEIKDTKEAL	HIV-1 infection	human (B60)	Yang2002
	Keywords class I down-regulation by Nef. • Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL43 infected cells. The CTL clone 161JD27, specific for the class I B60 presented epitope IEIKDTKEAL, was one of four used in this study.				
p17 (92–101)	Gag (p17) (92–101 NL43)	IEIKDTKEAL	HIV-1 infection	human (B60)	Yang2003
	Keywords escape. **Epitope name** IL10. **Assay type** Chromium-release assay, CTL suppression of replication. • Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts. • There was one cloned cell line that recognized IEIKDTKEAL, 161JD27. After 2 weeks of passaging HIV-1 in the presence of 161JD27, no mutations were observed within the epitope in 10 sequences; one of the 10 had a single E -> K substitution 6 amino acids beyond the C-terminal end of the epitope.				
p17 (92–101)	p17 (SF2)	IEIKDTKEAL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes. • B60 is present in 10-20% of the Caucasoid and very common in Asian populations.				
p17 (92–101)	p17 (92–101)	IEIKDTKEAL	HIV-1 infection	human (B60/B61)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to five B61-restricted epitopes tested.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.				
p17 (93–101)	p17 (SF2)	DVKDTKEAL	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ Caucasian from Boston, who was A1/*0201 B8/63 Cw7/- – this epitope fell outside the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p17 (93–101)	p17 (93–101)	EIKDTKEAL	Peptide-HLA interaction	human (B8)	DiBrino1994b
	• Examined in the context of motifs important for HLA-B8 binding, predicted epitope based on Achour *et al*.				
p17 (93–101)	p17 (93–101)	EIKDTKEAL	HIV-1 infection	human (B8)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (93–101)	p17 (93–101 LAI)	EIKDTKEAL		human (B8, B60)	Brander1997
	• Pers. comm. from A. Trocha and S. Kalams to C. Brander and B. Walker.				
p17 (121–132)	p17 (121–132 HXB2R)	DTGHSNQVSQNY	HIV-1 infection	human (A33)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.				
p17 (121–132)	Gag (121–132 LAI)	DTGHSNQVSQNY	HIV-1 infection	human (A33)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag.				
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	HIV-1 or HIV-2 infection	human (B*3501)	Frahm2004
	• Noted by Brander to be B*3501 epitope.				
p17 (124–132)	p17	NSSQVSQNY	HIV-1 infection	human (B*3501)	Dorrell2001
	Keywords binding affinity. • The crystal structure of this epitope bound to HLA-B*3501 shows that a serine can fit into the B pocket, which is shared between B35 and B53, with the hydroxyl group of the P2 serine occupying a position almost identical to the P2 proline that was previously considered the anchor motif. • Novel B53 epitopes (DTINEEAAEW and QATQEVKNM) were defined in this study that showed that A and T can also serve as P2 anchor residues for the B pocket of HLA-B35 and B53 – while S, T, and P could all fit into the B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53.				
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	HIV-1 infection	human (B35)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (124–132)		NSSKVSQNY	HIV-1 infection	human (B35)	Wilson2000a
	Keywords dynamics, acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
p17 (124–132)	p17 (124–132)	NSSKVSQNY	HIV-1 infection	human (B35)	Birk1998b
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs.				
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	HIV-1 or HIV-2 infection	human (B35)	Rowland-Jones1995b
	• Established by titration.				
p17 (124–132)	p17 (124–132 LAI)	NSSKVSQNY	in vitro stimulation or selectio	human (B35)	Lalvani1997
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers. • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.				
p17 (124–132)	p17	NSSKVSQNY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive. • HIV-2 version of this epitope is not conserved: PPSGKGGNY, but the CTLs are cross-reactive – this is one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				
p17 (124–132)	p17	NSSKVSQNY	HIV-1 infection	human (B35)	Seth2001
	Keywords HAART. • CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.				
p17 (124–132)	p17 (124–132 SF2)	NSSKVSQNY	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3.				
p17 (124–132)		NSSKVSQNY	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Gag-NY9. • Among HIV+ individuals who carried HLA B35, 1/21 (5%) recognized this epitope.				

II-B-2 p17-p24 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17-p24 (127–3)	p17-p24 (127–135 subtype D)	QVSQNYPIV		human (A*6802)	Dong1998a
	• Epitope starts in p17 and ends in p24. • Predicted on binding motif, no truncations analyzed.				
p17-p24 (131–6)	p17-p24 (132–140 SF2)	NYPIVQNL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• The epitope starts in p17 and ends in p24. • Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • NYPIVQNL bound to A*2402 with medium strength, and the epitope can be processed in a vaccinia construct and presented – no CTL clone was obtained.				

II-B-3 p24 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (8–17)	p24 (140–149)	GQMVHQAISP	HIV-1 infection	human (B57)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others.				
p24 (8–20)	p24 (140–152 IIIB)	GQMVHQAISPRTL	HIV-1 infection	human (Cw3)	Littaua1991
	• Fine specificity of human Cw3 restricted Gag CTL epitope.				
p24 (8–27)	p24 (140–159)	GQMVHQAISPRTLNAWVKVV	HIV-1 infection	human (B14)	Musey1997
	• CTL specific for this epitope were found in the peripheral blood but not in the cervical mucosa of one donor.				
p24 (9–18)	Gag (173–182)	QMVHQAISPR	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
p24 (10–18)	Gag (144–152 SF2)	MVHQAISPR	HIV-1 infection, computer prediction	human (A*3303)	Hossain2003
	Keywords binding affinity, computational epitope prediction. **Assay type** Chromium-release assay. • HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing. • This epitope is one of the 4 that are properly processed.				
p24 (10–18)	Gag (174–182)	MVHQAISPR	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
p24 (11–24)	p24 (SF2)	VQHAISPRTLNAWV	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A34/68 B57/71 Cw3/7 – this epitope fell outside the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.			
p24 (11–25)	p24 (11–25 HXB2)	VHQAISPRTLNAWVK	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 29% of the study subjects, and it was the third most frequently recognized peptide.			
p24 (11–32)	p24 (143–164 BH10)	VHQAISPRTLNAWVKVVEE-KAF	HIV-1 infection	human (Bw57)	Johnson1991
	• Gag CTL response studied in three individuals.				
p24 (12–20)	Gag (146–154)	HQAISPRTL	HIV-1 infection	chimpanzee (Patr-B*02)	Balla-Jhagjhoorsingh1999b
	• Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57. • Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS. • CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57. • The human HLA protein which presents this Patr-B*02 epitope is HLA-B*5701 but the amino acid sequences in the binding pockets of HLA-B*5701 and Patr-B*02 are distinctive.				
p24 (13–20)	p24 (145–152)	QAISPRTL	HIV-1 infection, HIV-1 exposed seronegative	human (Cw3)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p24 (13–23)	p24 (145–155)	QAISPRTLNAW	HIV-1 infection	human	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to QAISPRTLNAW noted previously to be A25.				
p24 (13–23)	p24 (145–155 LAI) • C. Brander notes that this is an A*2501 epitope.	QAISPRTLNAW		human (A*2501)	Frahm2004
p24 (13–23)	p24 (145–155 SF2) **Keywords** HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3.	QAISPRTLNAV	HIV-1 infection	human (A25)	Altfeld2001b
p24 (13–23)	Gag (145–155 IIIB) **Assay type** Chromium-release assay. • Three CD8+ CTL cell clones were derived from 2 HIV-1 positive asymptomatic patients, and their epitope specificities and HLA presenting proteins were defined.	QAISPRTLNAW	HIV-1 infection	human (A25)	Kurane2003
p24 (13–23)	p24 (145–155 LAI)	QAISPRTLNAW		human (A5)	Kurane1998
p24 (15–23)	**Keywords** HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • ISPRTLNAW was consistently recognized by 1/22 HEPS sex worker controls (ML1250), and LSPRTLNAW was recognized by 2 additional HEPS sex worker controls (ML1693 and ML1589)	LSPRTLNAW	HIV-1 infection, HIV-1 exposed seronegative	human	Kaul2001c
p24 (15–23)	p24 **Keywords** HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.	LSPRTLNAW	HIV-1 infection	human (B*57)	Kaul2002
p24 (15–23)	p24 (147–155 IIIB) • C. Brander notes this is a B*5701 epitope.	ISPRTLNAW	HIV-1 infection	human (B*5701)	Frahm2004
p24 (15–23)	**Keywords** rate of progression, immunodominance.	ISPRTLNAW	HIV-1 infection	human (B*5701)	Migueles2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.				
p24 (15–23)		ISPTRTLNAW	HIV-1 infection	human (B*5701)	Migueles2003
	Keywords rate of progression, escape. **Assay type** Intracellular cytokine staining, Flow cytometric CTL assay. • cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4). • In general use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.				
p24 (15–23)	Gag (147–155 LAI)	ISPRTLNAW	HIV-1 infection	human (B*5701 B*5801)	Klein1998
	Keywords rate of progression. • B57 has been associated with long-term non-progression in the Amsterdam cohort. • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag.				
p24 (15–23)	p24 (147–155)	ISPRTLNAW	HIV-1 infection	human (B57)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others, but not SLYNTVATL.				
p24 (15–23)	Gag (SF2)	ISPRTLNAW	HIV-1 infection	human (B57)	Goulder2001a
	Keywords acute infection. **Epitope name** IW9. • This epitope elicited the second strongest CTL response in patient PI004 during acute infection, and maintained the response. • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.				
p24 (15–23)	p24 (147–155)	ISPRTLNAW	HIV-1 infection	human (B57)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** ISP. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• None of the 8 study subjects recognized this epitope but none were HLA B57+				
p24 (15–23)	p24 (15–23)	ISPRTLNAW	HIV-1 infection	human (B57)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (15–23)	p24 (147–155 SF2)	ISPRTLNAW	HIV-1 infection	human (B57)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3.				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Gag-IW9. • Among HIV+ individuals who carried HLA B57, 2/5 (40%) recognized this epitope. • Among HIV+ individuals who carried HLA B58, 0/4 (0%) recognized this epitope.				
p24 (15–23)		ISPRTLNAW	HIV-1 infection	human (B57)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** ISP. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (15–23)	Gag (147–155)	ISPRTLNAW	HIV-1 infection	human (B57)	Musey2003
	Keywords TCR usage, genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A3, A28, B53, B57; A31, B7, B57. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood and semen of one male subject, and blood and cervix of one female subject. • From the male patient, six clones that recognized this epitope had three different patterns of TCRbeta usage: 2 from the blood and 1 from the semen used Vβ6S2DJ2S2; 1 from the blood and 1 from the semen used Vβ6S2DJ1.1; and 1 from the semen used Vβ7S1DJ2.3. • From the female patient, five clones that recognized this epitope had different TCRbeta usage. Blood derived clones were Bbeta6S7DJ2.7, Bbeta6.4DJ2.3, and Bbeta6S3DJ2.1. Cervix derived clones were Bbeta6S3DJ1.4 and Bbeta6S5DJ2.5.				
p24 (15–23)	p24 (147–155 IIIB)	ISPRTLNAW	HIV-1 infection	human (B57, B*5801)	Goulder1996b
	Keywords rate of progression. • Five slow progressors made a response to this epitope, and in two it was the dominant response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations.				
p24 (15–23)	p24 (subtype A)	LSPRTLNAW	HIV-1 exposed seronegative	human (B57, B58)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
p24 (15–23)	p24 (147–155)	LSPRTLNAW	HIV-1 infection, HIV-1 exposed seronegative	human (B57, B58)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • Variants (L/I)SPRTLNAW are specific for the A/B clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B57/B58 women, 4/6 HEPS and 14/17 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 14/17 responsive HIV-1 infected women.				
p24 (16–24)	p24	SPRTLNAWV	HIV-1 infection	chimpanzee	Santra1999
	• 3/4 animals displayed HIV-1 Gag-specific CTL activity. • Effector cells from two chimpanzees were able to recognize epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14) • No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14.				
p24 (16–24)	p24 (148–156)	SPRTLNAWV		human (B*0702)	Frahm2004
	• C. Brander notes this is a B*0702 epitope. • Optimal peptide mapped by titration.				
p24 (16–24)		SPRTLNAWV	HIV-1 infection	human (B07)	Sabbaj2002b
	Epitope name Gag-SW9. • Among HIV+ individuals who carried HLA B07, 1/9 (11%) recognized this epitope. • Among HIV+ individuals who carried HLA B81, 1/6 (17%) recognized this epitope.				
p24 (16–24)	p24 (148–156)	SPRTLNAWV		human (B7)	Brander1997
	• Optimal peptide mapped by titration, pers. comm. from D. Lewinsohn to C. Brander and B. Walker.				
p24 (16–24)	p24 (148–156)	SPRTLNAWV	HIV-1 infection	human (B7)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL. • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism. • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p24 (16–24)	p24 (148–156)	SPRTLNAWV	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGVIRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.			
p24 (16–24)	p24 (16–24)	SPRTLNAWV	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.				
p24 (16–24)	p24 (16–24)	SPRTLNAWV	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-SV9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 positive individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.				
p24 (16–24)	p24 (subtype B)	SPRTLNAWV	HIV-1 exposed seronegative	human (B7, B*8101)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
p24 (16–24)	Gag (subtype B)	SPRTLNAWV	HIV-1 exposed seronegative	human (B7, B*8101)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B, and D clade viruses.				
p24 (18–26)	Gag (150–)	RTLNAWVKV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag150. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that induced CTL responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.				
p24 (19–27)	p24 (151–159)	TLNAWVKVV	HIV-1 infection	human (A*02)	Huang2000
	Keywords HAART, immunodominance. • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed. • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT. • In 3/3 HLA-A*02, -B*27 subjects the immunodominant epitope was against HLA B*27 Gag p24 epitope KRWIILGL, not A2 Gag epitopes.				
p24 (19–27)	p24 (151–159)	TLNAWVKVV	HIV-1 infection	human (A*02)	Rinaldo2000
	Keywords HAART. • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection.				
p24 (19–27)	p24 (151–159)	TLNAWVKVV	HIV-1 infection	human (A2)	Parker1992, Parker1994
	• Study of sequence motifs preferred for peptide binding to class I HLA-A2.				
p24 (19–27)	p24 (19–27)	TLNAWVKVV	HIV-1 infection	human (A2)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (19–27)	p24 (150–159)	TLNAWVKVI	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS). • Variants TLNAWVKV(I/V) are A/B clade specific.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p24 (19–27)	p24 (subtype B)	TLNAWVKVV	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B and D clade viruses.				
p24 (21–40)	p24 (153–172 SF2)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A2, -B21.				
p24 (21–40)	p24 (153–172 SF2)	NAWVKVVEEKAFSPEVIPMF	Vaccine	macaque	Wagner1998b
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* CD4BS, Gag, gp120, V3 • A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner1998b] • CTL specific for this epitope could be found both before and after SHIV challenge.				
p24 (21–40)	Gag (153–172)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human (B57)	Brodie1999
	• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptively transferring them. • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects.				
p24 (21–40)	p24 (153–172)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human (B57)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL. • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication. • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism. • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p24 (21–42)	p24 (153–174 BH10)	NAWVKVVEEKAFSPEVIPM-FSA	HIV-1 infection	human (Bw57)	Johnson1991
	• Gag CTL response studied in three individuals.				
p24 (28–36)	p24	EEKAFSPEV	HIV-1 infection	human (B*4415)	Bird2002
	Keywords HIV exposed persistently seronegative (HEPS). • 5/233, (4 HIV-1 positive, 1 HEPS) (2.1%) Kenyan female sex workers carried the novel HLA allele B*4415.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Residues forming the B pocket of HLA B*4415 were identical to HLA B*4001, B*4402 and B*4403. These alleles preferred E, an acidic residue, at the P2 position. • The amino acid residues forming the F pocket of allele B*4415 were not correlated with other known HLA molecules, but analogy suggests a binding preference for small, neutral amino acids. • Based on the binding motif x[DE]xxxxxx[VILA], 19 potential B*4415 epitopes were identified, and 1/19 was reactive in an Elispot, EEKAFSPEV.				
p24 (28–36)	p24 (28–36)	EEKAFSPEV		human (B*4415)	Frahm2004
p24 (28–47)	p24 (160–179)	EEKAFSPEVIPMFSALSEGA	HIV-1 infection	human (B27)	Musey1997
	• Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope.				
p24 (29–48)	Gag (161–180 C consensus)	EKAFSPEVPMFTALSEGAT	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (30–37)	p24 (162–170 LAI)	KAFSPEVI	HIV-1 infection	human (B*5703)	Frahm2004
	• C. Brander notes this is a B*5703 epitope.				
p24 (30–37)	p24 (30–37)	KAFSPEVI	HIV-1 infection	human (B57)	Goulder2000c
	• Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11. • Improved stabilization of the B57-peptide complex was demonstrated by the 11 mer which fits the B57 binding motif, relative to the 8 mer, which does not. • B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection.				
p24 (30–37)		KAFSPEVI	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Gag-KI8. • Among HIV+ individuals tested who carried HLA B57, 0/5 (0%) recognized this epitope.				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection, HIV-1 exposed seronegative	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized by 1/22 HEPS sex worker controls, ML1250.				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection	human (B*57)	Spiegel1999
	Keywords HAART. • Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children. • CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef, and CTLe were measured by ELISPOT.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL against B*57-KAFSPEVIPMF was a de novo response observed in one of the children when viral load increased as a result of stopping therapy. • HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses.				
p24 (30–40)	p24 (162–172 LAI)	KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Goulder1996b
	Keywords rate of progression. • This peptide was recognized by CTL from five slow progressors. • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations. • This epitope is highly conserved.				
p24 (30–40)	p24 (162–172 LAI)	KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Frahm2004
	• C. Brander notes this is a B*5701 epitope.				
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • Attempts to make all for HLA B*5701-epitope tetramers were made, but only the HLA B*5701-KAFSPEVIPMF tetramer folded properly. The percentage of CD8+ T cells staining with this HLA B*57 gag tetramer and the fraction of CD69+IFN-+ cells responding to autologous B cells pulsed with KAFSPEVIPMF was highly correlated (r = 0.84; P = 0.005). The percent of CD8+ T cells that stain with the A*2 gag SLYNTVATL tetramer was low (0-0.31%) in a A2+ B57+ LTNP, emphasizing the focus of the immune response on the B*5701 epitopes.				
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong in individuals that carried both A2 and B57.				
p24 (30–40)	Gag (162–172)	KAFSPEVIPMF	HIV-1 infection	human (B*5701)	Migueles2003
	Keywords rate of progression, escape. **Epitope name** KAF11. **Assay type** Intracellular cytokine staining, Flow cytometric CTL assay. • cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4). • In general use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses. • This epitope tends to be quantitavtively immunodominant in B57+ people, including in some of the individuals in this study. It was extremely well conserved in the sequences obtained here, despite strong immune pressure, suggesting fitness constraints.				
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B*5701, B*5703)	Gillespie2002
	Keywords inter-clade comparisons, rate of progression. **Epitope name** KAFS.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL responses of eight HIV+ slow progressors from Nairobi Kenya or Oxford, UK who were B*5701 or B*5703 were studied, as B*57 is associated with slow progression. • This epitope is located between the structurally conserved alpha-helix 1 and alpha-helix 2 (H1-H2) region of the p24 capsid protein, and tends to elicit strong reactions in B*57 individuals. • Broad heterogeneous cross-clade reactivity to 6 clade variants of the KAFS peptide sequence were observed in one B*5701 and 5 B*5703 HLA-restricted patients, measured by IFNγ productionElispot assays as well as tetramer binding. The clade variants were: KAFSPEVIPMF (clades A and B), kGfNpevipmf (clades A/AC); kaLspevipmf (clade A); kafspevipVf (clade A); kafNpeIipmf (group O); kafspeIipmf (A/C); kafsQevipmf (A/C); and kaLspevipmf KNFSPEVIPMF A/G). Not all variants were well recognized in all patients, for example kafsQevipmf was not able to induce IFN gamma production in 3/6 tested, and had a diminished capacity to sensitize target cells for lysis.			
p24 (30–40)	p24 (162–172 LAI) • C. Brander notes this is a B*5703 epitope.	KAFSPEVIPMF	HIV-1 infection	human (B*5703)	Frahm2004
p24 (30–40)	**Keywords** HAART. **Epitope name** Gag-KF11. **Donor HLA** A*3402 A*7401 B*0801 B*5703 Cw*0302 Cw*0701. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 00RCH59 was African American, on HAART, viral load 170, CD4 count 477. • Among HIV+ individuals who carried HLA-B57, 6/6 (100%) recognized this epitope.	KAFSPEVIPMF	HIV-1 infection	human (B*5703)	Sabbaj2002b
p24 (30–40)	p24 (30–40) • Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11. • Improved stabilization of the B57-peptide complex was demonstrated by the 11mer which fits the B57 binding motif, relative to the 8 mer, which does not. • B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection.	KAFSPEVIPMF	HIV-1 infection	human (B57)	Goulder2000c
p24 (30–40)	p24 (162–172) **Keywords** immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others.	KAFSPEVIPMF	HIV-1 infection	human (B57)	Betts2000
p24 (30–40)	p24 (SF2) **Keywords** inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope is not among the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.	KAFSPEVIPMF	HIV-1 infection	human (B57)	Goulder2000a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (30–40)	Gag (SF2)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Goulder2001a
	Epitope name KF11. • Three CTL responses in patient PI004, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.				
p24 (30–40)	p24 (162–172)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** KAF. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B57+				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection	human (B57)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load. • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional. • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.				
p24 (30–40)	p24 (162–172 SF2)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3.				
p24 (30–40)	p24 (163–174)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p24 (30–40)		KAFSPEVIPMF	HIV-1 infection	human (B57)	Sabbaj2002b
	• Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope.				
p24 (30–40)	p24	KAFSPEVIPMF	HIV-1 infection	human (B57)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** KAF. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Cao2003
	Keywords acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A3, B44, B57, Cw5, Cw6. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • Alleles A3, B35, B57, and B62 were more frequently recognized than alleles A1, A2, A30, and A44 e.g., during primary infection. 2/10 patients, 1372 and 1397, recognized A2-restricted epitopes. The common A2-restricted epitopes Gag SL9 and Pol IV9 were not recognized in peptide tetramer-binding assays.				
p24 (30–40)	Gag (p24)	KAFSPEVIPMF	HIV-1 infection	human (B57)	Kaul2003
	Keywords immunodominance, genital and mucosal immunity. **Assay type** Intracellular cytokine staining. • Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher. • The immunodominant response was to this epitope in the PBMC of 10/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).				
p24 (30–40)	p24 (153–164)	KAFSPEVIPMF	HIV-1 infection, HIV-1 exposed seronegative	human (B57, B58)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B57/B58 women, 4/6 HEPS and 12/17 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 12/17 HIV-1 infected women.				
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B57/B58)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (30–40)	p24 (30–40)	KAFSPEVIPMF	HIV-1 infection	human (B58)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (31–44)	p24 (31–44 HXB2)	AFSPEVIPMFSALS	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 22% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (31–50)	p24 (163–182)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
p24 (31–50)	p24 (163–182 SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A2, B21.				
p24 (31–50)	p24 (163–182 SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
p24 (31–50)	p24 (SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual. • The response to the peptide was CD4 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
p24 (32–40)	Gag (164–172)	FSPEVIPMF	HIV-1 infection	human (B57)	Musey2003
	Keywords TCR usage, genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A3, A28, B53, B57. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood and semen. • The TCRbeta VDJ rearrangement of a CTL clone from the blood was Vβ21S3DJ1.2, and a clone from the semen used Vβ7S1DJ2.3.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (35–43)	p24 (167–175 LAI)	EVIPMFSAL		human (A*2601)	Goulder1996a
	Keywords inter-clade comparisons. • Identified as optimal epitope within Gag sequence AFSPEVIPMFSALSEGATPQ. • Relatively conserved epitope within B clade and in other clades. • Suspected binding motif for HLA-A26 includes T or V anchor at position 2, negative charge at position 1. • C. Brander notes that this is an A*2601 epitope in the 1999 database.				
p24 (35–43)	p24 (167–175 LAI)	EVIPMFSAL		human (A*2601)	Frahm2004
	• C. Brander notes that this is an A*2601.				
p24 (35–43)	p24 (167–175)	EVIPMFSAL	HIV-1 infection	human (A26)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.				
p24 (35–49)	p24 (35–48 HXB2)	EVIPMFSALSEGATP	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (36–43)	p24 (168–175 LAI)	VIPMFSAL		human (C*0102(Cw1))	Frahm2004
	• C. Brander notes this is a C*0102(Cw1) epitope.				
p24 (36–43)	p24 (168–175 LAI)	VIPMFSAL		human (Cw*0102, Cw1)	Goulder1997b
p24 (36–43)	p24 (168–175)	VIPMFSAL	HIV-1 infection	human (Cw01, 02)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.				
p24 (37–52)	Gag (169–184 LAI)	IPMFSALSEGATPQDL	HIV-1 infection	human (B12)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic. • Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (37–52)	p24 (169–184 LAI)	IPMFSALSEGATPQDL	HIV-1 infection	human (B12(44))	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.				
p24 (37–52)	p24 (37–52)	IPMFSALSEGATPDQL	HIV-1 infection	human (B44)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (39–58)	Gag (171–190)	MFTALSEGTPQDLNTMLNT	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons.				
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.				
	• Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.				
	• This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (41–60)	p24 (173–192 SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.				
	• Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag.				
	• Three of these 12 had CTL response to this peptide.				
	• The responding subjects were HLA-A3, A32, B7, B14; and HLA-A2, A3, B14, B44.				
p24 (41–60)	p24 (173–192 SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
p24 (41–60)	p24 (SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
	• The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
p24 (41–60)	p24 (179–188 subtype A)	SALSEGATPQDLNMMLNIVG	HIV-1 infection	human (B*8101)	Dorrell1999
	Keywords inter-clade comparisons.				
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa.				
	• This CTL epitope is presented by B*8101 in one of the patients with an A subtype infection – B*8101 is a newly discovered HLA allele found in Africans, and the epitope has yet to be mapped precisely.				
	• This epitope is distinct in subtype A relative to subtypes B, C, and D which share the dominant sequence: SALSEGATPQDLNTMLNTVG.				
p24 (41–62)	p24 (173–194 BH10)	SALSEGATPQDLNTMLNTV-GGH	HIV-1 infection	human (B14)	Johnson1991
	• Gag CTL response studied in three individuals.				
p24 (43–52)	p24 (subtype A)	LSEGATPQDL	HIV-1 infection	human (B42, B44)	Cao2000
	Keywords inter-clade comparisons.				
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype. • This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection (patient SP 511), is cross-reactive with subtypes A, B and D peptides.				
p24 (44–52)	p24 (176–184)	SEGATPQDL		human (B*4001)	Frahm2004
	• C. Brander notes this is a B*4001, B60 epitope.				
p24 (44–52)	Gag (p24)	SEGATPQDL	HIV-1 infection	human (B60)	Montefiori2003
	Keywords HAART, supervised treatment interruptions (STI), acute infection, early treatment. **Epitope name** SL9. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2, A24, B38, B60, Cw2, Cw12. • HIV-1+ patient AC10 underwent early HAART treatment, which was discontiuned 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.				
p24 (44–52)	p24 (44–52 NL43)	SEGATPQDL	HIV-1 infection	human (B60)	Yang2003
	Keywords escape. **Assay type** Chromium-release assay, CTL suppression of replication. • Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts. • One CTL clone, 161Jx12, recognized this epitope, and apparently no resistance mutations were selected by this clone, although the data was no shown in the paper.				
p24 (44–52)	p24 (SF2)	SEGATPQDL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes. • B60 is present in 10-20% of the Caucasoid and very common in Asian populations.				
p24 (44–52)	p24 (44–52)	SEGATPQDL	HIV-1 infection	human (B60/B61)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to five B61-restricted epitopes tested. • All five B60-restricted epitopes were reactive in another subject, the strongest CTL response directed against the B60-epitope p24 SEGATPQDL, and the B60-restricted responses together contributed over one-third of the total CTL response.				
p24 (46–59)	p24 (SF2)	GATPQDLNTMLNTV	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston with HLA A*3002/68 B14/*5802 Cw6/8 – this epitope fell within the most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (47–55)	p24 (47–55)	ATPQDLNTM	HIV-1 infection	human (B7)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (47–56)	p24 (subtype A)	ATPQDLNMML	HIV-1 exposed seronegative	human (B53)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
p24 (47–58)	p24 (181–192)	CTPYDINQMLNC	HIV-2 infection	human (B58)	Bertoletti1998a
	• HIV-2 epitope defined from an infection in Gambia, Bertoletti, pers. comm.				
p24 (48–56)	Gag (96ZM651.8)	TPQDLNTML		human (A*4201, B*8101)	Novitsky2001
	Keywords inter-clade comparisons, immunodominance. **Epitope name** G180-TL9. • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 19 of 46 (41.3%) had CTL responses to one or more peptides within the first immunodominant region of Gag (peptides TLNAWVKVIEEKAFSPEVIP, EKAFSPEVIPMFTALSEGAT, and MFTALSEGATPQDLNTMLNT), with magnitudes of response with ELISPOT results median and range 495 (103 to 1,447) SFC/10^6 PBMC. • 7 of 11 HLA-A*4201+ subjects (64%) responded to peptide MFTALSEGATPQDLNTMLNT. • TPQDLNTML is a A*4201 epitope within TLNAWVKVIEEKAFSPEVIP.				
p24 (48–56)	p24 (180–188 IIIB)	TPQDLNTML	HIV-1 infection	human (B*0702)	Frahm2004
	• C. Brander notes this is a B*0702 epitope.				
p24 (48–56)	p24 (179–187 LAI)	TPQDLNTML		human (B*4201)	Frahm2004
	• C. Brander notes this is a B*4201 epitope.				
p24 (48–56)	Gag (173–181 HIV-2)	TPYDINQML	HIV-2 infection	human (B*5301)	Frahm2004
	• C. Brander notes this is a B*5301 epitope.				
p24 (48–56)	p24 (180–188 LAI)	TPQDLNTML	HIV-1 infection	human (B*8101)	Frahm2004
	• C. Brander notes this is a B*8101 epitope.				
p24 (48–56)		TPQDLNTML	HIV-1 infection	human (B*8101, B*5301, B07)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-TL9. **Donor HLA** A*3402 A*7401 B*5301 B*8101 Cw*0401 Cw*0802.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subjects 00RCH86 and 03RCH59 both recognized this epitope, both restricted by HLA B*8101. • Subject 00RCH86 was African American, not on HAART, viral load 51000, CD4 count 520. • Subject 03RCH59 was African American, male, on HAART, viral load 22000, CD4 count 769. • Among HIV+ individuals who carried HLA B07, 2/9 (22%) recognized this epitope. • Among HIV+ individuals who carried HLA B*5301, 3/15 (20%) recognized this epitope. • Among HIV+ individuals who carried HLA B81, 4/6 (67%) recognized this epitope.				
p24 (48–56)	p24 (C consensus)	TPQDLNTML	HIV-1 infection	human (B42)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • B42 and B81 are very similar, and both can present this epitope to B42-positive effector cells – this epitope is almost certainly optimal for B81 as well – B42 and or B81 are expressed in 40-45% of Zulu and Xhosa infected individuals in South Africa, and in 14/18 B42 or B81+ individuals, the dominant gag response was to TPQDLNTML. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects.				
p24 (48–56)	Gag	TPQDLNTML	HIV-1 infection	human (B42)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.				
p24 (48–56)	p24	TPQDLNQML		human (B53)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: TPYDINQML, no cross-reactivity, [Gotch1993]				
p24 (48–56)	Gag (173–181 HIV-2)	TPYDINQML	HIV-2 infection	human (B53)	Gotch1993
p24 (48–56)	Gag (180–188 subtype A)	TPQDLNMML	HIV-1 infection, in vitro stimulation or selectio	human (B53)	Dorrell2001
	Keywords inter-clade comparisons. • In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins.				
p24 (48–56)	p24 (180–188 subtype A consensus)	TPQDLNMML	HIV-1 infection	human (B53)	Dorrell2001
	Keywords inter-clade comparisons, immunodominance, TCR usage. • In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This optimal epitope was identified within the 20 mer reactive peptide that carried it by homology with a B53 epitope from HIV-2, a B subtype B7 peptide that corresponds to it, as B53 is part of the B7 superfamily, and by the proline in the anchor at position 2. • TPQDLNMML was recognized in 6/7 HLA-B53 subjects and was immunodominant in most subjects. • TPQDLNMML was A subtype-specific with no cross-recognition of the subtype B, C, and D variant, TPQDLNTML, although the B/C/D variant bound more efficiently to B53 – position 7 show great positional variation in crystal structures of two HLA-B53 complexes, suggesting variation here might significantly alter the position of the peptide in the binding groove and thus affect TCR interactions. • Only one subject might have had a cross-reactive response with the HIV-2 and Mamu-A*01 variant CTPYDINQML, and this subject might have been dual infected with HIV-2.				
p24 (48–56)	Gag (p24)	TPQDLNMML	HIV-1 infection	human (B53)	Kaul2003
	Keywords immunodominance, genital and mucosal immunity. **Assay type** Intracellular cytokine staining. • Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher. • The immunodominant response was to this epitope in the PBMC of 2/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).				
p24 (48–56)	p24 (180–188 IIIB)	TPQDLNTML	HIV-1 infection	human (B7)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope.				
p24 (48–56)	p24 (180–188)	TPQDLNTML	HIV-1 infection	human (B7)	Jin2000b
	Keywords immunodominance. • This is the optimal epitope for the immunodominant response defined using a conventional approach in an HLA B7+ long-term non-progressor. • Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject – this was followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes.				
p24 (48–56)	p24 (SF2)	TPQDLNTML	HIV-1 infection	human (B7)	Goulder2001a
	Epitope name TL9. • Recognized by patient 9354 during chronic infection, used as a positive control in a study of the SLYNTVATL epitope.				
p24 (48–56)	p24 (48–56)	TPQDLNTML	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.				
p24 (48–56)	p24 (48–56)	TPQDLNTML	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-TL9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.				
p24 (48–56)	p24	TPQDLNTML	HIV-1 infection	human (B7)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** B7-TL9(p24). **Donor HLA** A32,A?,B7,B14. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT).				
p24 (48–56)	p24 (180–188 LAI)	TPQDLNTML	HIV-1 infection	human (C*0802(Cw8))	Frahm2004
	• C. Brander notes this is a C*0802(Cw8) epitope.				
p24 (48–57)	Gag	TPQDLNMMLN		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay. • TPQDLNMMLN was newly defined as an HLA-B7 epitope in this study, athough it was previously published as a B*8101 epitope. • TPQDLNMMLN was shown to stimulate an ELISPOT response, but could not be shown to bind to HLA-B7. • The variant TPQDLNTMLN was cross-reactive, had previously been identified as a HLA-B14 epitope, and could bind to HLA-B7.				
p24 (49–57)	p24 (181–189 LAI)	PQDLNTMLN	HIV-1 infection	human (B14, Cw8)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response. • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Despite this being a well defined conserved epitope, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 RAEQASQEV. • Christian Brander notes that B14 and Cw8 are in linkage disequilibrium, and that this epitope may be Cw8.				
p24 (51–59)	p24	DLNTMLNTV	HIV-1 infection	chimpanzee	Santra1999
	• 3/4 animals displayed HIV-1 Gag-specific CTL activity. • Effector cells from two chimpanzees were able to recognize two epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14) • No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14.				
p24 (51–59)	p24 (subtype A)	DLNMMLNIV	HIV-1 exposed seronegative	human (B14)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
p24 (51–59)	p24	DLNMMLNIV	HIV-1 infection	human (B14)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls, ML1792.				
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (B14)	Mollet2000
	Keywords HAART. **Epitope name** G5. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
p24 (51–59)	p24 (183–191)	DLNMMLNIV	HIV-1 infection, HIV-1 exposed seronegative	human (B14)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • Variants DLNMMLNIV/DLNTMLNVV are specific for clades A/B. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B14 women, 4/4 HEPS and 3/7 HIV-1 infected women recognized this epitope, likelihood ratio 4.8, p value 0.1, and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA. • The dominant response to this HLA allele was to this epitope for all 4/4 HEPS cases and in only one of the 3/7 HIV-1 infected women. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort. • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24.			
p24 (51–59)	p24	DLNMMLNIV	HIV-1 infection	human (B14)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.			
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (B14, Cw8)	Johnson1992, Nixon1988
	• Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–59)	p24	DLNTMLNTV	HIV-1 exposed seronegative	human (B14, Cw8)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is identical to the B clade epitope. • The D subtype consensus is dLNmMLNiV. • Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–59)	p24 (183–191 LAI)	DLNTMLNTV	HIV-1 infection	human (Cw8)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes – defined by B14 motif found within a larger peptide. • Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–59)	p24 (subtype B)	DLNTMLNTV	HIV-1 exposed seronegative	human (Cw8, B*1402)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among B and D clade viruses. • The Clade A version of the epitope, DLNNMLNIV, was preferentially recognized by CTL. • Recent evidence indicates this is a Cw8 epitope;B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24 (51–70)	p24 (183–202 SF2)	DLNTMLNTVGGHQAAMQMLK	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A26, A30, B38.				
p24 (51–82)	Gag (183–214 LAI)	DLNTMLNTVGGHQAAMQML-KETINEEAAEWDR	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 2/10 reacted to this peptide. • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual. • None of the 12 tested had an IgG response to this peptide.				
p24 (61–69)	Gag (p24) (61–69)	GHQAAMQML	HIV-1 infection	human (B*1510)	Frahm2004
p24 (61–69)	p24 (193–201 LAI)	GHQAAMQML		human (B*3901)	Frahm2004
	• C. Brander notes this is a B*3901 epitope.				
p24 (61–69)	Gag (193–201 IIIB)	GHQAAAMQML	HIV-1 infection	human (B38)	Kurane2003
	Assay type Chromium-release assay. • Three CD8+ CTL cell clones were derived from 2 HIV-1 positive asymptomatic patients, and their epitope specificities and HLA presenting proteins were defined.				
p24 (61–69)	p24 (193–201 LAI)	GHQAAMQML		human (B39)	Kurane1998
	• Optimal peptide defined by titration.				
p24 (61–71)	p24 (193–203 BRU)	GHQAAMQMLKE	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes first predicted, then shown to stimulate HLA-A2 restricted CTL line.				
p24 (61–80)	p24 (193–212 SF2)	GHQAAMQMKETINEEAAEW	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A26, A30, B38.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (61–82)	p24 (193–214 BH10)	GHQAAMQMLKETINEEAAE-WDR	HIV-1 infection	human (Bw52)	Johnson1991
	• Gag CTL response studied in three individuals.				
p24 (62–70)	p24 (194–202 LAI)	HQAAMQMLK		human (B52)	Brander1996b
	• P. Goulder, pers. comm.				
p24 (64–80)	p24 (63–80 HXB2)	AAMQMLKETINEEAAEW	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 22% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (65–72)	Gag (p24)	AMQMLKET	Vaccine	mouse (H-2d)	Bojak2002b
	Vaccine *Vector/Type:* DNA *HIV component:* Gag **Epitope name** A9I. **Assay type** Chromium-release assay. • Codon-optimized gag gene DNA vaccines were compared to wild type by vaccination of BALB/c mice. Codon optimized DNA gave a Th1 polarized Th response, a strong antibody response that persisted from more than 20 weeks, and CTL responses, while wild-type DNA induced weak and inconsistent immune respones.				
p24 (65–73)	Gag (199–207)	AMQMLKETI	Vaccine	mouse	Vajdy2001
	Vaccine *Vector/Type:* vaccinia, Sindbis *HIV component:* Gag **Keywords** genital and mucosal immunity. **Epitope name** p7g. **Assay type** CD8 T-cell Elispot - IFNγ. • Nasal, vaginal, rectal and i.m. immunization was performed with Sindbis virus expressing HIV-1 Gag (SIN-Gag), followed by intravaginal or intrarectal challenge with vaccinia virus expressing either Gag (VV-Gag) or gp160 (VV-gp160) as a control. • Intranasal and intramuscular immunization followed by intravaginal challenge induced HIV-1 Gag specific, IFN-γ producing CD8+ T cells in the vaginal/uteral mucosal tissue, as well as in the draining iliac lymph nodes and in the spleen, but could not protect against a VV-Gag infection of the ovaries. Local vaginal or rectal immunization, despite lower CD8+ T cells responses, did provide protection.				
p24 (65–73)	Gag (Du422)	AMQMLKDTI	Vaccine	mouse	vanHarmelen2003
	Vaccine *Vector/Type:* DNA *Strain:* C clade Du422 *HIV component:* Gag **Keywords** inter-clade comparisons, variant cross-recognition or cross-neutralization. **Assay type** Chromium-release assay.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA H-2d. • The pTHgagC DNA vaccine employed in this study expressed the gag gene derived from the South African isolate Du422, which was selected on the basis of being the natural strain most similar to the South African subtype C consensus sequence (aa distance of 1.8%). • A E7D mutation was introduced into the epitope to match the gag subtype C sequence in the vaccine. Mice vaccinated with the gag DNA made strong CTL responses against AMQMLKDTI, boosting enhanced the response, and memory cells persisted for 15 weeks.				
p24 (65–73)	Gag (p24) (197–205)	AMQMLKETI?	Vaccine	mouse	Yoshizawa2003
	Vaccine *Vector/Type:* protein *HIV component:* Gag *Adjuvant:* Cholera toxin (CT) **Keywords** TCR usage, genital and mucosal immunity. **Assay type** CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining, Chromium-release assay. **Donor HLA** H-2d. • Intranasal immunization triggered CTL response in the nasal-associated lymphoid tissue (NALT), posterior cervical lymph nodes (pCLNs) and the spleen, but not in the mesenteric lymph nodes (MLNs). Rectal immunzation elicited CTL responses only in the MLNs. By immunizing mice nasally following rectal immunization, CTL responses were detected in NALT, pCLNs, spleen and MLNs. Epitope-specific CD8+ T-cells were primarily located in NALT after 6 days and in pCLNs after 2 months. • The strongest specific lysis was induced by NALT-specific CTL clones. pCLNs derived memory CTL clones originated from NALT CTL clones, as determined by T cell receptor Vβ usage.				
p24 (65–73)	Gag (199–207 HXB2)	AMQMLKETI	Vaccine	mouse (H-2^d)	Qiu1999
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB2 *HIV component:* Gag • Different expression vectors were tested to increase Gag expression in cell lines and create suitable vectors for DNA vaccines. • Stable Gag expression was achieved in murine p815 cells, using a Gag gene that had mutated silent base positions that disrupt inhibitory RNA sequences which promote RNA degradation. • Silent mutations were more effective than introduction of the D retrovirus cis-acting posttranscriptional control element (CTE) for enhancing Gag expression. • The gag vector with silent mutations given as a vaccine to BALB/c mice gave CTL responses in splenic mononuclear cells, using peptide pulsed cells as targets.				
p24 (65–73)	p24 (199–207 SF2)	AMQMLKETI	Vaccine	mouse (H-2^d)	Neidleman2000
	Vaccine *Vector/Type:* protein, vaccinia *Strain:* B clade SF2 *HIV component:* Gag, Gag-Pol *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Epitope name** p7g. • Intranasal immunization of CB6F1 (H2bxd) mice with soluble gag p55 with LT ADP-ribosyltransferase mutants (LTK63 and LTK73) from Escherichia coli as adjuvants was tested. • Intranasal and intramucosal immunization of p55 gag protein with LTK63 or LTK72 adjuvant induced a CTL response comparable to intramuscular immunization responses. • Oral co-administration of LTR72, with residual ADP-ribosyltransferase activity, induced systemic CTL responses, but LTK63 with no ADP-ribosyltransferase activity did not.				
p24 (65–73)	p24 (66–74)	AMQMLKETI	Vaccine	mouse (H-2^d)	Marsac2002
	Vaccine *Vector/Type:* DNA *HIV component:* Gag *Adjuvant:* vesicular stomatitis virus glycoprotein (VSV-G) • BALB/c mice were injected with plasmids expressing HIV-1 Gag with or without coinjection of a plasmid expressing vesicular stomatitis virus glycoprotein (VSV-G). The combination encodes VSV-G pseudotyped Gag particles that can be taken up by cells for presentation in either the class I or class II pathways, while exogenous Gag alone can only be taken into the class II pathway.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Vaccination with DNA expressing VSV-G pseudotyped Gag particles rather than just Gag increase Gag-specific CTL responses generally as well as the specific H-2d restricted anti-AMQMLKETI response.				
p24 (65–73)	Gag (p24) (199–207 SF2)	AMQMLKETI	Vaccine	mouse (H-2^{kd})	O'Hagan2002
	Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* Gag *Adjuvant:* DDA, DOTAP, CpG immunostimulatory sequence (ISS), MF59, PLG, urea **Keywords** dendritic cells. **Epitope name** p7G. • Intramuscular or intraperitoneal immunization of BALB/c or CB6F1 mice with urea-solubilized, emulsified, or PLG-microparticle associated p55 Gag was studied in conjunction with the adjuvant CpG. CpG did not enhance CTL immunity when combined with urea solubilized p55, but did when combined with emulsions and PLG-microparticle antigen. • CpG shifted the Ab response towards a IgG2a, and CpG was shown to upregulate CD86 on mouse bone-marrow derived dendritic cells.				
p24 (65–73)	p24 (199–207 SF2)	AMQMLKETI	Vaccine	mouse (H-$2K^d$)	Doe1996
	Vaccine *Vector/Type:* vaccinia *HIV component:* Gag, Pol **Keywords** immunodominance. • Immunodominant murine CTL response to this peptide observed after immunization with vaccine VVgagpol. • Optimal peptide was defined.				
p24 (65–73)	Gag (197–205)	AMQMLKETI	Vaccine	mouse (H-$2K^d$)	Rayevskaya2001
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* Gag • BALB/c mice were immunized with a highly attenuated recombinant Listeria monocytogenes, Lmdaldat, that can grow only when supplemented with D-alanine, and that expresses HIV-1 HXB2 Gag. • Parenteral immunization provided protection against systemic and mucosal challenges with a recombinant vaccinia virus expressing HIV-1 gag, and a long lasting memory CTL response against Gag in spleen, mesenteric lymph nodes, and Peyer's patches directed against the gag protein. • Oral immunization gave protection only against mucosal virus challenge and was associated with a transient CTL response in the three lymphoid tissues examined. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.				
p24 (65–73)	Gag (197–205 SF2)	AMQMLKETI	Vaccine	mouse (H-$2K^d$)	Mata1998
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag **Keywords** immunodominance. • BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • This is the immunodominant CTL epitope in Gag in BALB/c mice. • AMQMLKETI does not contain established Kd anchoring residue in position 2, tyrosine or phenylalanine, thus deviating from the typical Kd anchoring motif – the lack of the aromatic anchor residue is compensated for by interaction of the glutamine at P3 with pocket D of Kd.				
p24 (65–73)	Gag (HXB2)	AMQMLKETI	Vaccine	mouse (H-$2K^d$)	Haglund2002a
	Vaccine *Vector/Type:* vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2, B clade IIIB *HIV component:* Env, Gag **Keywords** immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Different HIV strains were used for different regions: Env IIIB, Gag HXB2 • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag, Env, or both, and compared to using rec Env and Gag in vaccinia virus (rVVs). The primary response was determined by cell lysis, cytokine production and tetramer staining. • Primary CTL responses to the immunodominant Gag (AMQMLKETI) epitope peaked in 7 days for GAG-rVSV, 3% of the cells were tetramer positive, and this response was 8-fold higher than for Gag-rVV. • Vaccinating with GagEnv-rVSV carrying both Gag and Env allowed recognition of both HIV-1 proteins, but at reduced levels compared to either Gag-rVSV or Env-rVSV alone. • Intranasal immunization with Env-rVSV yielded CTL responses that were strong but reduced compared to an intraperitoneal route.				
p24 (65–73)	Gag (HXB2)	AMQMLKETI	Vaccine	mouse (H-2K^{d})	Haglund2002b
	Vaccine *Vector/Type:* vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2, B clade IIIB *HIV component:* Env, Gag **Keywords** immunodominance. • Different HIV strains were used for different regions: Env IIIB, Gag HXB2 • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag or Env, or both, and retention of memory responses and recall responses were studied by tetramer staining and IFN-gamma production. • Seven months after vaccination with Env-rVSV, 6% of the CD8+ cells were tetramer positive for the immunodominant Env epitope; these cells had a memory phenotype, CD44-Hi positive. • Env in rec vaccinia virus (Env-rVV) elicited a strong recall response, with up to 45% to the CD8+ T-cell population tetramer positive and activated (expressing CD62L-Lo), and capable of IFN-gamma production. • A prime with Env-rVSV and heterologous boost of Env-rVV gave remarkably high levels of memory cells, with approximately 1/3 of the CD8+ splenocytes being Env specific memory cells 150 days after the boost. • A Gag-rVSV or EnvGag-rVSV prime and with a heterologous Gag-rVV or EnvGag-rVV boost combination gave 40% tetramer positive CD8+ cells, but the fraction of IFN-gamma producing cells was only about 25%. Still the heterologous vector prime-boost combination showed a profound benefit. • A HIV-1 protein rVSV prime, rVV boost was a more potent combination than a vector reversal of a rVV prime and rVSV boost.				
p24 (65–73)	Gag	AMQMLKETI	Vaccine	mouse (H-2Kd)	Peters2003
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* Gag **Keywords** genital and mucosal immunity. **Assay type** Tetramer binding, Intracellular cytokine staining. **Donor HLA** H-2d. • Intravenous, rectal, and oral vaccination of recombinant L. monocytogenes expressing HIV-1 Gag antigen, were compared for their ability to stimulate a mucosal CTL response; mucosal administration of this vaccine gave strong mucosal response that was readily boosted. • This CTL epitope is the immunodominant epitope in Gag for BALB/c mice, and was used to characterize the vaccine responses.				
p24 (65–73)	Gag (197–205)	AMQMLKETI	Vaccine	mouse (H-2Kd)	Rayevskaya2003
	Vaccine *Vector/Type:* vaccinia, Listeria monocytogenes *HIV component:* Gag, Nef **Keywords** memory cells. **Assay type** cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay. **Donor HLA** H-2d. • Splenocytes derived from BALB/c mice immunized and boosted with Lmdd-gag were stimulated with gag-peptide specific antigen *in vitro*. In culture, CTL activity against this epitope reached a maximum at 9 days, then declined. Peptide restimulation gave a delayed (18 hours) but potent response, and growth was IL-2 or IL-15 dependent. Adoptive transfer of 5000 of the sorting purified cells could protect recipient BALB/c against vaccinia-gag challenge up to 3 months after transfer.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (69–86)	Gag (201–218 LAI)	LKETINEEAAEWDRVPV	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.				
p24 (70–78)		KETINEEAA	HIV-1 infection	human (B*4002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-KA9. **Donor HLA** A*0201 A*0217 B*0801 B*4002 Cw*0303 Cw*070. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized GELDRWEKI, p17(11-19), HLA B*4002, and TAFTIPSI, RT(128-135), HLA A*0217. • Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope.				
p24 (70–78)	p24 (70–78)	KETINEEAA	HIV-1 infection	human (B*4002)	Frahm2004
p24 (71–80)	p24 (203–212)	ETINEEAAEW	HIV-1 infection	human (A*2501)	Klenerman1996
	Keywords inter-clade comparisons. • The epitope was defined through direct stimulation of PBMC with 20-mer peptides. • It is in a conserved region, ETINEEAAEW is found in most B, D, and E subtype isolates. • DTINEEAAEW is found in A and some D subtype sequences.				
p24 (71–80)	p24 (203–212)	ETINEEAAEW	HIV-1 infection	human (A*2501)	Frahm2004
	• C. Brander notes this is an A*2501 epitope.				
p24 (71–80)	p24 (203–212)	ETINEEAAEW	HIV-1 infection	human (A*2501)	vanBaalen1996
	• Conserved between B and D subtypes, variable in other clades; a consensus of clades A, C, F, G, and H and a peptide of HIV-2ROD over this region were not recognized by CTL recognizing the index peptide. • C. Brander notes that this is an A*2501 epitope in the 1999 database.				
p24 (71–80)	p24	ETINEEAAEW		human (A25)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: EIINEEAAEW, no cross-reactivity [vanBaalen1996]				
p24 (71–80)	p24 (203–212 SF2)	ETINEEAAEW	HIV-1 infection	human (A25)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3.				
p24 (71–80)		DTINEEAAEW	HIV-1 infection	human (B*5301)	Sabbaj2002b
	Epitope name Gag-DW10. • Among HIV+ individuals who carried HLA B*5301, 2/15 (13%) recognized this epitope.				
p24 (71–80)		ETINEEAAEW	HIV-1 infection	human (B*5301)	Sabbaj2002b
	Epitope name Gag-EW10. • Among HIV+ individuals who carried HLA B*5301, 2/15 (13%) recognized this epitope.				
p24 (71–80)	p24 (203–212)	DTINEEAAEW	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B53 women, 0/2 HEPS and 7/9 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in 4 of the 7/9 responsive HIV-1 infected women.				
p24 (71–80)	p24 (203–212 subtype A consensus)	DTINEEAAEW	HIV-1 infection	human (B53)	Dorrell2001
	Keywords binding affinity, inter-clade comparisons, epitope processing. • In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays. • Two of the new epitopes lacked the predicted by P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35. • Two overlapping 20 mer peptides carry this complete epitope, but only one stimulates recognition, which could be due to different peptide processing. • DTINEEAAEW was recognized in only 2/7 HLA-B53 subjects. • DTINEEAAEW was not A subtype specific and there was cross-recognition although diminished, of the subtype B, C, and D variant, ETINEEAAEW. • In one of the two subjects there was cross-recognition of the HIV-2 version of the epitope, EIINEEAADW.				
p24 (71–90)	p24 (203–222 SF2)	ETINEEAAEWDRVHPVVHA-GP	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A2, B21.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (78–86)		AEWDRVHPV	HIV-1 infection	human (B*4002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-AV9. **Donor HLA** A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized TERQANFL, p2p7p1p6(64-71), HLA-B*4002, and KEKGGLEGL, Nef(92-100), HLA-B*4002. • Among HIV+ individuals who carried HLA B40, 4/5 (80%) recognized this epitope.				
p24 (78–86)	p24 (78–86)	AEWDRVHPV	HIV-1 infection	human (B*4002)	Frahm2004
p24 (83–92)	p24 (215–223 IIIB)	VHPVHAGPIA	HIV-1 infection	human (B55)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • LHPVHAGPVA, a variant found in HIV-1 PH136, was also recognized. • LHPVHAGPIA, a variant found in HIV-1 RF, was also recognized. • LHPVHAGPIT, a variant found in HIV-1 MN, was also recognized. • LHPAQAGPIA, a variant found in HIV-1 JH3, was recognized at high peptide concentrations.				
p24 (84–92)	p24 (84–92)	HPVHAGPIA	HIV-1 infection	human (B*07)	Frahm2004
p24 (84–92)	p24 (84–92)	HPVHAGPIA	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-HA9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection—10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.				
p24 (87–101)	Gag (219–233 LAI)	HAGPIAPGQMREPRG	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.				
p24 (87–101)	p24 (219–233 BRU)	HAGPIAPGQMREPRG	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes predicted then shown to stimulate HLA-A2 restricted CTL line.				
p24 (91–110)	p24 (223–242 SF2)	IAPGQMREPRGSDIAGTTST	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A2, A24, B13, B35.				
p24 (101–120)	p24 (233–252 SF2)	GSDIAGTTSTLQEQIGWMTN	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A26, A30, B38.				
p24 (107–115)	Gag (239–247 SF2)	TTSTLQEQI	Vaccine	mouse (H-2K^{d})	Mata1998
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag • BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.				
p24 (108–117)		TSTLQRQIGW	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls (ML1250)				
p24 (108–117)		TSTLQEQIGW	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW.				
p24 (108–117)		TSTLQEQIGW	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their immune response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.				
p24 (108–117)		TSTLQEQIGN	HIV-1 infection	human (B*5701)	Migueles2003
	Keywords rate of progression, escape. **Assay type** Intracellular cytokine staining, Flow cytometric CTL assay. • cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4). • In general use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (108–117)	p24 (241–250 LAI)	TSTVEEQQIW	HIV-2 infection	human (B*5801)	Frahm2004
	• C. Brander notes this is a B*5801 epitope.				
p24 (108–117)	p24 (240–249 LAI)	TSTLQEQIGW	HIV-1 infection	human (B*5801)	Frahm2004
	• C. Brander notes this is a B*5801 epitope.				
p24 (108–117)	p24 (233–252)	TSTLQEQIGW	HIV-1 infection	human (B57)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population. • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs. • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XSXXXXXXXW is a B57 binding motif, and CTL activity against TSTLQEQIGW has been found in two other B57 long-term non-progressors.				
p24 (108–117)	Gag (SF2)	TSTLQEQIGW	HIV-1 infection	human (B57)	Goulder2001a
	Keywords HAART, acute infection. **Epitope name** TW10. • Dominant epitope in acute infection in patient PI004, who did not receive any antiviral therapy. • 1-2 months post seroconversion, subject PI004 displayed a significant decrease in TW10 peptide recognition, followed by an increased CTL response against epitope SL9, SLYNTVATL and other epitopes. • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.				
p24 (108–117)	p24 (108–117)	TSTLQEQIGW	HIV-1 infection	human (B57)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** TST. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B57+				
p24 (108–117)	p24 (108–117)	TSTLQEQIGW	HIV-1 infection	human (B57)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (108–117)	p24	TSTLQEQIGW	HIV-1 infection	human (B57)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
p24 (108–117)	p24	TSTLQEQIGW	HIV-1 infection	human (B57)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** TST.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (108–117)	p24 (108–117)	TSTLQEQIGW	HIV-1 infection	human (B57, B58)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins, cross-presentation by different HLA. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A26, B35, B57, Cw4, Cw0601; A1, A30, B42, B52, Cw7, Cw17; A1, A*0201, B44, B57, Cw5, Cw6. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • This epitope was recognized in three of the acutely infected individuals and was presented by both HLA-B57 and B58. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				
p24 (108–117)	p24 (235–243)	TSTLQEQIGW	HIV-1 infection, HIV-1 exposed seronegative	human (B57, B58)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • TSTLQEQIGW cross reacts with both for the A and B clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p24 (108–117)	p24 (241–250)	TSTVEEQQIW	HIV-2 infection	human (B58)	Bertoletti1998a
	• HIV-2 epitope defined from an infection in Gambia, Bertoletti, pers. comm. • All HIV-2 sequences from the database are TSTVEEQIQW in this region, not TSTVEEQQW as in the paper.				
p24 (108–117)	p24	TSTLQEQIGW	HIV-1 exposed seronegative	human (B58)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: TSTVEEQIQW, CTL are cross-reactive, [Bertoletti1998b]				
p24 (108–117)	p24 (240–249)	TSTLQEQIGW	HIV-2 infection	human (B58)	Bertoletti1998b
	Keywords inter-clade comparisons, rate of progression, immunodominance. • CTL responses in HLA-B*5801 positive HIV-2 infected individuals have a dominant response to Gag and tolerate extensive substitution, thus HLA-B*5801+ individuals may have an enhanced potential for cross-protection between HIV-1 and HIV-2. • This can be an immunodominant epitope in HLA-B57 and B*5801 infected individuals, and is associated with long-term non-progression [Goulder1996b]				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-2 sequence: HIV-2 ROD has the epitope sequence TSTVEEQIQW, and the CTL from a person infected with HIV-2 was cross-reactive with HIV-1 epitopes. • The epitope is TSTLQEQIGW in HIV-1 B clade, and TSTVEEQIQW in HIV-2 ROD. • HLA B*5801 and B35 may preferentially select HIV-1 and HIV-2 cross-reactive epitopes.				
p24 (108–117)	p24 (240–249 SF2)	TSTLQEQIGW	HIV-1 infection	human (B58)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B58+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3.				
p24 (108–117)	p24 (108–117)	TSTLQEQIGW	HIV-1 infection	human (B58)	Goulder2001c
	Keywords acute infection. **Epitope name** TW10. • Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection. • Mutations in this epitope were observed in autologous clones of subjects who were B58-positive with a higher frequency than those who were B58-negative (P = 0.02) • These mutations are being sexually transmitted in adult infections.				
p24 (108–118)	p24 (240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human (B*57, B*5801)	Goulder1996b
	Keywords rate of progression. • Response to this epitope was found in 4 slow progressing HLA-B*57 individuals, in 2 it was dominant or very strong. • For one donor (from Zimbabwe) this was defined as the optimal peptide. • This epitope can be presented in the context of the closely related HLA molecules B*5801 and B*57.				
p24 (108–118)	p24 (240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human (B*5701)	Frahm2004
	• C. Brander notes this is a B*5701 epitope.				
p24 (108–118)		TSTLQEQIGWF	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Gag-TF11. • Among HIV+ individuals who carried HLA B57, 2/5 (40%) recognized this epitope.				
p24 (109–117)	Gag (241–249 LAI)	STLQEQIGW	HIV-1 infection	human (B*5701 B*5801)	Klein1998
	Keywords rate of progression. • B57 has been associated with long-term non-progression in the Amsterdam cohort. • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag.				
p24 (109–117)		STLQEQIGW	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Gag-SW9. • Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B58, 1/4 (25%) recognized this epitope.				
p24 (110–118)	Gag (242–)	TLQEQIGWM	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag242. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.				
p24 (118–126)	Gag (282–290)	MTNNPPIPV	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
p24 (121–135)	p24 (121–135 HXB2)	NPPIPVGEIYKRWII	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (121–135)	p24 (253–267)	NPPIPVGEIYKRWII	HIV-1 infection	human (B8)	Gotch1990
	• High frequency of memory and effector Gag-specific CTL.				
p24 (121–135)	p24 (255–274 SF2)	NPPIPVGEIYKRWII	HIV-1 infection	human (B8)	Goulder1997a, Phillips1991
	Keywords review, immunodominance, escape. • Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.				
p24 (121–135)	p24 (121–135)	NPPIPVGEIYKRWII	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (121–140)	p24 (253–272)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
p24 (121–140)	p24 (253–272 SF2)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • Two of these 12 had CTL response to this peptide. • The responding subjects were HLA-A2, A3, B8, B62, and HLA-A1, B8, B18.				
p24 (121–140)	p24 (253–272 SF2)	NPPIPGEIKRWIILGNIK	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
p24 (121–140)	p24 (255–274 SF2)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human	vanBaalen1993
	• Gag CTL epitope precursor frequencies were estimated and peptide mapping was performed.				
p24 (121–142)	p24 (253–274 BH10)	NPPIPVGEIYKRWIILGLN-KIV	HIV-1 infection	human (B8)	Johnson1991
	• Gag CTL response studied in three individuals.				
p24 (121–152)	Gag (183–214 LAI)	NPPIPVGEIYKRWIILGLN-KIVRMYSPTSILD	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 9/10 reacted to this peptide. • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees. • All of the 12 tested had an IgG response to this peptide.				
p24 (121–152)	Gag	NPPIPVGEIYKRWIILGLN-KIVRMYSPTSILD	HIV-1 infection, Vaccine	human (A*0201)	Seth2000
	Vaccine *Vector/Type:* lipopeptide *HIV component:* Gag • Immunization of 2/4 HIV seropositive HLA selected individuals with a 32 amino acid Gag lipopeptide that contains CTL epitopes restricted by HLA A33, B8, B27, B35, and Bw62 gave a transient increase in peptide-specific bulk CTL response, but they did not decrease plasma viral load. • Placebo and HLA mis-matched controls showed no change in CTL. • The responders carried HLA Bw62 and B35 – the two HLA-matched that did not respond carried B35 and B8.				
p24 (122–130)	p24	PPIPVGDIH	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls, ML887.				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	HIV-1 or HIV-2 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
p24 (122–130)	p24 (245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human (B*3501)	Rowland-Jones1995b
p24 (122–130)	p24 (245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	HIV-1 or HIV-2 infection	human (B35)	Rowland-Jones1995b
	• Defined as minimal peptide by titration curve, PPIPVGEIY and HIV-2 form NPVPVGNIY are also recognized.				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	in vitro stimulation or selectio	human (B35)	Lalvani1997
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers. • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.				
p24 (122–130)	p24 (260–268 LAI)	PPIPVGDIY	HIV-1 infection	human (B35)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes.				
p24 (122–130)	p24 (subtype B)	PPIPVGEIY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among B and D clade viruses. • The Clade A version of the epitope, PPIPVGDIY, was preferentially recognized by CTL.				
p24 (122–130)		PPIPVGEIY	HIV-1 infection	human (B35)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers—high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.				
p24 (122–130)	p24	PPIPVGDIY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 version of this epitope is not conserved: NPVPVGNIY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				
p24 (122–130)	p24 (260–268)	PPIPVGDIY	HIV-1 infection	human (B35)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** PPI. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • One of two HLA B35+ among the eight study subjects recognized this epitope. • Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment.				
p24 (122–130)	p24 (122–130)	PPIPVGDIY	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (122–130)	p24 (254–262 SF2)	PPIPVGDIY	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3.				
p24 (122–130)	p24 (260–268)	PPIPVGDIY	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B35 women, 1/3 HEPS and 3/4 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in the 1/3 HEPS case and in the all 3/4 responsive HIV-1 infected women. • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion.				
p24 (122–130)		PPIPVGDIY	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Gag-PY9. • Among HIV+ individuals who carried HLA B35, 2/21 (10%) recognized this epitope. • Among HIV+ individuals who carried HLA B*5301, 0/11 (0%) recognized this epitope.				
p24 (122–130)	p24	PPIPVGEIY	HIV-1 infection, Vaccine	human (B35)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (124–138)	p24 (256–270 LAI)	IPVGEIYKRWIILGL	HIV-1 infection	human (B8)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.				
p24 (124–138)	Gag (256–270 LAI)	IPVEGEIYKRWIILGL	HIV-1 infection	human (B8)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Two children, EM16 (CDC P2A+D2) and EM18 (CDC P2A), had a CTL response to this epitope, and it was shown to be presented by B8 in EM18.				
p24 (126–140)	p24 (126–140 HXB2)	VGEIYKRWIIGLNK	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (127–135)	p24 (259–267 SF2)	GDIYKRWII	HIV-1 infection	human (B*0801)	McAdam1998
	• GDIYKRWII specific CTL clone also recognized GEIYKRWII.				
p24 (127–135)	p24 (261–269)	GEIYKRWII	HIV-1 infection	human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide NPPIPVGEIYKRWII.				
p24 (127–135)	p24 (259–267)	GEIYKRWII	in vitro stimulation or selectio	human (B8)	Zarling1999
	Keywords dendritic cells. • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses. • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA. • A weak response to KLTPLCVSL was stimulated using macrophages as the APC. • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.				
p24 (127–135)	p24 (259–267 LAI)	GEIYKRWII	HIV-1 infection	human (B8)	Klenerman1994
	• Naturally occurring variant GDIYKRWII may act as antagonist.				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others.				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	Nowak1995
	Keywords dynamics, escape. • Longitudinal study of CTL response and study of immune escape – GDIYKRWII could also stimulate CTL, reactivity fluctuated.				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	McAdam1995
	• Equivalent sequence GDIYKRWII also recognized by CTL from some donors.				
p24 (127–135)	p24 (259–267)	GEIYKRWII	HIV-1 infection	human (B8)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, escape, acute infection. **Epitope name** GEI. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Six of the 7/8 study subjects that were HLA B8 recognized this epitope. • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones. • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQ-GYFPDWQNY, and GEIYKRWII and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent. • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197. • Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088. • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy. • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy.			
p24 (127–135)	p24 (259–267 SF2)	GEIYKRWII	HIV-1 infection	human (B8)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 2/3 group 1, 2/3 group 2, and 2/2 group 3.				
p24 (127–135)	p24	GEIYKRWII	HIV-1 infection	human (B8)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** GEI. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (127–135)	p24	GEIYKRWII	HIV-1 infection, Vaccine	human (B8)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (127–136)		GEIYKRWIIL	HIV-1 infection	human (B*0801)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-GL10. **Donor HLA** A*0101 A*0301 B*0801 B*5802 Cw*0602 Cw*0701. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 00RCH87 was not on HAART, viral load 8300, CD4 count 313. • Among HIV+ individuals who carried HLA B08, 3/6 (50%) recognized this epitope.				
p24 (128–135)	p24 (260–267 LAI)	EIYKRWII		human (B*0801)	Frahm2004
	• C. Brander notes this is a B*0801 epitope.				
p24 (128–135)	p24 (260–267 LAI)	EIYKRWII		human (B8)	Goulder1997g
	• Defined in a study of the B8 binding motif.				
p24 (128–135)	p24 (SF2)	EIYKRWII	HIV-1 infection	human (B8)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (128–135)	p24 (C consensus)	DIYKRWII	HIV-1 infection	human (B8)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ South African – this epitope did not fall within the five most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (128–135)	p24 (SF2)	EIYKRWII	HIV-1 infection	human (B8)	Goulder2001a
	Epitope name EI8. • This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Three CTL responses to epitopes, TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.				
p24 (128–135)	p24	EIYKRWII	HIV-1 infection	human (B8)	Kostense2001
	Keywords rate of progression. • HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load. • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional. • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival. • 4/13 patients that reacted with EIYKRWII displayed epitope mutations in a minority of sequences, which did not correlate with disease progression or viral load – these mutations were: Patient 156 (KIYKRWMI), Patient 36 (EIYKRRII), Patient 656 (KIYKRWII, EIYERWMI), and Patient 159 (EIYKRWVI). • Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113) • There were more functional IFN-gamma producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells.			
p24 (128–135)	p24 (259–267)	DIYKRWII	HIV-1 infection	human (B8)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p24 (128–135)	p24 (128–135)	EIYKRWII	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
p24 (128–135)	Gag	EIYKRWII	HIV-1 infection	human (B8)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.				
p24 (128–135)	p24	DIYKRWII	HIV-1 infection	human (B8)	Appay2002
	Keywords HAART. **Donor HLA** A2,A11,B8,B60,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
p24 (128–135)	Gag (260–267 IIIB)	EIYKRWII	HIV-1 infection	human (B8)	Kurane2003
	Assay type Chromium-release assay. • Three CD8+ CTL cell clones were derived from 2 HIV-1 positive asymptomatic patients, and their epitope specificities and HLA presenting proteins were defined.				
p24 (129–136)	p24 (263–270 SF2)	IYKRWIIL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide induced CTL in 1/4 HIV-1+ people tested. • IYKRWIIL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
p24 (129–138)	p24 (263–272 SF2)	IYKRWIILGL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • IYKRWIILGL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
p24 (129–138)	p24 (263–272)	IYKRWIILGL	HIV-1 infection	human (B27)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was B27 and responded to IYKRWIILGL.				
p24 (129–148)	Gag (261–280)	IYKLWIILGLNKIVRMYSPT	HIV-1 infection	human (B27, B62)	Musey2003
	Keywords genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A3, A31, B27, B38; A24, B27, B62. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood and rectum of one individual, and blood and semen of another. Both individuals are HLA-B27 positive, and within the peptide there is a B27 epitope that was recognied in the blood and rectum of the first patient, and in the blood of the second. A HLA-B62 epitope is also recognized in this peptide in the second individual, and the CD8+ T cells clones from both the blood and semen recognized this epitope.				
p24 (130–148)	p24 (265–280 BRU)	YKRWIILGLNKIVRMYSPT	HIV-1 infection	human (B27)	Dadaglio1991
	• Used as a positive control for HLA specificity.				
p24 (131–139)	Gag (265–273)	KRWIILGLN	HIV-1 infection	chimpanzee (Patr-B*03)	Balla-Jhagjhoorsingh1999b
	• Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57. • Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS. • CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57. • The human HLA protein which presents this Patr-B*03 epitope is HLA B*2705 but the amino acid sequences in the binding pockets of HLA-B*2705 and Patr-B*03 are distinctive.				
p24 (131–140)	Gag (263–272 LAI)	KRWILLGLNK	HIV-1 infection	human	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.				
p24 (131–140)	p24 (263–272)	KRWIILLGLNK	HIV-1 infection	human (B*27)	Huang2000
	Keywords HAART. • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed. • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT. • In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both gamma IFN production and T cell lysis was to the B27 epitope, KRWIILLGLNK, not the A2 SLYNTVATL epitope.				
p24 (131–140)	p24 (263–272 SF2)	KRWIILGLNK	HIV-1 infection	human (B*27)	McAdam1998
	• Epitope invariant across clades A, B, C, and D.				
p24 (131–140)	p24 (260–269 HIV-2)	RRWIQLGLQK		human (B*2703)	Frahm2004
	• C. Brander notes this is a B*2703 epitope.				
p24 (131–140)	p24	KRWIILGGLNK	HIV-1 infection	human (B*2705)	Wilson2000a
	Keywords dynamics, acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • Tetramers with peptide variants KRWIILGGLNK and KRWIIMGGLNK were used – CTL from most B27 donors recognize both variants, although one of the three subjects recognized only KRWIILGGLNK. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B*2705)	Frahm2004
	• C. Brander notes this is a B*2705 epitope.				
p24 (131–140)	p24 (263–272)	KRWIILGLNK	HIV-1 infection	human (B*2705)	Kelleher2001b
	Keywords escape. • A mutation in 4/5 B*2705 patients had substitution to lysine (K) at HIV-1 gag residue 264 (R264K), in three the change occurred late in infection – in one patient a substitution of glycine at HIV-1 gag residue 264 (R264G) was detected – these substitutions reduce binding to B27. • The R264K mutations were associated with a L268M mutation that may be compensatory, and R264G occurred in conjunction with E260D. • Positions 260, 264, and 268 all lie along one aspect of helix seven of the capsid protein, a region that is important for capsid self-association and assembly. • R264G and R264K escape mutation outgrowth occurred in conjunction with high viral loads.				
p24 (131–140)	p24 (263–272)	KRWIIMGLNK	HIV-1 infection	human (B*2705)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
p24 (131–140)	p24	KRWIILLGLNK	HIV-1 infection, Vaccine	human (B*2705)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag				
	Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.				
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B*2705, B27)	Goulder1997c, Goulder1997a
	Keywords review, rate of progression, immunodominance, escape.				
	• HLA-B*2705 is associated with slow HIV disease progression.				
	• 11/11 HLA-B*2705 donors make a response to this epitope, usually an immunodominant response.				
	• This is a highly conserved epitope.				
	• The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position.				
	• [Goulder1997a] is a review on CTL immune escape that discusses this epitope in the context of the difficulty in detection of immune escape – KRWIILGLNK and an R2K change, KKWIILGLNK, show little difference in titration curves, yet the K2 variants fail to bind to targets for more than 1 hour, while the R2 form can sensitize lysis by CTL for over 24 hours – minigene transfection experiments confirmed the importance of this for the CTL response.				
p24 (131–140)	p24 (260–269 HIV-2)	RRWIQLGLQK		human (B27)	Brander1996b
	• HIV-2, HLA-B*2703, S. Rowland-Jones, pers. comm.				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B27)	Fan1997
	Keywords dendritic cells.				
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied.				
p24 (131–140)	Gag (263–272)	KRWIILGLNK	HIV-1 infection	human (B27)	Zheng1999
	Keywords epitope processing, dendritic cells.				
	• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone.				
	• Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway.				
	• The CTL response to p24 was measured in individuals with a response to B27-KRWIILGLNK.				
p24 (131–140)	p24 (263–272 LAI)	KRWIILGLNK	HIV-1 infection	human (B27)	Wilson1998a
	Keywords dynamics, TCR usage.				
	• HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo*.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls. • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases.				
p24 (131–140)	p24 **Keywords** review. • Described in this review as the first identified HIV CTL epitope.	KRWIILGLNK	HIV-1 infection	human (B27)	Rowland-Jones1997
p24 (131–140)	p24 (263–272 LAI) • Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.	KRWIILGLNK	HIV-1 infection	human (B27)	Buseyne1993b
p24 (131–140)	p24 (263–272 LAI) **Keywords** review. • Review of HIV CTL epitopes.	KRWIILGLNK	HIV-1 infection	human (B27)	McMichael1994
p24 (131–140)	p24 (263–272) • Naturally occurring variant KRWIILGLNK may act as antagonist.	KRWIIMGLNK	HIV-1 infection	human (B27)	Klenerman1994
p24 (131–140)	p24 (263–272) • Naturally occurring variant KRWIILGLNK may act as antagonist.	KRWIIMGLNK	HIV-1 infection	human (B27)	Klenerman1995
p24 (131–140)	p24 (265–274) **Keywords** dynamics, TCR usage. • In one individual, TCR usage changed over time indicating that new populations of CTL can be recruited. • TCR usage showed a CTL clonal response to this epitope that persisted over 5 years. • CTL clones specific for HIV epitopes may represent between 0.2 and 1% of the total CD8+ population of T cells.	KRWIILGLNK	HIV-1 infection	human (B27)	Moss1995
p24 (131–140)	p24 (265–276) • Included in HLA-B27 binding peptide competition study.	KRWIILGLNK		human (B27)	Carreno1992
p24 (131–140)	p24 (265–274 SF2) **Keywords** dynamics, review, immunodominance, escape. • Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to B8 epitope. • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.	KRWIILGLNK	HIV-1 infection	human (B27)	Goulder1997a, Phillips1991
p24 (131–140)	p24 (263–272) **Keywords** review, escape. • Single point mutations were introduced and viral viability and CTL recognition tested – an Arg to Lys change at anchor position P2 abrogates binding to B27, but doesn't change viral viability *in vitro*. • [Goulder1997a] is a review of immune escape that summarizes this study.	KRWIILGLNK	HIV-1 infection	human (B27)	Goulder1997a, Nietfeld1995
p24 (131–140)	p24 (263–272) **Keywords** escape. • Longitudinal study of CTL response and immune escape – the form KRWIILGNK was also found, and both forms stimulate CTL.	KRWIIMGNK	HIV-1 infection	human (B27)	Nowak1995
p24 (131–140)	p24 (263–272) **Keywords** inter-clade comparisons.	KRWIILGNK	HIV-1 infection	human (B27)	Durali1998

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia. • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested. • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag. • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef. • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env. • One of the patients was shown to react to this epitope: KRWIILGNK.				
p24 (131–140)	p24 (263–272)	KRWIIMGLNK	HIV-1 infection	human (B27)	Goulder1997f, Goulder1997a
	Keywords review, immunodominance, escape. • Six HLA-B27 donors studied make a strong response to this epitope. • In 4/6 cases, this was the immunodominant or only CTL response. • Two of the cases had an epitope switch to the form KKWIIMGLNK during a period of rapid decline to AIDS, following their asymptomatic period. • The arginine to lysine switch is in an anchor residue, and results in immune escape due to severely diminished binding to the B27 molecule. • [Goulder1997a] is a review of immune escape that summarizes this study in the context of CTL escape to fixation.				
p24 (131–140)	p24	KRWIILGLNK		human (B27)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: RRWIQLGLQK – this epitope was not HIV-1 and HIV-2 cross-reactive.				
p24 (131–140)	Gag (263–)	KRWILGLNK	computer prediction	(B27)	Schafer1998
	Keywords inter-clade comparisons. • This study uses EpiMatrix for T cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV. • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule. • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV. • This peptide sequence is not conserved between clades, but is found in most B clade isolates.				
p24 (131–140)	p24 (263–282)	KRWIILGLNK	HIV-1 infection	human (B27)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population. • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs. • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XRXXXXXXXK is a B*2705 binding motif.				
p24 (131–140)	p24 (265–274 SF2)	KRWIILGLNK	HIV-1 infection	human (B27)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3.				
p24 (131–140)	p24 (263–272)	KRWIILGLNK	HIV-1 infection, HIV-1 exposed seronegative	human (B27)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion.				
p24 (131–140)	p24 (131–140)	KRWIILGLNK	HIV-1 infection	human (B27)	Day2001
p24 (131–140)	p24 (260–299)	RRWIQLGLQK	HIV-1 infection	human (B27)	Day2001
p24 (131–140)	p24 (131–140)	KRWIILGLNK	HIV-1 infection	human (B27)	Goulder2001b
	Keywords responses in children, mother-to-infant transmission, immunodominance, escape, acute infection. **Epitope name** KK10. • 85% of B27+ adults have CTL that recognize this epitope, but only 2/6 children did. • Responses to this dominant B27-restricted Gag epitope are present during the time of decreasing viral load in acute infection. • Three children who shared B27 with their mothers did not respond to this epitope and inherited escape mutations from their mothers. • A transmitted R132T anchor residue mutation abrogated binding to B27. • In the three children infected with the non-binding KK10 variants, the dominant CTL specificity was still HLA-B27-restricted, but it was directed against an epitope in p17, IRLRPGGKK, only rarely recognized in adults when KRWIILGLNK is the dominant response. • Mutations in this epitope were observed in autologous clones of subjects who were B27-positive with a higher frequency than those who were B27-negative (P = 0.0005) • These mutations are being sexually transmitted in adult infections.				
p24 (131–140)		KRWIILGLNK	HIV-1 infection	human (B27)	Sabbaj2002b
	Epitope name Gag-KK10. • Among HIV+ individuals who carried HLA B27, 2/3 (66%) recognized this epitope.				
p24 (131–140)	p24 (263–272 LAI)	KRWIIMGLNK	HIV-1 infection	human (B27)	Kelleher2001a
	Keywords HAART, epitope processing, immunodominance. • Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context. • RTV did not reduce antigen presentation and concentration of the two immunodominant Gag CTL epitopes (KRWIIMGLNK (B27) and SLYNTVATL (A2)).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
p24 (131–140)	p24	KRWIILGLNK	HIV-1 infection	human (B27)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** B27-KK10(p24). **Donor HLA** A24,A?,B7,B27; A30,A32,B18,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef). Patient D also displayed the greatest response to B27-KK10(p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
p24 (131–140)	Gag (263–272)	KRWIILGLNK	HIV-1 infection	human (B27)	Currier2002a
	Keywords inter-clade comparisons. **Donor HLA** B27. • Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades. • Subject AIHP-6 (Thai, CDF01-AE infected) recognized this epitope. This subject showed cross-subtype CTL responses to gag constructs derived from subtypes A, B, C, D, F, G, and H, and this epitope was perfectly preserved in all of these but subtype A which had the sequence KRWMILGLNK. • This subject didn't respond to a Gag CRF01 sequence which had a R->K mutation in position 2.				
p24 (131–142)	p24 (265–276)	KRWIILGLNKIV	Peptide-HLA interaction	human (B27)	Jardetzky1991
	• Epitope examined in the context of peptide binding to HLA-B27.				
p24 (131–142)	p24 (263–274 LAI)	KRWIILGLNKIV	HIV-1 infection	human (B27)	Fan1997
	Keywords dendritic cells. • The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied.				
p24 (131–142)	p24 (131–142)	KRWIILGLNKIV	HIV-1 infection	human (B27)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (131–145)	p24 (SF2)	KRWILGLNKIVRMY	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston with unknown HLA – this epitope did not fall within the three most recognized peptides in the study.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (131–145)	p24 (131–145 HXB2)	KRWIILGLNKIVRMY	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** CD8 T-cell Elispot - IFNγ. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (131–145)	p24 (263–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human (A33)	Buseyne1993b
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people.				
p24 (131–145)	p24 (266–277)	KRWIILGLNKIVRMY	Vaccine	human (B27)	Nixon1988
	Vaccine *Vector/Type:* vaccinia *HIV component:* Gag • Gag CTL epitope mapped with rec gag-vaccinia and synthetic peptides. • This was the first HIV-1 epitope to be mapped.				
p24 (131–145)	p24 (266–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human (B27)	Meyerhans1991
	• Longitudinal study showing persistence of epitope despite CTL activity.				
p24 (131–145)	p24 (265–279)	KRWIILGLNKIVRMY	HIV-1 infection	human (B27)	Nixon1990, Rowland-Jones1999
	• HIV-1 and HIV-2 cross-reactive CTL clone, highly conserved epitope. • Reviewed in Rowland-Jones99, notes that it did not appear cross-reactive with HIV-2 in Rowland-Jones98, HIV-2 form: RRWIQLGLQK.				
p24 (131–146)	p24 (265–279)	KRWIILGLNKIVRMYC	HIV-1 infection	human (B27)	Bouillot1989
	• HLA-B27 restricted epitope also binds to HLA-A2 and HLA-B37 in solid phase assay.				
p24 (131–150)	p24 (263–282 SF2)	KRWIILGLNKIVRMYSPTSI	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 A-2 had CTL response to this peptide. • The responding subject was HLA-A3, A32, B51, B62.				
p24 (131–150)	p24 (265–284 SF2)	KRWIILGLNKIVRMYSPTSI	HIV-1 infection	human (Bw62?)	vanBaalen1993
	• Gag CTL epitope precursor frequencies estimated.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (131–152)	p24 (263–284 BH10)	KRWIILGLNKIVRMYSPTS-ILD	HIV-1 infection	human (Bw62)	Johnson1991
	• Gag CTL response studied in three individuals.				
p24 (132–140)	Gag (261–280)	RWIILGLNK	HIV-1 infection	human (B27)	Musey2003
	Keywords genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A24, A33, B14, B27; A2, A32, B27, B62. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones that recognize this epitope were derived from both blood and cervix from a woman, and the blood and semen from a man.				
p24 (132–145)	Gag	KWILGLNKIVRMY	HIV-1 infection	human	Weekes1999a
	• Peptide 728: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.				
p24 (132–145)	Gag	KWILGLNKIVRMY	HIV-1 infection	human (B27)	Weekes1999b
	Keywords TCR usage. • Peptide 728: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population. • HIV CTL responses to 3 Env and 2 Gag peptides were studied. • The clonal composition of the TCR Vβ responses were studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ22.1.				
p24 (134–143)	p24 (subtype B)	IILGLNKIVR	HIV-1 exposed seronegative	human (A33)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B and D clade viruses.				
p24 (136–145)	p24 (268–277 LAI)	LGLNKIVRMY	HIV-1 infection	human (Bw62)	McMichael1994
	Keywords review. • Predicted from larger peptide. • Review of HIV CTL epitopes. • Also P. Johnson, pers. comm.				
p24 (136–146)	p24 (271–281)	LGLNKIVRMYS	HIV-1 infection	human (B62)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response. • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response. • A subject who was B62+ had CTL that recognized this peptide, p17 KIRLRPGGKKKYKL, and one additional unknown epitope. • The two clones that recognized this epitope used two different Vβ genes, further demonstrating a polyclonal response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (136–146)	p24 (136–146)	LGLNKIVRMYS	HIV-1 infection	human (B62)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (136–150)	p24 (136–150 HXB2)	LGLNKIVRMYSPTSI	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized—the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (137–145)	p24 (C consensus)	GLNKIVRMY	HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ South African living in Durban, HLA A2/- B5802/62 Cw4/6 – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (137–145)	p24 (272–280 LAI)	GLNKIVRMY	HIV-1 infection	human (B*1501)	Frahm2004
	• C. Brander notes this is a B*1501 epitope.				
p24 (137–145)	p24 (272–280 LAI)	GLNKIVRMY	HIV-1 infection	human (B62)	Goulder1997a
	Keywords review, escape. • This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY. • As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form.				
p24 (137–145)	p24 (SF2)	GLNKIVRMY	HIV-1 infection	human (B62)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ African American living in Boston – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (137–145)	p24 (267–277 SF2)	GLNKIVRMY	HIV-1 infection	human (B62)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B62+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/1 group 2, and 1/1 group 3.				
p24 (137–145)	p24 (137–145)	GLNKIVRMY	HIV-1 infection	human (B62)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to four B62-restricted epitopes tested.				
p24 (137–145)	p24 (137–145)	GLNKIVRMY	HIV-1 infection	human (B62)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A3, B8, B62, Cw3, Cw7. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
p24 (137–145)	Gag (269–277)	GLNKIVRMY	HIV-1 infection	human (B62)	Musey2003
	Keywords genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A2, A24, B27, B62. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood, rectum and semen.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The TCRbeta VDJ rearrangement of the CTL clones was Vβ22S1DJ1.2, demonstrating expansion of CTL clones in all three compartments from the same progenitor cell.				
p24 (143–150)	p24 (273–283 IIIB)	RMYSPTSI	HIV-1 infection	human (B*5201)	Frahm2004
	• C. Brander notes this is a B*5201 epitope.				
p24 (143–150)	p24 (273–283 IIIB)	RMYSPTSI	HIV-1 infection	human (B52)	Brander1999
	Keywords epitope processing, immunodominance, escape. **Epitope name** SL9. • Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope. • The CTL response to RMYSPTSI was used as a control.				
p24 (143–150)	p24 (273–283 IIIB)	RMYSPTSI	HIV-1 infection	human (B52)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope.				
p24 (143–150)	p24 (143–150)	RMYSPTSI	HIV-1 infection	human (B52)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (151–170)	p24 (283–302 SF2)	LDIRQGPKEPFRDYVDRFYK	HIV-1 infection	human	McAdam1998
p24 (155–177)	p24 (287–309)	QGPKEPFRDYVDRFYKTLR-AEQA	Vaccine	mouse	Nakamura1997
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag • Mice immunized with this synthetic peptide generated specific CTLs, a proliferative response, and antibodies. • The amino acids shown in the epitope field were based on the numbering provided by Nakamura *et al.*, and may not be correct. • The CTL epitope was shown to be located in positions 291-300.				
p24 (157–178)	p24 (290–309)	PKEPFRDYVDRFYKTLRAE-QAS	HIV-1 infection	human (B14)	Musey1997
	• Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope.				
p24 (159–168)	Gag (291–300)	EPFRDYVDRF	Vaccine	mouse (H-2^{d})	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18 **Keywords** Th1. • DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization. • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost. • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.				
p24 (159–168)	Gag (p24)	EPFRDYVDRF	Vaccine	mouse (H-2d)	Bojak2002b
	Vaccine *Vector/Type:* DNA *HIV component:* Gag **Epitope name** E10F. **Assay type** Chromium-release assay. • Codon-optimized gag gene DNA vaccines were compared to wild type by vaccination of BALB/c mice. Codon optimized DNA gave a Th1 polarized Th response, a strong antibody response that persisted from more than 20 weeks, and CTL responses, while wild-type DNA induced weak and inconsistent immune respones.				
p24 (159–178)	Gag (291–310)	EPFRDYVDRFFKTLRAEQAT	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (159–178)	Gag (96ZM651.8)	EPFRDYVDRFFKTLRAEQAT		human (B*44031)	Novitsky2001
	Keywords inter-clade comparisons, immunodominance. • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 16 of 46 (34.8%) had CTL responses to one or more peptides within the second immunodominant region region of Gag (peptides SILDIKQGPKEPFRDYV-DRF, EPFRDYVDRFFKTLRAEQAT, and FKTLRAEQATQEVKNWMTDT) with ELISPOT results median and range 500 (100 to 1,250) SFC/10^6 PBMC. • 3 of 6 (50%) carriers of HLA-B*44031 showed CTL responses to the peptide EPFRDYVDRFFKTLRAEQAT.				
p24 (161–170)		FRDYVDRFFK	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls, ML1732.				
p24 (161–170)	p24 (subtype B, D)	FRDYVDRFYK	HIV-1 infection	human (B*1801)	Ogg1998a
	• Noted in Brander 1999, this database, to be B*1801, FRDYVDRFY.				
p24 (161–170)	p24 (subtype B, D)	FRDYVDRFYK	HIV-1 infection	human (B*1801)	Frahm2004
	• C. Brander notes this is a B*1801 epitope.				
p24 (161–170)	p24 (161–170)	FRDYVDRFYK	HIV-1 infection	human (B18)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (161–170)	p24 (293–302)	FRDYVDRFYK	HIV-1 infection, HIV-1 exposed seronegative	human (B18)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Variants FRDYVDRF(Y/F)K are specific for the B,D/A,C clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B18 women, 3/4 HEPS and 1/9 HIV-1 infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYVDRFY/FK, while infected women tended to respond to YPLTFGWCY/F. • The dominant response to this HLA allele was to this epitope for all 3/4 HEPS cases and for the single HIV-1 infected women that responded to this epitope. • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLNM/TLN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.				
p24 (161–170)	p24	FRDYVDRFYK	HIV-1 infection, Vaccine	human, macaque (B18)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (161–174)	p24 (161–174 HXB2)	FRDYVDRFYKTLRA	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (161–180)	p24 (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A2, A3, B8, B62.				
p24 (161–180)	p24 (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
p24 (161–180)	p24 (293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human (B71)	McAdam1998
p24 (162–172)	p24 (296–306 subtype A)	RDYVDRFFKTL	HIV-1 infection	human (A*2402)	Dorrell1999
	Keywords inter-clade comparisons. • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa. • This epitope is similar to the A24 DYVDRYFKT epitope found for B subtype, but CTL from this A subtype infection required the additional Arg – the B clade sequence change from F to Y diminished CTL reactivity. • C. Brander notes that this is an A*2402 epitope in the 1999 database.				
p24 (162–172)	p24 (296–306 subtype A)	RDYVDRFFKTL	HIV-1 infection	human (A*2402)	Frahm2004
	• C. Brander notes this is an A*2402 epitope.				
p24 (162–172)	p24 (296–306)	RDYVDRFFKTL	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-A24 women, 0/4 HEPS and 6/10 HIV-1 infected women recognized this epitope, likelihood ratio 7.2, p value 0.03, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only. • The dominant response to this HLA allele was to this epitope in all of the 6/10 HIV-1 infected women. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort. • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion.				
p24 (162–172)	p24 (293–312 LAI)	RDYVDRFYKTL	HIV-1 infection	human (B*4402)	Frahm2004
	• C. Brander notes this is a B*4402 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (162–172)	p24 (162–172)	RDYVDRFYKTL	HIV-1 infection	human (B44)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (162–172)	p24 (162–172)	RDYVDRFYKTL	HIV-1 infection	human (B44)	Day2001
p24 (162–172)	p24	RDYVDRFYKTL	HIV-1 infection, Vaccine	human, macaque (B44)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
p24 (162–172)	p24 (293–312 LAI)	RDYVDRFYKTL	HIV-1 infection	human (B44, A26 or B70)	Ogg1998a
p24 (163–172)	p24 (163–172)	DYVDRFYKTL	HIV-1 infection	human (A24)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (163–173)	Gag (297–307 SF2)	DYVDRFYKTLR	HIV-1 infection, computer prediction	human (A*3303)	Hossain2003
	Keywords binding affinity, computational epitope prediction. **Assay type** Chromium-release assay. • HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing. • This epitope is one of the 2/6 peptides that could induce CTL responses in the PBMC of infected individuals, but was not properly processed in a vaccinia-HIV infected target cell.				
p24 (164–172)	Gag (296–304)	YVDRFYKTL	HIV-1 infection	human (A*0207)	Currier2002a
	Keywords inter-clade comparisons. **Donor HLA** A*0207. • Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades. • The Thai subject VAIP-4 demonstrated broad CTL cross-reactivity towards gag constructs derived from subtypes A, B, C, D, F, G, H, and CRF-01_AE. Sequence alignments of this epitope showed conservation for clades B and D, and Y->F substitutions at position 6 for subtypes A, C, CDR01-AE, F, G, and H. YVDRFYKTL and the variant epitope YVDRFFKTL are recognized equally well.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (164–172)	p24 (164–172)	YVDRFYKTL	HIV-1 infection	human (A*0207)	Frahm2004
p24 (164–172)	p24 (298–306 subtype A) **Keywords** inter-clade comparisons. • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa. • This CTL epitope is conserved in A and C subtype, and B clade sequences tend to have a change from F to Y, YVDRFYKTL – both variants showed strong CTL reactivity. • CTL reacted with targets presenting either in the context A26 or B70 – the epitope has the HLA-26 motif of Val at position 2 and Leu at the carboxy terminus, and the B70 anchor residue motif is unknown.	YVDRFFKTL	HIV-1 infection	human (A26 or B70)	Dorrell1999
p24 (164–172)	Gag (298–306 subtype A) **Keywords** inter-clade comparisons. • In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins.	YVDRFFKTL	HIV-1 infection, in vitro stimulation or selectio	human (A26 or B70)	Dorrell2001
p24 (164–172)	Gag (296–304 96ZM651.8) **Keywords** inter-clade comparisons. • This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 4 subjects who responsed to the CTL epitope YVDRFFKTL – all were HLA-B*1510 and also shared HLA-Cw03, suggesting linkage disequilibrium. • An HIV-1 B variant of the epitope YVDRFYKTL has been described, and was recognized byCTL from an HIV-1 subtype A-infected patient, and the HLA restriction of the epitope was suggested to be A26 or B70 – HLA-B*1510 is equivalent to the serological specificity HLA B70.	YVDRFFKRL		human (B*1510, B70)	Novitsky2001
p24 (164–172)	p24 (164–172) • One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.	YVDRFYKTL	HIV-1 infection	human (B70)	Ferrari2000
p24 (164–172)	Gag (p24) (164–172)	YVDRFFKTL		human (Cw*0303)	Frahm2004
p24 (164–172)	Gag (p24) (164–172)	YVDRFFKTL		human (Cw*0304)	Frahm2004
p24 (165–178)	p24 (165–177 HXB2) **Keywords** supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.	VDRFYKTLRAEQAS	HIV-1 infection	human	Addo2003

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (166–174)	p24 (298–306 LAI)	DRFYKTLRA	HIV-1 infection	human (B*1402)	Frahm2004
	• C. Brander notes this is a B*1402 epitope.				
p24 (166–174)	p24 (298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human (B14)	Wilson1996
	Keywords responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • DRFYKILRA, a naturally occurring variant, was found in mother, and is recognized although less reactive. • DQFYKTLRA, a naturally occurring variant, was found in infant and is not recognized.				
p24 (166–174)	p24 (298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human (B14)	Cao1997a
	• The consensus peptide for clades B and D is DRFYKTLRA. • The consensus peptide for clades A and C is DRFFKTLRA and it is equally reactive.				
p24 (166–174)	p24 (298–306 HXB2)	DRFYKTLRA	HIV-1 infection	human (B14)	Yang1997b
	Keywords kinetics. • A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transducing into CD8+ cells. • The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency. • A CTL clone specific for this epitope was used for the comparison.				
p24 (166–174)	p24	DRFWKTLRA	HIV-1 exposed seronegative	human (B14)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The D subtype consensus is identical to the B clade epitope. • The A subtype consensus is drFfKtLRA.				
p24 (166–174)	p24 (298–306 LAI)	DRFYKTLRA	HIV-1 infection	human (B14)	Harrer1996b
p24 (166–174)	p24 (298–306)	DRFYKTLRA	HIV-1 infection	human (B14)	Yang1996
	• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL. • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones. • The distinction was thought to be due to lower expression of RT relative to Env and Gag. • CTL can lyse infected cells early after infection, possibly prior to viral production.				
p24 (166–174)	p24 (298–306)	DRFYKTLRA	HIV-1 infection	human (B14)	Yang1997a
	Assay type CTL suppression of replication. • CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*. • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation. • CTL suppress HIV replication more efficiently in HLA-matched cells.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (166–174)	p24 (298–306)	DRFYKTLRA	in vitro stimulation or selectio	human (B14)	Zarling1999
	Keywords dendritic cells. • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses. • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA. • A weak response to KLTPLCVSL was stimulated using macrophages as the APC. • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.				
p24 (166–174)	p24	DRFYKLTRA		human (B14)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: DRFYKSLRA is cross-reactive, [Harrer1993]				
p24 (166–174)	p24 (298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human (B14)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • DRFYKILRA and DQFYKTLRA were escape mutants.				
p24 (166–174)	p24 (SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in 2/5 HIV+ individuals who were HLA B14 living in Boston – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (166–174)	p24 (SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Goulder2001a
	Keywords acute infection. **Epitope name** DA9. • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia. • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.				
p24 (166–174)	p24 (166–174)	DRFYKTLRA	HIV-1 infection	human (B14)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (166–174)	p24 (298–306 SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3.			
p24 (166–174)	p24 (298–306)	DRFFKTLRA	HIV-1 infection, HIV-1 exposed seronegative	human (B14)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • Variants DRF(F/W)KTLRA are specific for clades A/B. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B14 women, 0/4 HEPS and 6/7 HIV-1 infected women recognized this epitope, likelihood ratio 14.4, p value 0.004 and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA. • The dominant response to this HLA allele was to this epitope for all of the 6/7 HIV-1 infected women. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.			
p24 (166–174)	p24 (SF2)	DRFYKTLRA	HIV-1 infection	human (B14)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
p24 (166–174)	p24	DRFYKTLRA	HIV-1 infection	human (B14)	Cao2002
	Keywords epitope processing. • AC13 is a B14 restricted CTL clone that recognizes DRFYKTLRA. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
p24 (166–174)	p24	DRFWKTLRA	HIV-1 infection	human (B14)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (166–174)	p24	DRFYKTLRA	HIV-1 infection, Vaccine	human (B14)	Hanke2000, Wee2002

Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].

p24 (166–174)	p24 (166–174)	DRFYKTLRA	HIV-1 infection	human (B14)	Cao2003

Keywords acute infection, early-expressed proteins.
Assay type CD8 T-cell Elispot - IFNγ.
Donor HLA A1, A3, B7, B14, cw*0702, Cw*0802; A1, A1, B8, B14, Cw7, Cw8.

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- This epitope was recognized in two subjects early in infection, presented by B14 in each case.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

p24 (166–174)	p24 (subtype B)	DRFYKTLRA	HIV-1 exposed seronegative	human (B14, B*1402)	Rowland-Jones1998b

Keywords inter-clade comparisons.

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.
- This epitope is conserved among B and D clade viruses.
- The Clade A version of the epitope, DRFFKLTRA, was preferentially recognized by CTL.
- This epitope was recognized by two different exposed and uninfected prostitutes.

p24 (166–175)	p24 (298–306 HX10)	DRFYKTLRAE	HIV-1 infection	human (B14)	Wagner1999

Keywords immunodominance.

- The immunodominant CTL response in a long-term survivor was to this highly conserved and functionally relevant epitope.
- By testing mutations in an HXB2 background, it was found that all mutations within the epitope that abrogated CTL recognition also abolished viral infectivity.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The epitope in this study overlaps the major homology region for which highly conserved residues exist in all known lenti- and onco-viruses and yeast transposons. • Patient was part of the study in [Harrer1996a]				
p24 (166–175)	Gag (298–307)	DRFYKTRAE	HIV-1 infection	human (B14)	Musey2003
	Keywords TCR usage, genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A24, A33, B14, B27. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood and cervix.				
p24 (169–185)	p24 (169–184 HXB2)	YKTLRAEQASQDVKNWN	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • Responses to this peptide were detected in 17% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p24 (169–188)	Gag (301–320)	FKTLRAEQATQDVKNWMTDT	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (169–188)	Gag (301–320)	YKTLRAEQASQEVKNWMTET	HIV-1 infection	human (B57)	Musey2003
	Keywords TCR usage, genital and mucosal immunity. **Assay type** Chromium-release assay. **Donor HLA** A1, A66, B52, B57. • CTL clones from blood, semen, cervix and rectum samples from 12 individuals were compared. CTL clones derived from blood and mucosal samples had similar high lysis efficiency, primarily perforin dependent, and TCRbeta VDJ region sequencing revealed cases of expansion of the same clone in different compartments. • CD8+ T cell clones directed at this epitope were derived from blood and rectum.				
p24 (173–181)		RAEQASQEV	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls ML1792.				
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection	human (Cw8)	Johnson1991
	• Originally reported as HLA-B14 restricted, but subsequently found not to be presented by cells transfected with B14. • Thought to be HLA-Cw8 restricted (C. Brander and B. Walker)				
p24 (173–181)	p24	RAEQASQEV	HIV-1 exposed seronegative	human (Cw8)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is RAeQAtQEV. • The D subtype consensus is RAEQsQdV. • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)				
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection	human (Cw8)	Price1995
	• Study of cytokines released by HIV-1 specific activated CTL. • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)				
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection	human (Cw8)	Lubaki1997
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response. • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response. • Despite this being a well defined conserved epitope, and thought to be presented by B14, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 PQDLNTMLN. • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)				
p24 (173–181)	p24 (305–313)	RAEQASQEV	HIV-1 infection, HIV-1 exposed seronegative	human (Cw8)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p24 (174–184)	p24 (306–316 LAI)	AEQASQDVKNW		human (B*4402)	Frahm2004
	• C. Brander notes this is a B*4402 epitope.				
p24 (174–184)	p24 (306–316 LAI)	AEQASQDVKNW		human (B*4402, B44)	Brander1997
	• Pers. comm. from D. Lewinsohn to C. Brander and B. Walker, C Brander *et al.*, this database, 1999.				
p24 (174–184)	Gag (306–316)	AEQASQEVKNW	HIV-1 infection	human (B44)	Brodie1999
	• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptively transferring them. • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects.				
p24 (174–184)	p24 (306–316)	AEQASQEVKNW	HIV-1 infection	human (B44)	Brodie2000
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication. • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1alpha and MIP-1beta, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism. • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p24 (174–184)	p24 (306–316 LAI) **Keywords** HAART. **Epitope name** G3. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.	AEQASQDVKNW	HIV-1 infection	human (B44)	Mollet2000
p24 (174–184)	p24 (174–184) • B44-restricted CTL response was strongest to this epitope in one individual.	AEQASQDVKNW	HIV-1 infection	human (B44)	Day2001
p24 (174–184)	p24 **Keywords** HAART, supervised treatment interruptions (STI). **Epitope name** B44-AW11(p24). **Donor HLA** A32,A?,B44,B?. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample.	AEQASQDVKNW	HIV-1 infection	human (B44)	Altfeld2002
p24 (174–185)	Gag (p24) (174–185)	AEQASQEVKNWM		human (Cw*05)	Frahm2004
p24 (175–186)	p24 (307–318) • HIV is found in semen both as cell-associated and cell-free forms, and HIV-specific CTL could be found in the semen of 5/5 men with CD4 greater than 500 – 3 of the men were analyzed in detail and had broad CTL to gag, env and pol. • Two CTL lines from one donor recognized this epitope. • Isolation of CTLs specific to HIV in both male and female urinal tracts provide evidence that virus-specific lymphocytes come from the urogenital mucosa, and the authors speculate that CTL in mucosal tissues may be correlated with lower viral load in semen and reduced transmission.	EQASQEVKNWMT	HIV-1 infection	human (B44)	Quayle1998

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (176–184)	p24 (308–316 LAI)	QASQEVKNW	HIV-1 infection	human (B*5301)	Frahm2004
	• C. Brander notes this is a B*5301 epitope.				
p24 (176–184)		QASQEVKNW	HIV-1 infection	human (B*5301, B57)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-QW9. **Donor HLA** 01RCH59 A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 01RCH59 was Hispanic, was not on HAART, viral load 5100, CD4 count 349, and she also recognized PIQKETWETW, RT(392-401), A*3201. • Among HIV+ individuals who carried HLA B*5301, 11/15 (73%) recognized this epitope. • Among HIV+ individuals who carried HLA B57, 3/6 (60%) recognized this epitope.				
p24 (176–184)	p24 (309–317 LAI)	QASQEVKNW	HIV-1 infection	human (B*5701)	Goulder1996b
	• Recognition of this peptide by two long-term non-progressors. • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations. • Described as B*5701 in C. Brander *et al.*, this database, 1999.				
p24 (176–184)	p24 (311–319 LAI)	QASQEVKNW	HIV-1 infection	human (B*5701)	Frahm2004
	• C. Brander notes this is a B*5701 epitope.				
p24 (176–184)		QASQEVKNW	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • HLA B*5701 was found in a very high frequency in HIV-1 infected non-progressors, 11/13 (85%) versus 19/200 (9.5%) of progressors. Non-progressors tended to have an immune response that was highly focused on four p24 epitopes that were presented by B*5701, ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, and QASQEVKNW. • Only QASQEVKNW was recognized in all of the LTNP's tested.				
p24 (176–184)		QASQEVKNW	HIV-1 infection	human (B*5701)	Migueles2001
	Keywords rate of progression, immunodominance. • CTL activity was monitored in 27 individuals, including 10 LTNP with an over-expression of HLA B*5701 – these individuals have viral loads below the threshold of infection without therapy, and their CD8+ T-cell response tends to be focused on peptides that contain B*5701 epitopes ISPRTLNAW, KAFSPEVIPMF, TSTLQEQIGW, or QASQEVKNW. • CTL responses are broader in B*5701+ individuals with progressive viremia than those that control viremia. • The HLA-A*0201 SLYNTVATL epitope response was not as strong individuals that carried both A2, B57.				
p24 (176–184)	Gag (308–316)	QASQEVKNW	HIV-1 infection	human (B*5701)	Migueles2003
	Keywords rate of progression, escape. **Epitope name** QW9. **Assay type** Intracellular cytokine staining, Flow cytometric CTL assay. • cDNA Gag sequences from a set of 17 HLA-B*5701+ progressors and 10 LTNPs were obtained, and the variation in four p24 B*5701 epitopes examined. Sequence variants were more common ($p < 0.01$) in the epitopes in the progressors (median 3, range 1-7) than LTNPs (median 2, range 0-4). • In general use of the autologous protein in a target cell did not diminish the overall CD8+ T-cell responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The substituion E312D (qasqDvknw) was common in progressors (8/17) and rare in LTNP (1/8) (p = 0.06). qasqDvknw and qasqEvknw peptides were made; this mutation does not affect binding to B*57. 2/4 progressors that carried only the D variant could not recognize the D variant peptide, but could recognize the E variant peptide, demonstrating immune escape.				
p24 (176–184)	p24 (308–316 LAI)	QASQEVKNW	HIV-1 infection	human (B53)	Buseyne1997
	• Minimal sequence determined through epitope mapping. • This is a relatively conserved epitope. • HLA-Cw*0401 was defined as the restricting element, but cells that carry Cw*0401 varied in their ability to present this epitope – this could be the result of diminished cell-surface expression of Cw*0401 in some cells. • The HLA presenting molecule for this epitope was originally described as Cw*0401, but subsequent experiments with an HLA B53+ C4- cell line and with C1R cells transfected with HLA-B53 have shown that the HLA restricting element is HLA-B53 (F. Buseyne, pers. comm. 2000)				
p24 (176–184)	(LAI)	QASQEVKNW		human (B53)	Buseyne1999, Frahm2004
p24 (176–184)	p24 (NL43)	QASQEVKNW	in vitro stimulation or selectio	human (B53)	Buseyne2001
	Keywords epitope processing, dendritic cells. **Epitope name** QW9. • Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL. • Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in QASQEVKNW specific CTL clone 141 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency. • Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion.				
p24 (176–184)	p24 (308–316)	QATQEVKNW	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B53 women, 1/2 HEPS and 7/9 HIV-1 infected women recognized this epitope.				
p24 (176–184)	p24 (308–316 subtype A consensus)	QATQEVKNM	HIV-1 infection	human (B53)	Dorrell2001
	Keywords binding affinity, inter-clade comparisons. • In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays. • Two of the new epitopes lacked the predicted by P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35. • While S, T, and P could all fit into the HLA-B35 or HLA-B53 B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53. • QATQEVKNM was recognized in 6/7 HLA-B53 subjects.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Cross-recognition of QATQEVKNM was not studied here, but it was noted that both the A, QATQEVKNM, and B, QASQDVKNW, subtype version of this epitope, are also presented by HLA-B57 and B58, common HLA alleles in Africans.				
p24 (176–184)	Gag (SF2)	QASQEVKNW	HIV-1 infection	human (B57)	Goulder2001a
	Keywords acute infection. **Epitope name** QW9. • This peptide elicited a weak CTL response during acute infection of patient PI004. • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond.				
p24 (176–184)	(LAI)	QASQEVKNW		human (Cw4)	Buseyne1999
p24 (176–184)	p24 (176–184)	QASGEVKNW	HIV-1 infection, HIV-1 exposed seronegative	human (Cw4)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p24 (176–185)	p24 (311–319 SF2)	QASKEVKNWV	HIV-1 infection	human (B57)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3.				
p24 (177–185)	p24 (177–185)	ATQEVKNWM	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • Variants A(T/S)QEVKNWM are specific for the A/B clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B53 women, 1/2 HEPS and 5/9 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in the 1/2 HEPS case and in only one of the 5/9 HIV-1 infected women.				
p24 (180–189)	p24 (313–322)	EVKNWMTETL	HIV-1 infection, HIV-1 exposed seronegative	human (B53)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
p24 (181–190)	p24 (313–322 LAI) • P. Johnson, pers. comm.	VKNWMTETLL		human (B8)	Brander1996b
p24 (191–205)	Gag (320–328 BH10, LAI) • This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is TLLVQNANP) has similarity with growth differentiation factor 11, fragment THLVQQANP.	VQNANPDCKTILKAL	HIV-1 infection	human	Maksiutov2002
p24 (191–205)	p24 (191–205) • One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.	VQNANPDCKTILKAL	HIV-1 infection	human (B51)	Ferrari2000
p24 (191–205)	p24 (323–337) • Two CTL epitopes defined (see also p17(21-35))	VQNANPDCKTILKAL	HIV-1 infection	human (B8)	Nixon1991
p24 (191–205)	p24 (325–339 SF2) **Keywords** review, immunodominance, escape. • Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to the B8 epitopes, which varied over time. • [Goulder1997a] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients.	VQNANPDCKTILKAL	HIV-1 infection	human (B8)	Goulder1997a, Phillips1991
p24 (191–210)	p24 (323–342 SF2) • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • Three of these 12 had CTL response to this peptide. • The responding subjects were HLA-A3, A24, B8, B55; HLA-A1, A11, B8, B27.	VQNANPDCKTILKALGPAAT	HIV-1 infection	human	Lieberman1997a
p24 (191–210)	p24 (323–342 SF2) • CTL expanded *ex vivo* were later infused into HIV-1 infected patients.	VQNANPDCKTILKALGPAAT	HIV-1 infection	human	Lieberman1997b
p24 (193–201)	Gag (327–335 SF2) **Keywords** inter-clade comparisons, rate of progression. • HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed. • Four of the six epitopes were highly conserved among B subtype sequences, NANPDCKTI is conserved.	NANPDCKTI	HIV-1 infection	human (B*5101)	Tomiyama1999
p24 (193–201)	p24 (325–333) **Keywords** immunodominance.	NANPDCKTI?	HIV-1 infection	human (B51)	Betts2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 3/11 of the HLA A2+ individuals were HLA B51 and two of these responded to this epitope as well as to other epitopes.				
p24 (193–201)	p24 (324–335 IIIB)	NANPDCKTI	HIV-1 infection	human (B51)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope.				
p24 (193–201)	p24 (323–333)	NANPDCKTI	HIV-1 infection	human (B51)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** NAN. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B51+				
p24 (193–201)	p24 (191–205)	NANPDCKTI	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (195–202)	p24 (323–342)	NPDCKTIL	HIV-1 infection	human (B35)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population. • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs. • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XPXXXXXL is a B35 binding motif.				
p24 (195–202)		NPDCKTIL	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Gag-NL8. • Among HIV+ individuals who carried HLA B35, 3/17 (18%) recognized this epitope.				
p24 (197–205)	p24 (329–337 LAI)	DCKTILKAL		human (B*0801)	Frahm2004
	• C. Brander notes this is a B*0801 epitope.				
p24 (197–205)	p24 (329–337 LAI)	DCKTILKAL		human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide VQNANPDCKTILKAL.				
p24 (197–205)	p24 (329–337)	DCKTILKAL	HIV-1 infection	human (B8)	Nowak1995
	Keywords escape. • In a longitudinal study of CTL response and immune escape – the variant DCRTILKAL was also found, binds to B8, but is not recognized.				
p24 (197–205)	p24 (329–337)	DCKTILKAL		human (B8)	McAdam1995
	• Defined as minimal epitope by titration and binding studies.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (197–205)	p24 (197–205)	DCKTILKAL		human (B8)	Goulder1997g
	• Included in a study of the B8 binding motif.				
p24 (197–205)	p24 (329–337)	DCKTILKAL	HIV-1 infection	human (B8)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** DCK. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • This epitope was recognized at a low level by only 1 of the 7/8 study subjects that were HLA B8. • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy.			
p24 (197–205)	p24 (197–205)	DCKTILKAL	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (197–205)	p24 (197–205)	DCKTILKAL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
p24 (197–205)	p24	DCKTILKAL	HIV-1 infection	human (B8)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** DCK. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (199–218)	Gag (331–350)	KTILRALGPGATLEEMMTAC	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
p24 (209–217)	Gag (341–)	ATLEEMMTA	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag341. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice, although responses were detected in 2/17 HIV+ HLA-A2 subjects.				
p24 (211–230)	p24 (345–364 SF2)	LEEMMTACQGVGGPGHKARV	HIV-1 infection	human	vanBaalen1993
	• Gag CTL epitope precursor frequencies estimated, peptide mapping.				
p24 (211–230)	p24 (343–362 SF2)	LEEMMTACQGVGGPGHKARV	HIV-1 infection	human (B7)	McAdam1998
p24 (211–231)	p24 (343–362 SF2)	LEEMMTACQGVGGPGHKAR-VL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag. • One of these 12 had CTL response to this peptide. • The responding subject was HLA-A1, A2, B50, B57.				
p24 (213–221)	Gag (345–)	EMMTACQGV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag345. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced a response in 1/6 transgenic mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.				
p24 (217–227)	p24 (349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human (A*1101)	Frahm2004
	• C. Brander notes this is an A*1101 epitope.				
p24 (217–227)	Gag (349–359)	ACQGVGGPGHK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons, TCR usage. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • ACQGVGGPGHK was found to elicit clade-specific responses in clade B (ACQGVGGPGHK is most common in clades A and B) and clade E (acqgvggpShk is most common and is also common in clades C and D). ACQGVGGPGHK was recognized by CTL from 4/5 B clade infected Japanese subjects, and acqgvggpShk from 3/7 E clade infected Thai subjects. • The binding of the two variants to HLA A*1101 was almost identical, but bulk CTL generated from individuals did not cross-react with the cross-clade peptides, indicating the lack of cross-reactivity was due to TCR specificity.				
p24 (217–227)	p24 (349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ACQGVGGPSHK, a variant found in HIV RF, was also recognized.				
p24 (217–227)	p24 (SF2)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
p24 (217–227)	p24 (349–359)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** ACQ. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope. • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197. • Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up.				
p24 (217–227)	p24 (216–226)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
p24 (217–227)	p24 (349–359 SF2)	ACQGVGGPGHK	HIV-1 infection	human (A11)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3.				
p24 (217–227)	p24	ACQGVGGPGHK	HIV-1 infection	human (A11)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** ACQ. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
p24 (221–231)	p24 (353–363 LAI) **Keywords** HAART. **Epitope name** G1. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.	VGGPGHKARVL	HIV-1 infection	human (B7)	Mollet2000
p24 (223–231)	p24 (223–231 SF2) **Epitope name** GL9. • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • The response to GPGHKARVL was dominant.	GPGHKARVL	HIV-1 infection	human (B*0702)	Altfeld2001a
p24 (223–231)	p24 (355–363 LAI) **Keywords** review, escape. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. • One had a strong response to this peptide, the other a weak response. • [Goulder1997a] is a review of immune escape that summarizes this study.	GPGHKARVL	HIV-1 infection	human (B7)	Goulder1997e, Goulder1997a
p24 (223–231)	p24 (SF2) **Keywords** inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.	GPSHKARVL	HIV-1 infection	human (B7)	Goulder2000a
p24 (223–231)	p24 (SF2) **Keywords** inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study. • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.	GPSHKARVL	HIV-1 infection	human (B7)	Goulder2000a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (223–231)	(LAI)	GPGHKARVL		(B7)	Frahm2004, Goulder1999a
p24 (223–231)	p24 (223–231 SF2)	GPGHKARVL	HIV-1 infection	human (B7)	Altfeld2001b

Keywords HAART, acute infection.

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef.
- Previously described and newly defined optimal epitopes were tested for CTL response.
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 2/3 group 2, and 0/1 group 3.

p24 (223–231)	p24 (223–231)	GPGHKARVL	HIV-1 infection	human (B7)	Day2001

Keywords rate of progression, acute infection.

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.
- Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.
- An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.
- The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.
- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.

p24 (223–231)	p24 (223–231)	GPGHKARVL	HIV-1 infection	human (B7)	Yu2002a

Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection.
Epitope name B7-GL9.
Donor HLA A3, B7, Cw7.

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- Only two epitopes were detected during acute infection in patient AC-06, B7 restricted gp41 epitope IPRRIRQGL and Gag GPGHKARVL. GPGHKARVL was the first targeted peptide, and remained immunodominant through the 34 month study period.
- 3/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.

II-B-4 p24-p2p7p1p6 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24-p2p7p1p6 (223–1)	Gag	GPGHKARVLA		human (B7)	De Groot2001

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.
- GPGHKARVLA was confirmed as an HLA-B7 epitope in this study, and had been previously published.

p24-p2p7p1p6 (225–8)	Gag (357–372 LAI)	GHKARVLAEATLSQVN	HIV-1 infection	human	Buseyne1993a

- Vertical transmission of HIV ranges from 13% to 39%
- Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children.
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures.
- Patient EM28 (CDC P2A) had a CTL response to four epitopes in Gag.

p24-p2p7p1p6 (230–7)	Gag (386–)	VLAEAMSQV		human (A*0201)	Altfeld2001c

Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction, immunodominance.
Epitope name Gag-386.

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- VLAEAMSQV binds to all five HLA-A2 supertype alleles tested: A*0201, A*0202, A*0203, A*0206 and A*6802 (highest affinity)
- 4/22 individuals with chronic HIV-1 infection recognized this epitope, and it was immunodominant in 3/4 by ELISPOT.
- 0/12 acutely infected individuals recognized this epitope.

p24-p2p7p1p6 (230–7)		VLAEAMSQV	HIV-1 infection	human (A02)	Sabbaj2002b

Epitope name Gag-VV9.

- Among HIV+ individuals who carried HLA A02, 3/29 (10%) recognized this epitope.

p24-p2p7p1p6 (230–7)	Gag (362–)	VLAEAMSQV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003

Vaccine *Vector/Type:* peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Keywords binding affinity, inter-clade comparisons, computational epitope prediction.
Epitope name Gag362(9L).
Assay type T-cell Elispot, Chromium-release assay, Flow cytometric CTL assay.

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects. • The variant vlaeamsqA was also immunogenic in A2 transgenic mice, eliciting a CD8+ T-cell response, as was recognized in 3/17 HIV+ people, including the person that recognized the vlaeamsqV variant.				
p24-p2p7p1p6 (230–7)	Gag (397–405)	VLAEAMSQV	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				

II-B-5 p2p7p1p6 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p2p7p1p6 (1–10)	p2p7p1p6 (1–10)	AEAMSQVTNS		human (B*4501)	Frahm2004
p2p7p1p6 (5–13)	Gag (SF2)	SQVTNPANI	Vaccine	mouse (H-2D^b)	Paliard1998
	Vaccine *Strain:* B clade SF2 *HIV component:* Gag • HIV-1(SF2)p55gag vaccination of H-2 mice activates a CTL response against this epitope. • CTL that recognized SQVTNPANI in the context of H-2D^b cross-reacted with H-2 alloantigens H-2L^d and an unidentified self-peptide. • A postulate: heterozygosity at the MHC level could prevent the maturation of some T cell receptor combinations for foreign peptide and self-MHC constructs because of thymic depletion and tolerance.				
p2p7p1p6 (18–37)	Gag (96ZM651.8)	SNFKGNKRMVKCFNCGKEGH		human (A*02011)	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 4 of 8 individuals (50%) who were positive for HLA-A*02011 responded to the peptide SNFKGNKRMVKCFNCGKEGH.				
p2p7p1p6 (33–41)	p2p7p1p6 (33–41)	KELYPLTSL	HIV-1 infection	human (B*4001)	Frahm2004
p2p7p1p6 (42–50)	p15 (42–50)	CRAPRKKGC	HIV-1 infection	human (B*14)	Frahm2004
p2p7p1p6 (42–50)	p15 (42–50 SF2)	CRAPRKKGC	HIV-1 infection	human (B14)	Yu2002b
	Keywords immunodominance. **Donor HLA** B14. • 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T-cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6. • p15 contributed on average 17% of the total Gag response (rage 0-100%). • 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK. • 2/6 HLA-B14+ subjects recognized this epitope. The binding motif for B14 is C-term Cys, positions 2 and 5 Arg.				
p2p7p1p6 (55–70)	p15 (446–460 BRU)	KEGHQMKDCTERQANF	HIV-1 infection	human (A2)	Claverie1988
	• One of 4 epitopes first predicted, then subsequently shown to stimulate an HLA-A2 restricted CTL line.				
p2p7p1p6 (63–71)	p15 (63–71)	CTERQANFL	HIV-1 infection	human (B61)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A11, B51, B61, Cw2, Cw14. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
p2p7p1p6 (64–71)		TERQANFL	HIV-1 infection	human (B*4002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Gag-TL8. **Donor HLA** A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized AEWDRVHPV, p24(78-86), HLA-B*4002 and KEKGGLEGL, Nef(92-100), HLA-B*4002. • Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope.				
p2p7p1p6 (64–71)	p15 (64–71)	TERQANFL		human (B*4002)	Frahm2004
p2p7p1p6 (66–80)	p15 (66–80)	RQANFLGKIWPSYKG	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
p2p7p1p6 (70–77)	Gag (433–)	FLGKIWPS	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Gag *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Gag433. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 7/17 HIV+ HLA-A2 subjects.				
p2p7p1p6 (70–79)	p15 (70–79 SF2)	FLGKIWPSYK	HIV-1 infection	human (A*0201)	Yu2002b
	Keywords immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T-cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6. • p15 contributed on average 17% of the total Gag response (rage 0-100%). • 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK. • FLGKIWPSYK was embedded in a peptide recognized by 14/57 (25%) of subjects. • 13/24 (54%) of HLA-A*0201+ subjects recognized this peptide.				
p2p7p1p6 (70–79)	p2p7p1p6 (1–10)	FLGKIWPSYK	HIV-1 infection	human (A*0201)	Frahm2004
p2p7p1p6 (83–97)	Gag (453–462 BH10, LAI) • This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is PEPTAPPFLQ) has similarity with the T-cell surface glycoprotein CD5, fragment PEPTAPPRLQ.	GNFLQSRPEPTAPPF	HIV-1 infection	human	Maksiutov2002
p2p7p1p6 (83–97)	p15 (418–433 BRU) • One of 4 epitopes first predicted, then subsequently shown to stimulate an HLA-A2 restricted CTL line.	GNFLQSRPEPTAPPF	HIV-1 infection	human (A2)	Claverie1988
p2p7p1p6 (118–126)	p2p7p1p6 (118–126) • C. Brander notes that this is a B*4001 epitope.	KELYPLTSL		human (B*4001(B60))	Frahm2004
p2p7p1p6 (118–126)	p15 (118–126 SF2) **Keywords** immunodominance, cross-presentation by different HLA. **Epitope name** p15-24. • 26/57 HIV-1 infected subjects displayed Gag p15-specific CD8+ T-cell IFNgamma responses were measured by Elispot and intracellular staining. The immunodominant regions targeted by CD8+ T cells were mapped to three functional domains: the zinc finger structures, the protease cleavage site p7/p1, and to the Vpr binding site in p6. • p15 contributed on average 17% of the total Gag response (rage 0-100%). • 3 optimal CTL epitopes were mapped within p15: KELYPLTSL, CRAPRKKGC, and FLGKIWPSYK. • Four patients who were HLA-B60+ recognized KELYPLTSL. • The binding motif for B60 is C-term Leu and 2nd position Glu. • Four patients who did not carry HLA-B60 also recognized the 15 amino acid long peptide carrying KELYPLTSL, suggesting other epitopes in this immediate region can be presented by other HLA class I molecules.	KELYPLTSL	HIV-1 infection	human (B60, B*4001)	Yu2002b
p2p7p1p6 (121–130)	Gag (484–493) • This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor. • A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing.	YPLTSLRSLF	HIV-1 infection	human (B7)	Jin2000b

II-B-6 Gag CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	Gag (IIIB)		Vaccine	macaque	Paliard2000
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* Gag				
	• CTLs primed by HIV-1 p55 gag virus-like particle (VLP) vaccination recognized epitopes in four different 20 amino acid peptides p17/4, p17/8, p24/13 and p14/9.				
	• Cytotoxic T cell response lasted greater than 8.5 months.				
Gag	Gag (IIIB)		HIV-1 infection	human	Wasik2000
	Keywords rate of progression, Th1.				
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants.				
	• HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors.				
	• CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.				
Gag	Gag (LAI)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp41, Protease, V3				
	• The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))				
	• Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36.				
	• Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160.				
Gag	p24		Vaccine	human	Klein1997
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* p17 Gag, p24 Gag				
	• Immunization of HIV+ people with an HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load.				
	• Two of four subjects that received 500 or 1000 μg of p24-VLP had an increase in gag-specific CTL.				
Gag	p24 (SF2)		Vaccine	mouse, baboon	O'Hagan2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade SF2 *HIV component:* gp120, p24 Gag *Adjuvant:* MF59, PLG				
	• PLG (Polylactide co-glycolide polymer) microparticles administered in MF59 emulsion induced gp120 Ab responses and CTL immune responses against p24 gag.				
Gag	Gag		HIV-1 infection	human	Lubaki1999
	• Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20)				
	• A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20.				
Gag	Gag		HIV-1 infection	human	Kalams1999a
	• The presence of HIV-1 p24-specific proliferative responses was positively correlated with Gag-specific memory CTL and negatively correlated with viral load in untreated subjects.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Gag proliferative responses were the most readily detected – Gag CTL responses were the only responses with a significant correlation with Gag stimulated help, although there was a positive trend with Nef, Env and RT.				
Gag	p55 (IIIB)		HIV-1 infection	human	Greenough1999
	• 7/128 HIV-1 infected hemophiliac were identified as long-term non-progressors (LTNPs) and were monitored for viral and host immune parameters over 15 years – LTNPs maintained a low viral load, high frequencies of CTL precursors directed against Gag antigen and low levels of HIV-specific effector CTL activity – effector cell activity suggests low level ongoing viral replication.				
Gag	Gag		HIV-1 infection	human	Trickett1998
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection. • Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Gag was seen in one patient.				
Gag	Gag (IIIB)		HIV-1 infection	human	Betts1999
	Keywords rate of progression. • This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection.				
Gag	Gag (LAI)		HIV-1 infection	human	Legrand1997
	• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat. • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef. • Early responses to Pol, Rev, Vif and Tat were rare.				
Gag	Gag (IIIB)		HIV-1 infection	human	Betts1997
	Keywords inter-clade comparisons. • 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins. • A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients.				
Gag	Gag		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function. • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.				
Gag	Gag (LAI)		Vaccine	human	Belshe1998
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Protease • The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers.				
Gag	Gag (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.				
Gag	Gag (LAI)		HIV-1 infection	human	Buseyne1998b
	Keywords inter-clade comparisons. • In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	Gag		HIV-1 exposed seronegative	human	Goh1999
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype. • In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins.				
Gag	Gag (LAI)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT • A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.				
Gag	p17		HIV-1 infection	human	Kuiken1999
	Keywords epitope processing. • A correlation between conserved regions of p17 or Nef and CTL epitope density was noted – the authors suggest that this may be due to a biological reason such as epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents. • In contrast to p17 and Nef, p24 is a more conserved protein and known epitopes are evenly distributed across p24.				
Gag	Gag (LAI)		Vaccine	macaque	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag **Keywords** Th1, Th2. • Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone. • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.				
Gag	Gag/Pol (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease • A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers.				
Gag	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86 • The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.				
Gag	Gag (BRU)		HIV-1 infection	human	Aladdin1999
	Keywords rate of progression. • *In vitro* measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.				
Gag	p24 (C consensus)		HIV-1 infection	human	Goulder2000a
	Keywords inter-clade comparisons, immunodominance. • The CTL-dominant response was focused on this epitope in a HIV+ South African – this epitope did not fall within the five most recognized peptides in the study.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK (p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses. • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYV-DRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa.				
Gag	Gag		Vaccine	macaque	Akahata2000
	Vaccine *Vector/Type:* DNA *Strain:* ZF1 *HIV component:* complete genome • Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging. • Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153) • 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected. • PBMC from all vaccinated monkeys produced IFN-gamma, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response. • 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit. • 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit.				
Gag	Gag		HIV-1 infection	human	Salerno-Goncalves2000
	Keywords rate of progression. • A general test of CD8 anti-viral activity was developed based on proviral load of coculture of autologous CD8+ cells with CD4+ cells after homogeneous superinfection with NSI virus. • Significantly decreased the CD4+ T-cell proviral loads were found in 12 HIV+ slow progressors relative to 10 rapid progressors. • Significant CD8+ mediated cytotoxicity directed against autologous cells infected with vaccinia carrying the HIV-1 gag gene was observed in slow progressors in contrast to rapid progressors, but no correlation was found between plasma viral load in 22/22 asymptomatic HIV infected individuals.				
Gag	Gag		HIV-1 infection	human	Young2001
	• Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500. • 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12.				
Gag	p24		HIV-1 infection	mouse	deQuiros2000
	• CB-17 SCID-Hu mice engrafted with peripheral blood mononuclear cells of four long-term nonprogressors (viral load < 50 copies/ml) displayed resistance to challenge with HIV-1 SF162, mediated by CD8+ T-cells and associated with proliferation in response to p24 – these patients did not have a higher level of HIV-1 specific immunity *in vitro*, so the mechanism is unknown.				
Gag	Gag (subtype A, B, D)		HIV-1 infection	human	Cao2000
	Keywords inter-clade comparisons. • HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, RT or Nef from HIV-1 clades A, B, and D. • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	Gag		HIV-1 infection	human	White2001
• HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women.					
Gag	Gag (HXB2)		HIV-1 infection	human	Chun2001
• Suppression of viral replication in the resting CD4+ T-cell reservoir by autologous CD8+ T-cells via CD4+/CD8+ cell contacts was observed in long-term nonprogressors and patients undergoing antiretroviral treatment, but this activity appears to be independent of Gag-specific CTL activity.					
Gag	Gag (IIIB)		HIV-1 infection	human	Jin2000a
Keywords rate of progression.					
• The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets.					
• LTNPs have high memory CTL numbers and low viral load.					
Gag	Gag		HIV-1 exposed seronegative	human	Rowland-Jones2001
Keywords review, HIV exposed persistently seronegative (HEPS).					
• This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population.					
• The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays.					
• CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases.					
• CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response.					
• HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people.					
Gag			Vaccine	mouse	Nabel2002
Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol					
Keywords review, vaccine-specific epitope characteristics.					
• Using DNA that had humanized codon usage, CTL responses to DNA vaccines containing either Gag, Pol, Gag-Pol fusion protein, or Gag-Pol pseudoparticles suggested that the greatest breadth and most potent response was to the Gag-Pol fusion protein. The Gag-Pol fusion lacks the Gag precursor protein required for viral assemble, so does not form releaseable particles; the author speculates that longer retention of the Gag-Pol protein with in the cell may enhance antigen presentation.					
Gag			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission.					
• 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env.					
• Reviewed in [Kuhn2002].					
Gag			HIV-1 infection	human	Aldhous1994, Kuhn2002
Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission.					
• Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses to Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Kuhn2002, Wasik1999
	Keywords HAART, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission, rate of progression. • In HIV-infected infants HIV-specific, CTL responses were not detectable in icord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied. • The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies. • Stronger responses were detected after initiation of the antiretroviral therapy. • Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth. • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Kuhn2002, McFarland1994
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • Only 9% of HIV+ infants had HIV-specific CTL against Env or Gag in unstimulated PBMC. After CD3 stimulation of PBMC, Gag and Env specific CTL were found in PBMC from 91% and 78% of HIV-infected children, respectively, with high precursor frequencies. • Reviewed in [Kuhn2002].				
Gag			HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. p17 is much more variable than p24.				
Gag	p24 (HXB)		HIV-1 infection	human	Lu2000a
	Keywords epitope processing, vaccine-specific epitope characteristics. • Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and Nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs *in vitro*.				
Gag	(HXB2)		HIV-1 infection	human	Edwards2002
	• 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag. • Nef and/or Pol CTL responses were detected in 86% of the subjects. • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load. • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count. • Nef and Env responses did not correlate with either CD4 counts or viral load.				
Gag			HIV-1 infection	human	Larsson2002b
	Keywords HAART, dendritic cells. • Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	(IIIB)		HIV-1 infection	human	Trickett2002
	Keywords immunotherapy.				
	• Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.				
Gag	(IIIB)		HIV-1 and HCV co-infection	human	Lauer2002
	Keywords rate of progression.				
	• HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins.				
	• All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load.				
	• Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted.				
	• HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.				
Gag			HIV-1 infection	human	Luzuriaga1995
	Keywords responses in children.				
	• 2/3 infants infected in utero had detectable HIV-1 Gag and Env specific CTL responses, one by 4 months, one by 11 months of age. Levels of the responses varied at different time point. Pol responses were not detected.				
	• 2/4 infants infected intrapartum had detectable responses, one note until 11 months, one not until 42 months.				
	• HIV-specific CTL were not detected in ten HIV- infants that were born to HIV+ mothers.				
Gag			Vaccine	human	Gupta2002
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN *HIV component:* Env, Gag				
	• Different HIV strains were used for different regions: Gag, LAI; gp120, MN; and gp41, LAI				
	• A safety and immunogeniticity study of a vaccine dosing schedule was studied in a trial conducted in high and low risk study subjects. There was a 76% cumulative probability of detecting a Gag or Env CTL response by day 728.				
Gag			HIV-1 infection	human	Scott2001
	Keywords HAART, responses in children.				
	• CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.				
	• Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.				
	• One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.				
	• Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.				
Gag	(IIIB, MN)		HIV-1 infection	human	Larsson2002a
	Keywords dendritic cells.				
	• Dendritic cells acquire and present HIV-1 antigens derived from dead, apoptotic cells or from non-infectious, fusion-competent HIV-1 virions, and these DC cells could stimulate CD4+ and CD8+ T-cells resulting in IFNgamma production in an Elispot assay. Both HLA Class I and class II molecules were used for presentation. This may be an important aspect of the initial immune response to HIV-1 infection of CD4+ cells in the mucosal subepithelia.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	(IIIB)		HIV-1 infection	human	Ortiz2001

Keywords HAART, supervised treatment interruptions (STI).

- Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.

Gag	Gag			human	
Gag	Gag			human	
Gag	Gag		HIV-1 infection	human	Amicosante2002

Keywords HAART, computational epitope prediction, supervised treatment interruptions (STI).
Assay type Intracellular cytokine staining.

- A new assay was developed to detect CTL responses to HIV using 28 pooled 15-mer peptides from conserved regions in Gag that were selected to be rich in HLA class I motifs, carrying potential epitopes for more than 90% of HLA class I haplotypes, and to be conserved between subtypes. Some peptide variants were included, expanding the potential for cross-clade recognition. 12 Caucasians, even those on successful HAART, had detectable CTL responses using this assay, and as did five Africans. People with either B subtype or A-G recombinant infections all reacted.
- The Gag peptide ICS assay was more sensitive to picking up CTL reactivity than whole Gag in HAART treated people. Initiation of STI increased the number of IFN-gamma producing CD8+ T-cells detected using the peptide assay.

Gag	Gag		Vaccine	macaque	Caulfield2002

Vaccine *Vector/Type:* vaccinia *HIV component:* Gag *Adjuvant:* block copolymer CRL8623
Keywords vaccine-induced epitopes.
Assay type CD8 T-cell Elispot - IFNγ.

- Codon-optimized HIV Gag DNA vaccines were given i.m. with or without a nonionic block copolymer(CRL8623) as adjuvant. DNA-CRL8623 fourmulations induced 2-fold higher Elispot responses, shifting the response towards CD8+ T-cells.
- 23 monkeys recognized 25 different epitopes with an average of 2.7 epitopes per monkey, and a minimum of 1 and a maximum of 5 peptides per monkey.
- Responses were detected up to 18 months after vaccination.

Gag	Gag			human	Currier2003

Keywords inter-clade comparisons.
Assay type Flow cytometric CTL assay.

- CD8-cellular immune responses from 21 HIV-1 infected patients from Kenya infected with subtype A, C, D, and unique recombinants were studied for cross-recognition of Gag, Env, and Nef vaccinia-expressed proteins representing subtypes A-H, including CRF01.
- Both subtype-specific and cross-reactive CTL were observed, with a skewing of responses towards the infecting subtype in the nine subjects with full length sequence available. The magnitude of the responses to Gag were the highest, less to Nef, and still less to Env.
- For Gag, 8/21 subjects responded to at least 7/8 different subtype proteins, 7 had a mixed response, recognizing some subtypes but not others, and 6 responded to only one or none of the different subtype proteins. For Env, 4/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 7 responded to one or none. For Nef, 5/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 6 responded to one or none.

Gag	Gag (SF2)		Vaccine	macaque	Otten2003

Vaccine *Vector/Type:* DNA, protein, virus-like particle (VLP), PLG microparticle *Strain:* B clade SF2 *HIV component:* Gag *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), LTK63
Assay type proliferation, Chromium-release assay.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Immunization strategies for Gag (p55) in macaques were compared. GAG DNA prime with a boost of Gag adsorbed onto PLG (polyactide coglycolide) microparticles with LTK63 as adjuvant gave the strongest CD4+ T cell proliferative, CTL, and antibody responses, compared with Gag protein, or Gag virus-like particles (VLP). GAG DNA was best for inducing CTL responses, Gag-PLG for T-help and antibody; the prime-boost combination gave strong responses for all three.				
Gag	Gag		HIV-1 infection	human (A*0201 and Cw*08)	Shacklett2000
	• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples.				
Gag			computer prediction	(A*0201, B*3501)	Schönbach2002
	Keywords inter-clade comparisons, computational epitope prediction. • Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.				
Gag	Gag		HIV-1 infection	human (B*35)	Jin2002
	Keywords rate of progression. • Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501. • Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env. • The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Gag			Vaccine	human (B60)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol **Keywords** inter-clade comparisons, vaccine-specific epitope characteristics. • Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 • HLA-B60 responses dominated the responses against an Gag vaccine in an individual (022G0Z) who was HLA A1, A11, B8, B60. The strongest response was against the MN peptide 107-136. Low level Gag responses were observed against B8 and A11 epitopes, no response was observed against A1 epitopes. • Vaccinee 202T7 (HLA A2, B27, C25) made the strongest response to an epitope at positions 131-140 of Gag. The response was highly cross-reactive with D clade Gag expressed from vaccinia, less so with C, and only minimally cross-reactive with A and CRF01.				
Gag	p24		Vaccine	mouse (H-2^b, H-2^d, H-2^k)	Iroegbu2000
	Vaccine *Vector/Type:* DNA *HIV component:* p17/p24 Gag • The p24 sequence is more conserved than is p17 within patient, and nonsynonymous substitutions are spread evenly throughout its coding regions, not concentrated in CTL epitopes. • Minor changes in p24 did not alter the immunogenicity in H-2b,d, or k mice, while changes in p17 (92% similarity) did alter immunogenicity.				
Gag	Gag (SF2)		Vaccine	mouse (H-2^{bxd})	Otten2000
	Vaccine *Vector/Type:* DNA, vaccinia *Strain:* B clade SF2 *HIV component:* Gag, Pol • CB6F1 were primed with gag DNA by im injection and challenged with vaccinia expressing Gag/Pol (rVVgag-pol)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Gag-specific CTL responses were detected by IFNgamma secretion in the spleen, independent of the route (intraperitoneal, intranasal or intrarectal) of rVV gag-pol challenge. • The gag DNA vaccine induced CTL responses in 4/4 monkeys 2 weeks post immunization, but antibody responses were detected in only 1/4 monkeys after 3 immunizations. • CTL cross-reactivity against Gag sequences 1-80, 254-323, and 421-496 was observed, suggesting multiple CTL epitope recognition.				
Gag	p24		Vaccine	mouse (H-2^d)	Qiu2000
	Vaccine *Vector/Type:* DNA *HIV component:* Gag • Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein. • Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors. • IFN-gamma levels were increased compared to an undetectable IL-4 response. • CTL levels were also increased in secreted Gag expression vaccination studies.				
Gag	Gag (SF2)		Vaccine	macaque, mouse (H-2^d)	zurMegede2000
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade SF2 *HIV component:* Gag, Protease • Sequence-modified Rev-independent gag and gag-protease gene constructs lead to increased expression levels and elevated CTL and antibody immunogenicity in BALB/c and CB6F1 mice. • A CTL response in mice could be detected after a single immunization with codon-optimized gag, using 2 ng of plasmid; wild type gag required 200 ng to detect a response. • Recognition of 3 different Gag peptide pools was observed, indicating a polyclonal CTL response. • Significant gag-specific CTL responses were detected in 4/4 rhesus monkeys, in contrast to 1/4 using wildtype gag.				
Gag	p24		Vaccine	mouse (H-2^d)	Halim2000
	Vaccine *Vector/Type:* coxsackievirus *HIV component:* p24 Gag • An avirulent recombinant coxsackievirus (CB4-P) construct was generated that can express p24 Gag sequences – CB4-P is attenuated even in immunodeficient mice and T help responses can be elicited from peptides embedded in a surface loop of the VP1 capsid. • This paper describes the vaccine strategy and generation of constructs, and employs amino-terminal fusion of Gag sequences to the viral polyprotein with subsequent cleavage to elicit CTL responses via MHC class I presentation in BALB/c mice.				
Gag	Gag		Vaccine	mouse (H-2^d)	Huang2001
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB2, B clade NL43 *HIV component:* Gag, Pol • Different HIV strains were used for different regions: gag HXB2, pol NL43 • Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct. • The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti-Pol CTL.				
Gag	Gag (HXB)		Vaccine	mouse (H-2^d, H-2^b)	Mata2001
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag **Keywords** Th1. • BALB/c and C57BL/6 mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CD4+ Th1 T-cells mediated the Gag specific immunological protection in mice immunized with Lm-Gag and challenged with vaccinia-Gag. • Gag-specific CTL may enhance viral clearance via IFN-gamma secretion, but are not essential for immunity.				
Gag	Gag		Vaccine	mouse (H-2^d, H-2^b)	Mata2000
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag **Keywords** review, Th1. • BALB/c and C57BL/6 mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • This article is a review of L. monocytogenes biology and its potential as a vaccine vector for HIV, comparing to other vector systems, and discussing CD4+ Th1 T-cells mediated Gag specific immunological protection in mice and the Gag CTL response.				

II-B-7 Gag/Pol CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag/Pol	Gag/Pol (ARV-2 SF2)		Vaccine	macaque	Kent2000
	Vaccine *Vector/Type:* fowlpoxvirus *Strain:* B clade ARV-2, B clade SF2 *HIV component:* Gag, Pol *Adjuvant:* IFN-gamma				
	• Vaccination with FPV Gag/Pol-IFN-gamma increased HIV-1 specific CTL and T cell proliferative responses to Gag/Pol antigens, respectively, in infected Macaca nemestrina.				
	• HIV-1 viral loads remained low and unchanged following vaccinations.				
Gag/Pol	RT		Vaccine	mouse	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12				
	• A Gag/Pol or Env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.				
	• When CD86 was present, CTL response could be detected even without *in vitro* stimulation.				
Gag/Pol	RT		HIV-1 infection	human	Gamberg1999
	Keywords TCR usage.				
	• 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens.				
	• Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR Vβ gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases.				
Gag/Pol			Vaccine	mouse	Muthumani2002
	Vaccine *Vector/Type:* adenovirus *HIV component:* Gag-Pol, Nef, Vpr				
	• Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens.				
	• Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol.				
	• In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.				

II-B-8 Protease CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Protease (3–11)	RT (71–79 subtype A, B, D) • C. Brander notes this is an A*6802 epitope.	ITLWQRPLV		human (A*6802)	Frahm2004
Protease (3–11)	Pol	ITLWQRPLV	HIV-1 infection, Vaccine	human (A*6802)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Protease (3–11)	Protease (71–79 LAI) **Keywords** inter-clade comparisons. • Predicted on binding motif, no truncations analyzed. • Clade A/B/D consensus, S. Rowland-Jones, pers. comm.	ITLWQRPLV		human (A*6802, A*7401, A19)	Dong1998a
Protease (3–11)	RT (71–79 subtype A, B, D) • C. Brander notes this is an A*7401 epitope.	ITLWQRPLV		human (A*7401)	Frahm2004
Protease (3–11)	Pol (59–)	ITLWQRPLV	HIV-1 infection, Vaccine	transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Protease *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol59. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.				
Protease (3–11)	Pol (59–65) • One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.	ITLWQRPLV	HIV-1 infection	human (A28)	Ferrari2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Protease (3–11)	RT (71–79 LAI)	ITLWQRPLV	HIV-1 infection	human (A28supertype)	Mollet2000
	Keywords HAART, supertype. **Epitope name** P2. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
Protease (3–11)	Pol	ITLWQRPLV	HIV-1 infection, HIV-1 exposed seronegative	human (A74)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ITLWQRPLV cross-reacts with clades A, B and D. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Protease (4–14)	Pol (60–70 SF2)	TLWQRPLVTIR	HIV-1 infection, computer prediction	human (A*3303)	Hossain2003
	Keywords binding affinity, computational epitope prediction. **Assay type** Chromium-release assay. • HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing. • This epitope is one of the 4 that are properly processed.				
Protease (11–20)	Pol (91–100)	VTILIGGQLK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
Protease (12–20)	Pol (92–100)	TIKIGGQLK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Protease (30–38)	Pol (subtype B)	DTVLEEMNL	HIV-1 exposed seronegative	human (A*6802)	Rowland-Jones1998b
	Keywords inter-clade comparisons.				
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi—these CTL may confer protection.				
	• Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.				
	• Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.				
	• This epitope is conserved among B and D clade viruses.				
	• The Clade A version of the epitope: DTVLEDINL.				
	• This epitope was recognized by two different exposed and uninfected prostitutes.				
	• This epitope was identified by screening 49 HIV-1 peptides with the predicted A*6802 anchor residue motif x(VT)xxxxxx(VL)				
Protease (30–38)	Pol (subtype A)	DTVLEDINL	HIV-1 exposed seronegative	human (A*6802)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 IFNγ responses in the cervix—systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses.				
	• Low risk individuals did not have such CD8+ cells.				
	• CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
Protease (30–38)	RT (85–93 subtype D)	DTVLEEWNL		human (A*6802)	Frahm2004
	• C. Brander notes this is an A*6802 epitope.				
Protease (30–38)	Pol (subtype A)	DTVLEDINL	HIV-1 infection	human (A*6802)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS), escape.				
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.				
	• DTVLEDINL was recognized in 3 of the 6 women (ML857, ML1203, and ML1707), and the response was present in the last available sample prior to seroconversion, 3-7 months.				
	• In each of the three women, 20/20 sequences of the infecting strain had no substitutions in this epitope, all were DTVLEDINL, so there was no evidence for escape.				
	• The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire.				
	• This epitope was recognized in 3/22 HEPS sex worker controls, ML851, ML1432, and ML1601.				
Protease (30–38)	Pol (85–93)	DTVLEDINL	HIV-1 infection, HIV-1 exposed seronegative	human (A*6802)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance.				
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
	• Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women.				
	• 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.				
	• Among HLA-A*6802 women, 11/12 HEPS and 6/11 HIV-1 infected women recognized this epitope likelihood ratio 4.4, p value 0.08, and HEPS women tended to respond to DTVLEDINL, infected women tended to ETAYFYILKL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The dominant response to this HLA allele was to this epitope in 10 of the 11/12 HEPS cases, but in only 4 of the 6/11 HIV-1 infected women. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort. • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24. • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion, and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes. • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV. • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion, and the loss of the pre-seroconversion response was not due to sequence variation within the epitope. • Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAYFILKL post-seroconversion.			
Protease (30–38)	Pol	DTVLEDINL	HIV-1 infection	human (A*6802)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
Protease (34–42)	Protease (34–42)	EEMNLPGRW		human (B*44)	Frahm2004
Protease (45–54)	Pol (125–134)	KMIGGIGGFI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
Protease (75–84)	Protease (75–84 MN)	VLVGPTPVNI	in vitro stimulation or selectio	human (A*0201)	Konya1997
	Keywords binding affinity. • Peptide predicted to be reactive based on HLA-A*0201 binding motif. • Peptide could stimulate CTL in PBMC from 5/6 seronegative donors. • Peptide located in a highly conserved region of protease. • Both 9-mer and 10-mer could stimulate CTL: VLVGPTPVNI and LVGPTPVNI. • Binding affinity to A*0201 was measured, $C_{1/2\ max}\mu M = 6$ for 10-mer, 3 for 9-mer. • MAL variant of Pr(75-84 MN), with substitutions V77, G78, and P79, gave reduced binding and CTL recognition.				
Protease (76–84)	Pol (163–)	LVGPTPVNI	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name Pol-163. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • LVGPTPVNI binds to 4/5 HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802, but not A*0203. • 1/22 individuals with chronic HIV-1 infection recognized this epitope by ELISPOT. • 0/12 acutely infected individuals recognized this epitope.				
Protease (76–84)	Protease (76–84 HXB2)	LVGPTPVNI	HIV-1 infection	human (A2)	Karlsson2003
	Keywords HAART, escape. **Epitope name** PR82V. **Assay type** Intracellular cytokine staining, Chromium-release assay. • This epitope contains two positions that are commonly associated with protease inhibitor escape, lvgptpAni (V82A) and lvgptpvnV (I84V). 29 HIV-1 infected patients (15 were HLA-A2+) with a history of protease inhibitor failure were screened for mutations within the protease gene and CD8+ T cells recognition of the wt and V82A variant peptides. CTL pressure alone, despite high functional avidity, did not drive the V82A substitution. Suprisingly V82A was found more frequently among HLA-A2- individuals (10/14) than HLA-A2+ (7/15), despite the mutation conferring not only drug resistance but CTL escape. • 8/15 HLA-A2+ patients carried had a Val at position 82; 7/8 of these recognized the WT peptide, but only 3/8 could also recognize V82A. • 7/15 had the V82A substitution; 2/7 recognized the wt and the V82A mutation, 1/7 recognized only the peptide with the V82A substitution.				
Protease (76–84)	Pol (156–164)	LVGPTPVNI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				

II-B-9 Protease-RT CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Protease-RT (95–5)	Gag (175–184)	CTLNFPISPI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • The epitope starts in Protease and ends in RT. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				
Protease-RT (96–5)	Pol (176–184)	TLNFPISPI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				

II-B-10 RT CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (3–12)	RT (LAI)	SPIETVPVKL	HIV-1 infection	human (A2, B61)	vanderBurg1997
	• Recognized by CTL from a long-term survivor, EILKEPVGHGV was also recognized. • Highly conserved across clades.				
RT (3–12)	Pol	SPIETVPVKL		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay. • SPIETVPVKL was newly identified as HLA-B7 epitope in this study, it had been previously shown to be presented by HLA-A2 and B61.				
RT (5–12)	RT (5–12)	IETVPVKL	HIV-1 infection	human (B*4001)	Frahm2004
RT (5–29)	RT (160–184 HXB2)	IETVPVKLKPGMDGPKVKQ-WPLTEE	HIV-1 infection	human (B8)	Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study.				
RT (18–26)	RT (185–193 LAI)	GPKVKQWPL		human (B*0801)	Frahm2004
	• C. Brander notes this is a B*0801 epitope.				
RT (18–26)	RT (18–26)	GPKVKQWPL	HIV-1 infection	human (B8)	Meier1995, Menendez-Arias1998
	• HIV proteins with mutations in this epitope allowed transactive inhibition of specific CTL-mediated lysis. • Article reviewed in [Menendez-Arias1998], with a discussion of antagonism.				
RT (18–26)	RT (173–181)	GPKVKQWPL		human (B8)	Goulder1997g, Menendez-Arias1998
	• Included in a study of the B8 binding motif. • Article reviewed in [Menendez-Arias1998], with a discussion of antagonism.				
RT (18–26)	RT (185–193 LAI)	GPKVKQWPL		human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE.				
RT (18–26)	RT (185–193 LAI)	GPKVKQWPL	HIV-1 infection	human (B8)	Klenerman1995, Menendez-Arias1998
	• Naturally occurring antagonist GPRVKQWPL found in viral PBMC DNA and RNA. • Article reviewed in [Menendez-Arias1998] with a discussion of antagonism.				
RT (18–26)	RT (18–26)	GPKVKQWPL	in vitro stimulation or selectio	human (B8)	Zarling1999
	Keywords dendritic cells. • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses. • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA. • A weak response to KLTPLCVSL was stimulated using macrophages as the APC.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.				
RT (18–26)	RT (185–193)	GPKVKQWPL	HIV-1 infection	human (B8)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, escape, acute infection. **Epitope name** GPK. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • Two of the 7/8 study subjects that were HLA B8+ recognized this epitope. • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones. • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy.			
RT (18–26)	Pol	GPKVKQWPL	HIV-1 infection	human (B8)	Seth2001
	Keywords HAART. • CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized.				
RT (18–26)	RT (185–193 SF2)	GPKVKQWPL	HIV-1 infection	human (B8)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/3 group 2, and 2/2 group 3.				
RT (18–26)	Pol (171–180)	GPKVKQWPL	HIV-1 infection, HIV-1 exposed seronegative	human (B8)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • GPKVKQWPL is cross-reactive for clades A, B, C, and D. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
RT (18–26)	RT (18–26)	GPKVKQWPL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
RT (18–26)	RT	GPKVKQWPL	HIV-1 infection	human (B8)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** GPK.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
RT (18–27)	Pol	GPKVKQWPLT		human (B7, B8)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay. • GPKVKQWPLT was confirmed as a previously identified HLA-B8 epitope, and newly identified as an HLA-B7 epitope in this study.				
RT (33–41)	RT (33–41 LAI)	ALVEICTEM	HIV-1 infection	human (A*0201)	Frahm2004
	• C. Brander notes this is an A*0201 epitope.				
RT (33–41)	RT (33–41 LAI)	ALVEICTEL	HIV-1 infection	human (A*0201)	Samri2000
	Keywords binding affinity, computational epitope prediction. • This epitope contains the mutation M41L, a mutation induced by nucleosidee reverse transcriptase inhibitors. • Patient 201#5, (A*0201), was found by ELISPOT to recognize the mutated peptide after zidovudine treatment, but not the wild-type peptide – the mutation M41L gave an increased A2 binding score (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence. • Three additional A*0201 individuals and one B27 individual did not respond to this epitope before or after treatment. • M41L occurred at anchor positions p2 and p9 in several computer predicted RT epitopes (33-41, 32-41, and 40-49) (http//bimas.dcrt.nih.gov/molbio/hla_bind), and increased the predicted binding affinity for 6 HLA molecules (B2705, B5102, C3, A0201, B2705 and B3901)				
RT (33–41)	RT (33–41)	ALVEICTEM	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.				
RT (33–41)	RT (33–41)	ALVEICTEM	HIV-1 infection	human (A2)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes and who had a dominant A-2 response to ALVEICTEM.				
RT (33–43)	RT (33–43)	ALVEICTEMEK	HIV-1 infection	human (A*0301)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules. • C. Brander notes that this is an A*0301 epitope in the 1999 database, G. Haas, pers. comm.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (33–43)	RT (33–43)	ALVEICTEMEK	HIV-1 infection	human (A*0301)	Frahm2004
	• C. Brander notes this is an A*0301 epitope.				
RT (33–43)	RT (33–43)	ALVEICTEMEK	HIV-1 infection	human (A3)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.				
RT (38–52)	RT (203–209)	CTEMEKEGKISKIGP	Vaccine	mouse (H-2^{d})	Burnett2000
	Vaccine *Vector/Type:* Salmonella *HIV component:* RT • A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV epitope in the Lpp-OmpA-HIV fusion protein, induced a specific CTL response in BALB/c mice (<15% lysis assayed by Cr-release of target cells)				
RT (38–52)	RT (205–219 BRU)	CTEMEKEGKISKIGP	Vaccine	mouse (H2^{k})	De Groot1991, Menendez-Arias1998
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT **Keywords** review. • Murine and human helper and CTL epitope. • Epitope noted in a review by [Menendez-Arias1998] to be located in the "fingers" domain of RT and is a helper and CTL epitope.				
RT (38–52)	RT (205–219)	CTEMEKEGKISKIGP	HIV-1 infection	human (broad)	Hosmalin1990, Menendez-Arias1998
	Keywords review. • Murine and human helper and CTL epitope. • Epitope noted in a review by [Menendez-Arias1998] to be located in the "fingers" domain of RT and is a helper and CTL epitope.				
RT (39–47)	RT (206–214)	TEMEAEGKI	in vitro stimulation or selectio	mouse	Leggatt1997
	Keywords TCR usage. • Ala-substituted nonamer-peptide used to test a non-radioactive assay for murine CTL recognition of peptide-MHC class I complexes. • The new assay is CTL adherence assay (CAA), and is based on the discovery that CTL develop adhesive properties upon TCR triggering. • Substitutions in TEMEAEGKI that reduce cytolytic activity were correctly detected by CAA.				
RT (39–47)	RT	TEMEKEGKI		mouse (H-2K^{k})	Leggatt1998
	• Epitope variants were examined for CTL response in concert with H-2K^{k} MHC class I binding – all of the following combinations were observed: (i) two single mutations which did not alone abrogated CTL activity did abrogate activity when combined, (ii) loss of recognition of a single substitution could be restored by an additional substitution, and (iii) sometimes there was recognition of two single substitutions as well as the combination of those substitutions. • 2E and 9I are anchor residues for H-2K^{k} – if you have M in the third position, it enhances H-2K^{k} binding 10-fold, but polymorphism at this site is important for the overall conformation of the peptide and can influence T cell recognition.				
RT (42–50)	RT (42–50 LAI)	EKEGKISKI	HIV-1 infection	human (B*5101)	Frahm2004
	• C. Brander notes this is a B*5101 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (42–50)	RT (42–50 LAI)	EKEGKISKI	HIV-1 infection	human (B51)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.				
RT (57–65)	Pol (236–244)	NTPVFAIKK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
RT (73–82)	RT (73–82)	KLVDFRELNK	HIV-1 infection	human (A*03)	Frahm2004
RT (73–82)	RT (73–82 LAI)	KLVDFRELNK	HIV-1 infection	human (A3)	Samri2000
	• This epitope contains the mutation L74V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors. • The wild-type, but not the mutated peptide, was recognized before and after zidovudine treatment in A3-restricted patients 252#0 and 252#4. • Mutation L74V affects the p2 anchor position in RT epitopes and was predicted to reduce binding to A3 (http://bimas.dcrt.nih.gov/molbio/hla_bind)				
RT (73–82)	RT (228–237)	KLVDFRELNK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-KK10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 3/7 individuals began to have detectable responses to this epitope after STI.				
RT (93–101)	(LAI)	GIPHPAGLK		(A3)	Altfeld2000a, Frahm2004
RT (93–101)	RT (248–257)	GIPHPAGLK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-GK9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (93–102)	Pol (240–249 93TH253 subtype CRF01)	GIPHPAGLKK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P248-257. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11 and after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33.				
RT (93–102)	Pol (240–249 93TH253 subtype CRF01)	GIPHPAGLKK	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it. • This epitope was highly conserved in other subtypes, and exact matches were common.				
RT (98–113)	Pol (254–264 BH10, LAI)	AGLKKKKSVTVLDVGD	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is GLKKKKSVTVL) has similarity with the CD166 antigen (activated leukocyte-cell adhesion molecule), fragment GLKKRESLTLI.				
RT (98–113)	RT (252–266)	AGLKKKKSVTVLDVGD	HIV-1 infection	human (Cw4)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population. • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.				
RT (103–117)	RT (257–251)	KKSVTVLDVGDAYFS	HIV-1 infection	human (Cw4)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune. • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.				
RT (107–115)	RT (262–270 IIIB)	TVLDVGDAY		(B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
RT (107–115)	RT (262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human (B35)	Menendez-Arias1998, Wilson1996
	Keywords review, responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • TVLDMGDAC is a naturally occurring variant that is less reactive. • [Menendez-Arias1998], in a review, notes that this epitope includes a catalytic residue (Asp-110) in the active site of RT.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (107–115)	Pol (262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human (B35)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • An additional variant that gave a positive CTL response: TVLDMGDAC.				
RT (107–115)	Pol (262–270)	TVLDVGDAY	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (107–115)	RT (262–270 SF2)	TVLDVGDAY	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3.				
RT (107–115)		TVLDVGDAY	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Pol-TY9. • Among HIV+ individuals who carried HLA B35, 8/21 (38%) recognized this epitope.				
RT (107–115)	Pol	TVLDVGDAY	HIV-1 infection	human (B35)	Sabbaj2002a
	Keywords mother-to-infant transmission. **Donor HLA** A3, A11, B35, B51. • IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with either of two overlapping peptides that carry known B35 epitope TVLDVGDAY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
RT (108–118)	RT (267–277)	VLDVGDAYFSV	in vitro stimulation or selectio	human (A*0201)	vanderBurg1996
	• High dissociation rate, but immunogenic in primary CTL induction after repeated stimulations with peptide. • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.				
RT (108–118)	RT (267–277)	VLDVGDAYFSV	HIV-1 infection	human (A2)	Kundu1998b
	Keywords dendritic cells. • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated. • VLDVGDAYFSV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, but only one of these had a detectable CTL response – the other two had the sequences EEDVGDAYFSV and ELDVGDAYFSV and no detectable CTL response.				
RT (108–118)	RT (267–277)	VLDVGDAYFSV	in vitro stimulation or selectio	human (A2)	vanderBurg1995
	• Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor. • VLDVGDAYFSV is in a functional domain.				
RT (108–118)	Pol (263–273)	VLDVGDAYFSV	HIV-1 infection	human (A2, A*0201)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (108–122)	RT (257–251)	VLDVGDAYFSVPLDE	HIV-1 infection	human (Cw4)	Bernard1998
	• This study focuses on six rare long-term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population. • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs.				
RT (113–120)	Pol (268–275 SF2)	DAYFSVPL	HIV-1 infection	human (B*5101, B24)	Tomiyama1999
	Keywords inter-clade comparisons, rate of progression. • HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA -B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed. • Four of the six epitopes were highly conserved among B subtype sequences, DAYFSVPL is conserved.				
RT (116–135)	Pol (271–290)	FSVPLDEDFRKYTAFTIPSI	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
RT (117–126)	Pol (264–273 93TH253 subtype CRF01)	SVPLDESFRK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P272-281. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (117–126)	Pol (264–273 93TH253 subtype CRF01)	SVPLDESFRK	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 3/8 tested FSWs recognized it. • This epitope was only conserved in CRF01, and subtype A and B, and exact matches were uncommon.				
RT (118–127)	RT (273–282 SF2)	VPLDKDFRKY	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	Keywords review. • A CTL clone responsive to this epitope was obtained. • 4/7 B35-positive individuals had a CTL response to this epitope. • A K to E substitution at position 5 abrogates specific lysis, and reduces binding to B*3501. • [Menendez-Arias1998], in a review, notes that a Glu to Lys (E to K) change abrogates CTL activity, but that both VPLDEDFRKY and VPLDKDFRKY can serve as HLA-B35 epitopes, so the change must alter T cell receptor binding – residues in this epitope may be important for polymerase activity.				
RT (118–127)	RT (273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
RT (118–127)	Pol (273–282)	VPLDKDFRKY	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A. • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals. • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm. • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
RT (118–127)	(SF2)	VPLDEDFRKY	HIV-1 infection	human (B*3501)	Tomiyama2000b
	Epitope name HIV-B3501-SF2-4. • B*3501 VPLDEDFRKY tetramer binding did not inhibit CTL activity of a clone that react with both HLA-B*3501 than HLA-B*5101 presentation of the epitope IPLTEEAEL.				
RT (118–127)	RT (118–127)	VPLDEDFRKY	HIV-1 infection	human (B*3501)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*2301, B*3501, B*1503 (B72), Cw2, Cw7. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
RT (118–127)	RT (273–282 IIIB) • Binds HLA-B*3501.	VPLDEDFRKY	HIV-1 infection	human (B*3501, B35)	Shiga1996
RT (118–127)	(SF2) **Keywords** binding affinity, rate of progression, escape. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation. • ––E–– was found in 8/10 of the B35+ individuals, and three of the B35- individuals – the D –> E substituted peptide had similar binding affinity to B35 and was equally susceptible to a CTL clone.	VPLDKDFRKY	HIV-1 infection	human (B35)	Kawana1999
RT (118–127)	RT (273–282 IIIB) **Keywords** inter-clade comparisons. • HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB. • VPLDKDFRKY, a variant found in HIV MN, was not recognized. • VPHDEDFRKY, a variant found in HIV YU2, was not recognized. • This epitope was type-specific and conserved in only one other B subtype sequence.	VPLDEDFRKY	HIV-1 infection	human (B35)	Sipsas1997
RT (118–127)	RT (273–282 SF2) **Keywords** HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3.	VPLDEDFRKY	HIV-1 infection	human (B35)	Altfeld2001b
RT (118–127)	**Epitope name** Pol-VY10. • Among HIV+ individuals who carried HLA B35, 5/21 (24%) recognized this epitope.	VPLDEDFRKY	HIV-1 infection	human (B35)	Sabbaj2002b
RT (126–135)	RT (293–302 HXB) **Keywords** HAART. • A novel CTL clone was defined with a panel of recombinant vaccinia-RT-infected B-LCL target cells using PBMCs donated by a patient who was HIV-seropositive for 6 years and had not received any antiretroviral therapy. • There is evidence that some CTL epitopes are poorly presented on the surface of infected cells, but this RT epitope was recognized as effectively on HIV-infected cells as on peptide-pulsed targets.	KYTAFTIPSI	HIV-1 infection	human (A2)	Shankar1998

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (127–135)	RT (127–135)	YTAFTIPSV	HIV-1 infection	human (A*02)	Frahm2004
RT (127–135)	Pol (316–)	YTAFTIPSI	HIV-1 infection	human (A2)	Altfeld2001c

Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction.
Epitope name Pol-316.

- HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested.
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2)
- 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT.
- 0/12 acutely infected individuals recognized this epitope.
- YTAFTIPSI binds to five HLA-A2 supertype alleles: A*0201, A*0202,A*0203, A*0206 and A*6802 (highest affinity)

RT (127–135)	Pol (306–314)	YTAFTIPSI	HIV-1 infection	human (A2 supertype)	Propato2001

Keywords supertype, rate of progression.

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes.
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs.
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.
- This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

RT (128–135)		TAFTIPSI	HIV-1 infection	human (A*0217, B*5101)	Sabbaj2002b

Keywords HAART.
Epitope name Pol-TI8.
Donor HLA A*0201 A*0217 B*0801 B*4002 Cw*0303 Cw*070.

- This study monitored epitope responses in HIV-1 infected minority women living in the United States.
- 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described.
- Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release.
- Patient 01RCH46 was Hispanic, on HAART, and had a viral load of 21000 and CD4 count of 623 – she also recognized GELDRWEKI, p17(11-19), HLA B*4002, and KETINEEAA p24(70-78), HLA B*4002.
- Among HIV+ individuals who carried HLA A*02, 7/36 (19%) recognized this epitope, two of which also carried B*5101 which can also restrict this epitope.

RT (128–135)	RT (295–302 IIIB)	TAFTIPSI	HIV-1 infection	human (B*5101)	Frahm2004

- C. Brander notes this is a B*5101 epitope.

RT (128–135)	Pol (283–290 SF2)	TAFTIPSI	HIV-1 infection	human (B*5101)	Tomiyama1999

Keywords inter-clade comparisons, rate of progression.

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed. • Four of the six epitopes were highly conserved among B subtype sequences, but TAFTIPSI is somewhat variable.				
RT (128–135)	RT (295–302) **Keywords** HAART, escape. **Epitope name** P5. • The epitope TAFTIPSI was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition.	TAFTIPSI	HIV-1 infection	human (B*5101)	Samri2000
RT (128–135)	RT (128–135 IIIB) **Keywords** epitope processing, escape. • HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • TAFTIPSI was one of two epitopes characterized in detail. C-terminal I135x substitutions were associated with people who carried HLA-B5 – 39/40 (98%) of HLA-B*5101 individuals had substitutions in this position, while only 127/431 (29%) who did not have HLA-B*5101 did. The predominant substitution was kytaftipsT, and this mutation is predicted to abrogate binding to HLA-B*5101.	TAFTIPSI	HIV-1 infection	human (B*5101)	Moore2002b
RT (128–135)	RT (295–302 IIIB) **Keywords** review. • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • TAFTIPST, a variant found in HIV-1 CAM1, was also recognized but 100-fold more peptide was needed. • TAFTIPSV, a variant found in HIV-1 VE1RT, was also recognized, but 10-fold more peptide was needed. • TVFTIPSI, a variant found in HIV-1 MANC, was also recognized. • [Menendez-Arias1998], in a review, notes that this epitope includes a region near the active site of RT – the substitution of the position two conservative change from A to V decreases CTL recognition.	TAFTIPSI	HIV-1 infection	human (B51)	Menendez-Arias1998, Sipsas1997
RT (128–135)	RT (295–302) **Keywords** immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • Three of the four individuals that responded to SLYNTVATL recognized additional HIV epitopes, and all three were also HLA B51 and recognized this epitope as well as other epitopes.	TAFTIPSI	HIV-1 infection	human (B51)	Betts2000
RT (128–135)	RT (295–302) **Keywords** HAART, acute infection. **Epitope name** TAF. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B51+	TAFTIPSI	HIV-1 infection	human (B51)	Oxenius2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (128–135)	RT (295–302 LAI) **Keywords** HAART. **Epitope name** P5. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.	TAFTIPSI	HIV-1 infection	human (B51)	Mollet2000
RT (128–135)	Pol **Keywords** mother-to-infant transmission. **Donor HLA** A3, A11, B35, B51. • IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with either of two overlapping peptides that carry known B51 epitope TAFTIPSI. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.	TAFTIPSI	HIV-1 infection	human (B51)	Sabbaj2002a
RT (128–135)	RT (128–135) **Keywords** binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A11, B51, b61, Cw2, Cw14. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.	TAFTIPSI	HIV-1 infection	human (B51)	Cao2003
RT (151–159)	Pol (306–314 SF2) **Keywords** inter-clade comparisons, rate of progression. • HLA-B27, -B51, and -B57 are associated with slow progression to AIDS. • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed. • Four of the six epitopes were highly conserved among B subtype sequences, QGWKGSPAI is conserved.	QGWKGSPAI	HIV-1 infection	human (B*5101)	Tomiyama1999

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (151–168)	RT (151–168 HXB2)	QGWKGSPAIFQSSMTKIL	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.			
RT (153–165)	RT (308–320)	WKGSPAIFQSSMT	HIV-1 infection	human (B7)	Brander1995b
	Keywords responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.				
RT (153–165)	Pol (308–320)	WKGPAIFQSSMT	HIV-1 infection	human (B7)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (153–167)	RT (SF2)	WKGSPAIFQSSMTKI	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized.				
RT (156–164)	RT (311–319 SF2)	SPAIFQSSM	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	Keywords review. • A CTL clone responsive to this epitope was obtained. • Only 1/7 B35-positive individuals had a CTL response to this epitope. • [Menendez-Arias1998], in a review, notes that this epitope is near the active site of RT.				
RT (156–164)	RT (311–319 SF2)	SPAIFQSSM	HIV-1 infection	human (B35)	Menendez-Arias1998, Shiga1996
	Keywords review. • Binds HLA-B*3501. • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues in the active site of RT.				
RT (156–164)	Pol (311–319)	SPAIFQSSM	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (156–164)	Pol (156–164 HXB2)	SPAIFQSSM	HIV-1 infection	human (B7)	Hay1999b
	Keywords rate of progression, immunodominance. • CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201. • The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted. • Despite the initial narrow response to two epitopes, no other CTL responses developed. • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak. • Variants of this epitopes were observed *in vivo* (spaifqCsm, spSifqssm), but the binding motifs for B7 were preserved (P2, and C-term aromatic or hydrophobic)				
RT (156–164)	Pol	SPAIFQSSM	HIV-1 infection	human (B7)	Islam2001
	Keywords rate of progression, acute infection. • Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS. • This individual had a dominant response to IPRRIRQGL with strong *in vivo* activated responses and *in vitro* stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred with in both epitopes, but CTL clones specific for IPRRIRQGL persisted throughout.				
RT (156–164)	RT (323–331 SF2)	SPAIFQSSM	HIV-1 infection	human (B7)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.				
RT (156–164)	RT (156–164)	SPAIFQSSM	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-SM9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.				
RT (156–165)	RT (311–319 LAI)	SPAIFQSSMT	HIV-1 infection	human (B35)	Samri2000
	Keywords HAART, escape. **Epitope name** P4. • This epitope contains the mutation P157S which can be induced by nucleosidee reverse transcriptase inhibitors. • It was recognized by patient 252#0 in a study of the effects of therapy escape mutations on CTL recognition.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (156–165)	RT (311–319 SF2)	SPAIFQSSMT		human (B7)	Brander1997, Menendez-Arias1998
	Keywords review. • Pers. comm. from C. Hey and D. Ruhl to C. Brander and B. Walker. • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues in the active site of RT.				
RT (156–165)	RT (311–319 SF2)	SPAIFQSSMT	HIV-1 infection	human (B7)	Mollet2000
	Keywords HAART. **Epitope name** P4. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
RT (156–165)	Pol	SPAIFQSSMT		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay. • SPAIFQSSMT was confirmed as a previously identified HLA-B7 epitope in this study.				
RT (156–165)	RT (IIIB)	SPAIFQSSMT	HIV-1 infection	human (B7)	Moore2002b
	Keywords epitope processing, escape. • HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • HLA-B7+ individuals with a S162x (18/33) substitution had higher viral loads than those that did not, suggesting escape was associated with diminished immune control of viremia.				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A*0301)	Frahm2004
	• C. Brander notes this is an A*0301 epitope.				
RT (158–166)	Pol	AIFQSSMTK	HIV-1 infection, Vaccine	human, macaque (A*0301, A11, A33)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A*1101)	Frahm2004
	• C. Brander notes this is an A*1101 epitope.				
RT (158–166)	Pol (313–321)	AIFQSSMTK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • AIFQSSMTK is commonly found in viruses representing subtypes A-E. It was strongly recognized by CTL from 2/5 B clade infected Japanese subjects, and 5/6 E clade infected Thai subjects.				
RT (158–166)	RT (325–333)	AIFQSSMTK	HIV-1 infection	human (A*1101, A3, A*0301, A*6801)	Menendez-Arias1998, Threlkeld1997
	• Study of the fine specificity of an A3-like super-type epitope (the A3 super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801) • A3 super-type is characterized by a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position. • While most lines were specific, promiscuous cloned CTL lines were also derived from HIV+ donors that could recognize epitope presented by either A3 or A11 or A*6801. • Alanine substitutions throughout the epitope and natural variants indicate that the same amino acid positions are critical for presentation by either MHC molecule, A3 or A11. • AIFQSSMTK is presented by three members of the A3 superfamily: A*0301, A*1101, and A*6801, and the naturally occurring variants A1S and K9R are recognized with similar efficiency to wild type epitope – AIFQRSMTR can also bind to two additional members of the A3 superfamily, A*3101 and A*3301.				
RT (158–166)	RT	AIFQSSMTK	HIV-1 infection	human (A11)	Wagner1998a
	• CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	Peptide-HLA interaction	human (A11)	Menendez-Arias1998, Zhang1993
	• Exploration of A11 binding motif, based on Nixon *et al.* 1991.				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A11)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes.				
RT (158–166)	Pol (305–313 93TH253 subtype CRF01)	AIFQSSMTK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P313-321. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33. • This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.				
RT (158–166)	Pol (305–313 93TH253 subtype CRF01) **Keywords** inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined. • 6/8 tested FSWs recognized this epitope. • An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – and both subjects had expanded tetramer staining T-cell populations after *in vitro* stimulation. • This epitope was highly conserved in other subtypes, and exact matches were common.	AIFQSSMTK	HIV-1 infection	human (A11)	Bond2001
RT (158–166)	RT (158–166 IIIB) **Keywords** epitope processing, escape. • HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • HLA-A11+ individuals with a K166x (4/19) substitution had higher viral loads than those that did not, suggesting escape was associated with diminished immune control of viremia.	AIFQSSMTK	HIV-1 infection	human (A11)	Moore2002b
RT (158–166)	Pol **Keywords** HAART. **Donor HLA** A2,A11,B8,B60,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.	SIFQSSMTK	HIV-1 infection	human (A11)	Appay2002
RT (158–166)	RT (325–333 IIIB) **Keywords** responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • AIFQSSMTR and AILQSSMTK, naturally occurring variants, were found in infant, and are recognized. • TISQSSMTK, a naturally occurring variant, was found in infant and is not recognized.	AIFQSSMTK	HIV-1 infection	human (A3)	Wilson1996
RT (158–166)	RT (325–333 LAI) **Keywords** inter-clade comparisons.	AIFQSSMTK	HIV-1 infection	human (A3)	Cao1997a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The consensus peptide of B and D clade viruses is AIFQSSMTK. • The consensus peptide of a subset of As is AIFQASMTK and it is less able to stimulate the CTL clone. • The consensus peptide of a subset of As is SIFQSSMTK and is as reactive as the originally defined epitope.				
RT (158–166)	Pol (325–333 IIIB)	AIFQSSMTK	HIV-1 infection	human (A3)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • One variant found in an infant gave a positive CTL response: AIFQSSMTR. • AIFLSSMTK and TISQSSMTK were escape mutants.				
RT (158–166)	RT (325–333 SF2)	AIFQSSMTK	HIV-1 infection	human (A3)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 0/7 group 1, 0/4 group 2, and 1/2 group 3.				
RT (158–166)	RT (158–166)	AIFQSSMTK	HIV-1 infection	human (A3)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant. • In two of the subjects, AIFQSSMTK was the dominant epitope.				
RT (158–166)	RT Pol (313–321)	AIFQSSMTK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-ATK9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 3/7 individuals began to have detectable responses to this epitope after STI.				
RT (158–166)	Pol (337–345)	AIFQSSMTK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
RT (158–166)	Pol (313–321)	AIFQSSMTK	HIV-1 infection	human (A3, A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (158–166)	Pol (325–333)	AIFQSSMTK	HIV-1 infection, HIV-1 exposed seronegative	human (A3, A11, A33)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • Variants (S/A)IFQSSMTK are specific for the A/B clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-A3 women, 2/2 HEPS and 3/3 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in one of the 2/2 HEPS cases and in one of the 3/3 HIV-1 infected women.				
RT (158–166)	RT (325–333)	AIFQSSMTK	HIV-1 infection	human (A3.1)	Brander1995b
	Keywords responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.				
RT (158–166)	RT (325–333)	AIFQSSMTK	HIV-1 infection	human (A3.1)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A3 and reacted with this epitope as well as two other A3.1 epitopes.				
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK		human (A33)	Rowland-Jones1995a
	• Defined as minimal peptide by titration curve, S. Rowland-Jones, pers. comm.				
RT (158–166)		AIFQSSMTK	HIV-1 infection	human (A33)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls, ML1668.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (158–166)	RT (325–333 LAI)	AIFQSSMTK	HIV-1 infection	human (A3supertype)	Mollet2000
	Keywords HAART, supertype. **Epitope name** P3. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
RT (158–166)		AIFQSSMTK	HIV-1 infection	human (B*0301)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
RT (158–182)	RT (325–349 PV22)	AIFQSSMTKILEPFRKQNP-DIVIYQ	HIV-1 infection	human (A11)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.				
RT (158–182)	RT (325–349)	AIFQSSMTKILEPFRKQNP-DIVIYQ	HIV-1 infection	human (A11)	Price1995
	• Study of cytokines released by HIV-1 specific activated CTL.				
RT (164–172)	Pol (343–351)	MTKILEPFR	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 4/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
RT (173–181)	RT (173–181 LAI)	KQNPDIVIY		human (A*3002)	Frahm2004, Goulder2001a
	• C. Brander notes this is an A*3002 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (173–181)	RT	KQNPDIVIY	HIV-1 infection	human (A*3002)	Goulder2001a
	Epitope name KY9 (RT-53). • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule. • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood. • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean. • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant. • In subject 199 four additional A*3002 epitopes were identified. • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)			
RT (175–183)	RT (328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained. • 3/7 B35-positive individuals had a CTL response to this epitope. • D to E, or V to I, substitutions at positions 3 or 5, respectively, reduces CTL activity and binding to B*3501.				
RT (175–183)	RT (328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
RT (175–183)	RT (342–350 LAI)	HPDIVIYQY	HIV-1 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
RT (175–183)	Pol (330–338)	NPDIVIYQY	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A. • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals. • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm. • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)			
RT (175–183)	RT (175–183 IIIB)	NPDIVIYQY	HIV-1 infection	human (B*3501)	Moore2002b
	Keywords epitope processing, escape. • HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing. • NPDIVIYQY was one of two epitopes characterized in detail. D177x substitutions are know to specifically abrogate binding to HLA-B*3501, and not other B*35 subtypes. D177x substitutions were associated with people who carried HLA-B*3501 and not other B*35 subtypes; considering high resolution typing generally strengthened the B*35 associations.			
RT (175–183)	RT (175–183)	NPDIVIYQY	HIV-1 infection	human (B*3501)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA A*2301, B*3501, B*1503 (B72), Cw2, Cw7. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ INFγ T-cell responses in 21 men within 15-92days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFNγ secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
RT (175–183)	RT (342–350 LAI) **Keywords** review. • Review of HIV CTL epitopes.	HPDIVIYQY	HIV-1 infection	human (B35)	McMichael1994
RT (175–183)	RT (329–337) • NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized.	HPDIVIYQY	HIV-1 infection	human (B35)	Rowland-Jones1995b
RT (175–183)	(SF2) **Keywords** binding affinity, rate of progression, escape. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation. • npEiviyqy was found in 8/10 of the B35+ individuals, and two of the B35- individuals—the D–>E substituted peptide had reduced binding affinity to B35 and may be an escape mutant.	NPDIVIYQY	HIV-1 infection	human (B35)	Kawana1999
RT (175–183)	RT (329–337) • A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers. • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.	HPDIVIYQY	in vitro stimulation or selectio	human (B35)	Lalvani1997
RT (175–183)	RT (328–336 IIIB) • Binds HLA-B*3501. • CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding [Menendez-Arias1998]	NPDIVIYQY	HIV-1 infection	human (B35)	Menendez-Arias1998, Shiga1996
RT (175–183)	RT (328–336 IIIB) **Keywords** review, escape. • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • NPDIIIYQY, a variant found in HIV-1 JRCSF, was also recognized. • NPEIVIYQY, was also recognized.	NPDIVIYQY	HIV-1 infection	human (B35)	Menendez-Arias1998, Sipsas1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• NPDLVIYQY, was also recognized. • [Menendez-Arias1998], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding.				
RT (175–183)	RT	NPDIVIYQY	HIV-1 exposed seronegative	human (B35)	Menendez-Arias1998, Rowland-Jones1998a
	Keywords review, inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is HPDIVIYQY. • The D subtype consensus is NPEIVIYQY. • [Menendez-Arias1998], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding.				
RT (175–183)	Pol (subtype B)	NPDIVIYQY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • Clade A version of epitope HPDIVIYQY, Clade D NPEIVIYQY.				
RT (175–183)	Pol	HPDIVIYQY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 version of this epitope is not conserved: NPDVILIQY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				
RT (175–183)		HPDIVIYQY	HIV-1 infection	human (B35)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.				
RT (175–183)	Pol (subtype A)	HPDIVIYQY	HIV-1 infection	human (B35)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • HPDIVIYQY or NPDIVIYQY was recognized in 1 of the 6 women (ML857), and the response was present in the last available sample prior to seroconversion, 7 months. • 20/20 sequences of the infecting strain had three substitutions in this epitope, all 20 were NpQiIiyqy, and this form was not recognized by CTL from ML 857 – this was the only case in the study where a virus carrying an unrecognized form of the epitope broke through. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • NPDIVIYQY was recognized by 1/22 HEPS control sex workers, ML887.				
RT (175–183)	RT (175–183 SF2)	NPDIVIYQY	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3.				
RT (175–183)	Pol (342–350)	HPDIVIYQY	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • Variants (H/N)PDIVIYQY are specific for the A/B clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B35 women, 2/3 HEPS and 1/4 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in only one of the 2/3 HEPS cases, and was not to this epitope in the one responsive HIV-1 infected women. • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes.				
RT (175–183)		HPDIVIYQY	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Pol-HY9.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HIV+ individuals who carried HLA B35, 4/21 (19%) recognized this epitope.				
RT (175–183)	Pol	NPDIVIYQY	HIV-1 infection	human (B35)	Sabbaj2002a
	Keywords mother-to-infant transmission. **Donor HLA** A3, A11, B35, B51. • IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope NPDIVIYQY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
RT (175–183)	Pol	HPDIVIYQY	HIV-1 infection, Vaccine	human, macaque (B35)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (175–184)	RT (175–184 LAI)	NPDIVIYQYM	HIV-1 infection	human (B51)	Samri2000
	• This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors. • Patient 246#1 (B51), was found by ELISPOT to recognize the wild type and the mutated peptide after zidovudine treatment. • The resistance mutation M184V gave an increased predicted binding score to B51 (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence and also an increased ELISPOT reactivity.				
RT (175–199)	RT (342–366 LAI)	NPDIVIYQYMDDLYVGSDL-EIGQHR	HIV-1 infection	human (A11)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study.				
RT (179–187)	RT	VIYQYMDDL	Vaccine	human (A*0201)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia • This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.				
RT (179–187)	RT	VIYQYMDDL	HIV-1 infection	human (A*0201)	Tan1999
	• Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable.				
RT (179–187)	Pol (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Sewell1999
	Keywords epitope processing, immunodominance, escape. • Proteasome regulation influences epitope processing and could influence patterns of immunodominance. • The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome. • IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways. • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway. • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Harrer1996a, Menendez-Arias1998
	Keywords review. • The substitution VIYQYVDDL abrogates CTL response and confers drug resistance. • [Menendez-Arias1998], in a review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Frahm2004
	• C. Brander notes this is an A*0201 epitope.				
RT (179–187)	RT (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Brander1998a, Menendez-Arias1998
	Keywords review, escape. • Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape. • Only one subject had CTL against all three epitopes. • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area. • In the review [Menendez-Arias1998] the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) – substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC – substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors.				
RT (179–187)	RT	VIYQYMDDL	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** RT VL9. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, including RT VL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	RT (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Dela Cruz2000
	Epitope name VL9. • Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL. • These antigens could also be used to stimulate primary responses *in vitro*.				
RT (179–187)	Pol (346–354)	VIYQYMDDL	HIV-1 infection	human (A*0201)	Sewell2002
	Keywords epitope processing, immunodominance. • Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing. • ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.				
RT (179–187)	Pol	VIYQYMDDL	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (179–187)	RT (179–187)	VIYQYMDDL	Vaccine	mouse (A*0201)	Okazaki2003
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12 **Keywords** binding affinity, vaccine-induced epitopes. **Assay type** cytokine production, Chromium-release assay. **Donor HLA** A2.1. • Alanine substitutions of VIYQYMDDL were tested for importance of each amino acid for HLA-A2.1 binding. Peptide variant (vLyqymddV) showed an 8 fold higher MHC binding affinity than wild type. YLyqymddV had an even higher binding affinity, but the Y at positions one blocked TCR recognition. The higher affinity form of vLyqymddV induced CTL *in vivo* that could protect against a vaccinia virus expressing RT and the wild type epitope.				
RT (179–187)	RT	VIYQYMMDL	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A and D consensus sequences are both VIYQYMMDL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (179–187)	Pol (346–354)	VIYQYMDDL	Vaccine	human (A2)	Woodberry1999

Vaccine *Vector/Type:* DNA prime with vaccinia boost

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice.
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost.
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested.
- VIYQYMDDL was recognized by 3 of the HLA-A2 patients.

RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Schmitt2000

Keywords escape, immunotherapy.

- The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL.
- 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL.
- This suggests immunotherapy stimulating anti-VIYQYVDDL responses maybe helpful for reducing lamivudine escape.

RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Haas1998

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)

RT (179–187)	Pol (339–347 93TH253 subtype CRF01)	VIYQYMDDL	HIV-1 infection	human (A2)	Sriwanthana2001

Keywords HIV exposed persistently seronegative (HEPS).
Epitope name P334-342.

- This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand.
- HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed.
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.

RT (179–187)	Pol (339–347 93TH253 subtype CRF01)	VIYQYMDDL	HIV-1 infection	human (A2)	Bond2001

Keywords inter-clade comparisons.

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 2/4 tested FSWs recognized the E clade version of this epitope, which is identical to the previously defined B clade version VIYQYMDDL.
- This epitope was conserved in many subtypes, and exact matches were very uncommon.

RT (179–187)	RT (179–187)	VIYQYMDDL	HIV-1 infection	human (A2)	Day2001

Keywords rate of progression, acute infection.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
RT (179–187)	Pol (346–354 LAI)	VIYQYMDDL	HIV-1 infection	human (A2)	Kelleher2001a
	Keywords HAART, epitope processing. • Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in an intracellular context. • RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome. • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
RT (179–187)	Pol (334–)	VIYQYMDDL	HIV-1 infection	human (A2)	Corbet2003
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol334. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • 1/17 HIV-infected HLA-A2+ people in this study recognized this epitope.				
RT (179–187)	Pol (subtype B)	VIYQYMMDL	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B and D clade viruses.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR26. • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
RT (179–187)	RT (346–354 LAI)	VIYQYMDDL	Vaccine	mouse (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30 **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR26. • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
RT (180–189)	RT (LAI)	IYQYMDDLYV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a progressor, spans important RT functional domain. • A previous study determined that this was an epitope recognized by a long-term survivor.				
RT (181–189)	RT (181–189 LAI)	YQYMDDLYV	HIV-1 infection	human (A*0201)	Samri2000
	Keywords binding affinity, computational epitope prediction. • This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors. • High levels of recognition by ELISPOT were observed for zidovudine induced mutation YQYVDDLYV and for the wildtype peptide YQYMDDLYV in patient 250#0 (HLA-A*0201), but neither were recognized by patient 201#5 (also HLA-A*0201) • Both the wild-type and the mutated peptide were computer predicted to have a high binding affinity for A2 (http//bimas.dcrt.nih.gov/molbio/hla_bind)				
RT (192–201)	RT (192–201)	DLEIGQHRTK	HIV-1 infection	human (A3)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.				
RT (192–216)	RT (359–383 HXB2)	DLEIGQHRTKIEELRQHLL-RWGLTT	HIV-1 infection	human (Bw60)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study.				
RT (192–216)	RT (191–215)	DLEIGQHRTKIEELRQHLL-RWGFTT	HIV-1 infection	human (polyclonal)	Haas1997, Menendez-Arias1998
	Keywords HAART, escape. • Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably the escape variant, RT T215Y.				
RT (198–212)	RT (SF2)	HRTKIEELRQHLLRW	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
RT (201–209)	RT (201–209)	KIEELRQHL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.				
RT (201–210)	Pol	KIEELRQHLL		human (B58)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay. • KIEELRQHLL was newly identified as a HLA-B58 epitope in this study, it had been previously shown to be presented by HLA-A2 and Bw60. • KIEELRQHLL did not bind detectably to B7.				
RT (202–210)	RT (202–210 LAI)	IEELRQHLL		human (B*4001)	Altfeld2000b, Frahm2004
	• C. Brander notes this is a B*4001 epitope.				
RT (202–210)	RT (SF2)	IEELRQHLL	HIV-1 infection	human (B60)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3.				
RT (202–210)	RT	IEELRQHLL	HIV-1 infection	human (B60)	Montefiori2003
	Keywords HAART, supervised treatment interruptions (STI), early treatment. **Epitope name** IL9. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2, A24, B38, B60, Cw2, Cw12. • HIV-1+ patient AC10 underwent early HAART treatment, which was discontiuned 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.				
RT (202–210)	RT (SF2)	IEELRQHLL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes. • B60 is present in 10-20% of the Caucasoid and very common in Asian populations.				
RT (202–210)	RT (202–210)	IEELRQHLL	HIV-1 infection	human (B60/B61)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to five B61-restricted epitopes tested.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.				
RT (203–212)	RT (LAI)	EELRQHLLRW	HIV-1 infection	human (B44)	Menendez-Arias1998, vanderBurg1997
	• The only epitope recognized by CTL from a long-term survivor in two samples taken six years apart. • Recognized by CTL from a progressor, EILKEPVGHGV and TWETWWTEYW were also recognized.				
RT (209–220)	RT (209–220)	LLRWGLTTPDKK	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.				
RT (240–257)	RT (240–257 HXB2) **Keywords** supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.	TVQPIVLPEKDSWTVNDI	HIV-1 infection	human	Addo2003
RT (243–252)	RT (LAI) • Recognized by CTL from a progressor and a long-term survivor, KITTESIVIW was also recognized.	PIVLPEKDSW	HIV-1 infection	human (B*5701)	Menendez-Arias1998, vanderBurg1997
RT (243–252)	RT (LAI) **Keywords** binding affinity, escape. • Recognized by CTL from long-term survivor, whose CTL response persisted for more than 10 years – the substitution V3M reduced affinity but was well recognized, on the other hand V3T and D8G did not reduce affinity, but abrogated CTL response.	PIVLPEKDSW	HIV-1 infection	human (B*5701)	Menendez-Arias1998, vanderBurg1997
RT (243–252)	RT (410–419) **Keywords** HAART, acute infection. **Epitope name** PIV. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B57+	PIVLPEKDSW	HIV-1 infection	human (B57)	Oxenius2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (243–252)	RT	PIVLPEKDSW	HIV-1 infection	human (B57)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** PIV. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
RT (244–252)	RT (399–407)	IVLPEKDSW		human (B*5701)	Frahm2004
	• Subtype of B57 not determined. • C. Brander notes this is a B*5701 epitope.				
RT (244–252)	RT (244–252 LAI)	IVLPEKDSW	HIV-1 infection	human (B*5701, B*5801)	Klein1998
	Keywords binding affinity, rate of progression, escape. • This peptide was defined as the optimal epitope. • B57 has been associated with long-term non-progression in the Amsterdam cohort. • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag. • B57 restricted CTL responses are targeted at multiple proteins, but one LTS had a response that was dominated by reactivity to the epitope – two variants were found in this LTS: ITLPEKESW, which bound to B*5701 with similar affinity as the index peptide but was an escape mutant that was not recognized by CTL, and IMLPEKDSW, which bound to B*5701 with reduced affinity but could still be recognized. • In an additional HIV+ LTS, only the variant IELPEKDSW was found, and this epitope was recognized by CTL but had less affinity for B*5701 than the index peptide. • This epitope was recognized in the context of both HLA-B*5701 and B*5801.				
RT (244–252)	Pol (244–252)	IVLPEKDSW	HIV-1 infection	human (B*5801)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
RT (244–252)	RT (399–407)	IVLPEKDSW		human (B57)	vanderBurg1997
RT (244–252)	RT (244–252)	IVLPEKDSW	HIV-1 infection	human (B57)	Guillon2002
	Keywords early-expressed proteins, kinetics. • An early-expressed Nef protein was modified to contain Env and Pol epitopes to enable the study the effect of expression kinetics on CTL mediated suppression of replication. The "EpiNef" construct was inserted into a recombinant vaccinia virus which was used to infect a target cell line; the target cells were lysed by CTL clones specific for the Env and Pol epitopes indicating that they were properly processed.				
RT (244–252)	RT (244–252 ACH320.2A.2.1)	IVLPEKDSW	HIV-1 infection	(B57)	vanBaalen2002
	Keywords acute infection, early-expressed proteins, kinetics.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Tat, Rev and Nef are the first HIV proteins expressed upon acute infection of T-cells (< 6 hours), and RT is not expressed until after 24 hours. The B14-restricted Rev-SAEPVPLQL specific CD8 T-cell clone TCC108, and the B57-restricted RT-IVLPEKDSW specific CD8 T-cell clone TCL1C11 were co-incubated with CD4+ cultures innoculated with HIV-1 at low MOI. Co-incubation with the Rev-specific CTL resulted in two logs less HIV-1 production in ten days of culture. When the RT epitope was cloned into the Nef gene of the infecting strain, another early expressed protein, it proved as effective as the Rev epitope at inhibiting viral production. A mathematical model of CTL-target interactions suggest early proteins are important for vaccine design.				
RT (245–252)	Pol	IVPEKDSW	HIV-1 infection	human (B57)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load. • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional. • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.				
RT (259–267)	Pol	KLVGKLNWA	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802). • Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population.				
RT (260–271)	RT (415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human (B*1501)	Frahm2004
	• C. Brander notes this is a B*1501 epitope.				
RT (260–271)	RT (260–271)	LVGKLNWASQIY	HIV-1 infection	human (B62)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to four B62-restricted epitopes tested.				
RT (260–271)	RT (415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human (Bw62)	Brander1996b, Menendez-Arias1998
	• P. Johnson, pers. comm.				
RT (263–271)	RT (263–271 LAI)	KLNWASQIY		human (A*3002)	Frahm2004, Goulder2001a
	• C. Brander notes this is an A*3002 epitope.				
RT (263–271)	RT	KLNWASQIY	HIV-1 infection	human (A*3002)	Goulder2001a
	Epitope name KY9 (RT-35). • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule. • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood. • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant. • In subject 199 four additional A*3002 epitopes were identified. • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)				
RT (263–271)	RT	KLNWASQIY	HIV-1 infection	human (A30)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** A30-KY11(RT). **Donor HLA** A30,A32,B18,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).			
RT (266–285)	Pol (421–440)	WASQIYPGIKVRQLCKLLRG	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
RT (268–282)	RT (SF2)	SQIYPGIKVRQLCKL	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized.				
RT (269–277)	Pol (424–432)	QIYAGIKVK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords binding affinity, inter-clade comparisons. • binding affinity, inter-clade comparisons. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • QIYAGIKVK is commonly found in viruses representing subtypes A, B and E. It was strongly recognized by CTL from 1/5 B clade infected Japanese subjects, and 5/7 E clade infected Thai subjects. • QIYAGIKVK had the highest A*1101 binding affinity, but qiyagikvR and qiyPgikvR (the most common C and D clade variant both bound to A*1101). QIYAGIKVK and qiyagikvR were both cross-presented by a clone from a B clade infection, but qiyPgikvR was not.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (269–277)	(LAI)	QIYPGIKVR		(A3)	Altfeld2000a, Frahm2004
RT (269–277)	RT (269–277)	QIYPGIKVR	HIV-1 infection	human (A3)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.			
RT (269–277)	RT (424–432)	QIYPGIKVR	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-QR9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 4/7 individuals began to have detectable responses to this epitope after STI.			
RT (271–279)	(LAI)	YPGIKVRQL	HIV-1 infection	human (B*4201)	Frahm2004
	• C. Brander notes this is a B*4201 epitope.				
RT (271–279)	RT (438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human (B42)	Menendez-Arias1998, Wilson1996
	Keywords responses in children, mother-to-infant transmission. • YAGIKVRQL and YPGIKVKQL are naturally occurring variants that are both reactive. • YHKIKVRQL is a naturally occurring variant that has not been tested. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.				
RT (271–279)	Pol (438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human (B42)	Wilson1999a
	Keywords mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • An additional variant that gave a positive CTL response: YPGIKVKQL, YAGIKVRQL. • YHGIKVRQL was an escape mutant.				
RT (293–301)	RT (448–456 SF2)	IPLTEEAEL	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	• A CTL clone responsive to this epitope was obtained. • Only 1/7 B35-positive individuals had a CTL response to this epitope. • An E to K substitution at position 5 abrogates specific lysis, but not binding to B*3501. • An I to V substitution at position 1, P to Q at position 2, and E to K at 5, abrogates specific lysis and binding to B*3501.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• An I to V substitution at position 1 did not alter reactivity. • Reviewed in [Menendez-Arias1998], this epitope lies in the thumb region of RT.				
RT (293–301)	Pol (448–456 SF2-24)	IPLTEEAEL	HIV-1 infection	human (B*3501 AND B*5101)	Tomiyama2000b
	Epitope name HIV-B35-SF2-24. • This epitope is naturally processed and presented by both HLA-B*3501 and HLA-B*5101 and is cross-recognized by a single CTL clone. • IPLTEEAEL binds approximately four times more tightly to HLA-B*3501 than HLA-B*5101.				
RT (293–301)	Pol (489–456)	IPLTEEAEL	HIV-1 infection	human (B*3501, B*5301, B*5101, B*0702)	Ueno2002
	Keywords supertype, cross-presentation by different HLA, TCR usage. **Donor HLA** A24/A26, B35/B51, Cw3/-. • The IPLTEEAEL epitope was known to be presented by both HLA-B*3501 and -B*5101 to a dual specific CTL clone. A single TCR complex bearing Valpha12.1 and Vβ5.6 was shown recognize the epitope in either HLA-B*3501 and -B*5101. Furthermore, this TCR also recognized the peptide presented by B*5301 and B*0702 in cytolytic CTL assays, demonstrating that this single TCR complex recognizes the same peptide presented by a range of HLA class I molecules.				
RT (293–301)	(SF2)	IPLTEEAEL	HIV-1 infection	human (B35)	Kawana1999
	Keywords rate of progression. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals but this was one of the six that had no B35 associated pattern of mutation.				
RT (293–301)	RT (448–456 SF2)	IPLTEEAEL	HIV-1 infection	human (B35, B51)	Menendez-Arias1998, Shiga1996
	• Binds HLA-B*3501 and B*5101. • Reviewed in [Menendez-Arias1998], this epitope lies in the thumb region of RT.				
RT (293–301)	Pol (447–455)	IPLTEEAEL	HIV-1 infection, HIV-1 exposed seronegative	human (B51)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
RT (294–318)	RT (461–485 HXB2)	PLTEEAELELAENREILKE-PVHGVY	HIV-1 infection	human (A2)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study.				
RT (308–317)	RT (LAI)	EILKEPVGHV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a long-term survivor, SPIETVPVKL was also recognized. • Recognized by CTL from a progressor, EELRQHLLRW and TWETWWTEYW were also recognized.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human	Luzuriaga2000
	Keywords HAART, responses in children. **Donor HLA** A*0201. • Longitudinal study of 8 infants with prolonged viral suppression due to combination antiretroviral therapy showed no HIV-1 specific CTL responses in peripheral blood cells. 6/8 were studied using a Chromium release assay and no response was detected using Gag expressed in vaccinia in the target cells. Three HLA-A*0201 children were tested using SLYNTVATL or ILKEPVHGV HLA A*0201 tetramers and again no HIV-specific response was detected, either using PBMC specimens, or PBMC which had been stimulated *in vitro* for a week. • In contrast, one of the children with suppressed HIV viral replication who was co-infected with HIV and EBV, while HIV-tetramer negative, had EBV-tetramer staining cells at a frequency of 0.14% in the PBMC.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*02)	Huang2000
	Keywords HAART. • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed. • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*02)	Rinaldo2000
	Keywords HAART. • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection.				
RT (309–317)	RT	ILKEPVHGV	HIV-1 infection	human (A*02)	Scott-Algara2001
	Keywords HAART, immunodominance. **Epitope name** IV9. • This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV. • 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV) • There were no differences observed in children that had therapy versus those that did not. • Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells.				
RT (309–317)		ILKEPVHGV	HIV-1 infection	human (A*0201)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T cells and viral load. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Spiegel2000
	• High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen. • Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Sewell1999
	Keywords epitope processing, immunodominance. • Proteasome regulation influences epitope processing and could influence immunodominance. • The proteasome is inhibited by lactacystin treatment, and gamma IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome. • IFN-gamma induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways. • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway. • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Loing2000
	Keywords epitope processing. • The ILKEPVHGV was modified by the addition of an N-palmitoyl-lysine residue at the P0, P1 or P10 positions of the parent peptide to create a lipopeptide for direct antigen delivery to the cytoplasm for processing. • The N-terminal modification increased the life span for functional CTL recognition up to 48 hours in comparison to the parent peptide.				
RT (309–317)	Pol (510–518)	ILKEPVHGV	Vaccine	human (A*0201)	Larsson1999
	Vaccine *Vector/Type:* canarypox, vaccinia *HIV component:* Env, Gag, Nef, Pol • ELISPOT was used to assay the CD8 T cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia or canarypox vectors in 19 HIV+ people. • The highest CTL frequency was directed at epitopes in Pol. • In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Wilson1998a
	Keywords TCR usage. • HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo*. • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls. • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 2/11 of the A2+ individuals responded to ILKEPVHGV, and neither of these two responded to SLYNTVATL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A*0201)	Gray1999
	Keywords HAART.				
	• Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, Ogg1998b
	• HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load.				
	• Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity.				
	• No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells.				
RT (309–317)	RT	ILKEPVHGV	Vaccine	human (A*0201)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia				
	• This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.				
RT (309–317)	RT (476–484)	ILKEPVHGV	in vitro stimulation or selectio	human (A*0201)	Konya1997, Menendez-Arias1998
	Keywords binding affinity.				
	• This epitope was included as a positive control.				
	• Binding affinity to A*0201 was measured, $C\_1/2\max\mu M = 12$				
RT (309–317)	RT (468–476)	ILKEPVHGV	in vitro stimulation or selectio	human (A*0201)	vanderBurg1996
	• Immunogenic in humans, slow dissociation rate, and associated with immunogenicity in transgenic HLA-A*0201/K^b mice.				
	• CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.				
RT (309–317)	RT (468–476)	ILKEPVHGV	in vitro stimulation or selectio	human (A*0201)	vanderBurg1995
	• Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Menendez-Arias1998, Pogue1995
	• Mutational study: position 1 I to Y increases complex stability with HLA-A*0201.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Goulder1997e, Goulder1997a, Menendez-Arias1998
	Keywords review, escape.				
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII.				
	• One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV.				
	• Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL.				
	• 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL.				
	• Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL.				
	• [Goulder1997a] is a review of immune escape that summarizes this study.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Altman1996
	• This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs—HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and can quantify HIV-specific CD8+ cell lines in freshly isolated PBMCs. • Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%) • The A2-Pol CD8+ clones were CD45RO positive and HLA-DR and CD38 negative, suggesting a memory rather than effector phenotype.				
RT (309–317)	RT (476–484)	ILKEPVHGV	in vitro stimulation or selectio	human (A*0201)	Menendez-Arias1998, Walter1997
	Keywords epitope processing. • HLA-A2 heavy chain and β2-microglobulin expressed in E. coli were refolded in the presence of this peptide. • The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2. • Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens.				
RT (309–317)	RT (464–472)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Gray1999
	Keywords HAART. • Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells. • 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL. • After HAART, the majority of the epitope-specific CTL were apparently memory cells.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Brander1998a
	Keywords escape. • Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape. • Only one subject had CTL against all three epitopes. • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area. • C. Brander notes this is an A*0201 epitope.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Ogg1999
	Keywords HAART. • CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient. • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy. • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days.				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Frahm2004
	• C. Brander notes this is a A*0201 epitope.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection, in vitro stimulation or selectio	human (A*0201)	Dela Cruz2000
	Epitope name IV9. • Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• These antigens could also be used to stimulate primary responses *in vitro*.				
RT (309–317)	RT (309–317) **Keywords** HAART, escape. **Epitope name** P1. • The epitope was recognized by patient 250#0 but not in another A*0201+ patient, 201#5, in a study of the effects of therapy escape mutations on CTL recognition.	ILKEPVHGV	HIV-1 infection	human (A*0201)	Samri2000
RT (309–317)	Pol (LAI) **Keywords** dendritic cells. • Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors. • Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses.	ILKEPVHGV	in vitro stimulation or selectio	human (A*0201)	Engelmayer2001
RT (309–317)	Pol • In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found. • High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products. • 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope.	ILKEPVHGV	HIV-1 infection	human (A*0201)	Gea-Banacloche2000
RT (309–317)	Pol (476–484) **Keywords** HAART, rate of progression. • The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay. • LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load.	ILKEPVHGV	HIV-1 infection	human (A*0201)	Jin2000a
RT (309–317)	Pol (476–484) • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α	ILKEPVHGV	HIV-1 infection	human (A*0201)	Appay2000
RT (309–317)	Pol **Keywords** dendritic cells. • The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients. • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes. • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Ostrowski2000
RT (309–317)	RT (309–317) **Vaccine** *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT **Epitope name** RT2.	ILKEPVHGV	Vaccine	human, transgenic mouse (A*0201)	Guardiola2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A2 transgenic mice were injected with bacteriophage antigens expressing a Th epitope and the HIV CTL epitope ILKEPVHGV, and epitope-specific cytotoxic activity was induced.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Sewell2002
	Keywords epitope processing, immunodominance. • Epitope processing of three different HLA-A*0201 HIV epitopes was shown to use different pathways, which might influence patterns of immunodominance. .174 cells were used that lack TAP1 and TAP2 genes, as well as the LMP2 and LMP7 genes that encode the beta-subunits of the immunoproteasome. These genes could be added back through transfection to study processing. • ILKEPVHGV was efficiently presented in TAP-1 and -2 transfected cells while VIYQYMDDL and SLYNTVATL were not. VIYQYMDDL was destroyed by the MB1 subunit of the protease, and could be expressed in the presence of the proteasome inhibitor lactacystin, but SLYNTVATL expression was not restored. SLYNTVATL expression was unaltered by lactacystin in a wild type cell line.				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infected monocyte-derived	mouse (A*0201)	Poluektova2002
	Epitope name IL-9. • Nonobese diabetic NOD-C.B-17 SCID mice were reconstituted with HLA-A*0201 positive human PBL and injected with HIV-1 infected monocyte-derived macrophages MDM in the basal ganglia to provide a mouse model of HIV-1 encephalitis. • HLA-A*0201 CTL responses were detected by tetramer staining in the spleen in seven days, increased through day 14, and the numbers of productively infected were reduced >85% in the second week.				
RT (309–317)	RT (309–317)	ILKEPVHGV	Vaccine	transgenic mouse (A*0201)	Boissonnas2002
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** binding affinity, vaccine-specific epitope characteristics. • Ten naturally occurring variants of the Nef epitope VLMWQFDSRL were tested for their affinity to HLA-A*0201 and for their ability to induce gamma-IFN and cytotoxic functions through vaccination of HLA-A*0201 transgenic mice. • ILKEPVHGV could induce HLA-A*0201 vaccine responses, and was a positive control.				
RT (309–317)	Pol (468–476)	ILKEPVHGV	Vaccine	mouse (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 **Keywords** epitope processing, vaccine-specific epitope characteristics, immunodominance. • C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome. • A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members. • Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen. • The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (309–317)	Pol (476–484)	ILKEPVHGV	in vitro stimulation or selectio	human (A*0201)	Andrieu2003
	Keywords epitope processing, dendritic cells. • This study demonstrates that lipopeptides carrying epitopes can be taken up by human dendritic cells, processed using different pathways, and recognized by epitope-specific CD8+ T-cells originally derived from HIV+ individuals. The RT ILKEPVHGV peptide was embedded in a longer peptide fragment in the lipopeptide, and was internalized by endocytosis and processed in the cytosol by proteasomal cleavage by following an endosome-to-cytosol pathway for processing and presentation. Administration of epoxomycin, a proteasome inhibitor, completely abrogated epitope presentation to a CD8+ T-cell line, while monensin, an inhibitor of acid-dependent endosomal enzyme activity did not. • In contrast to the RT epitope, dendritic cell presentation of the Nef epitope QVPLRPMTYK embedded in a longer peptide in a lipopeptide was not inhibited by epoxomycin, but was inhibited by monensin, indicative of endocytolitic epitope processing.				
RT (309–317)		ILKEPVHGV	HIV-1 infection	human (A*0201)	Dagarag2003
	Epitope name IV9. **Assay type** cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay. • Telomer length is short in the CD8+ T-cell compartment of HIV-1 infected people, indicating excessive CTL activation and premature senescense. Here human telomerase RT (hTERT) transduction of HIV-1-specific CTL was used to study the functional impact of telomerase. Telomerase expression enhanced proliferative capacity, as well as cytolytic and antiviral capabilities; cytokine production was unchanged. hTERT transduced CTLs were 10-fold more efficient in controlling HIV-1 replication in culture. Thus telomerase transduction can restore CTL mediated cytolysis, and may have therapeutic potential. • Three polyclonal CD8+ T-cell lines derived from an HIV-1, HLA A*0201 positive patient were used in this study, including one specific for this epitope. An IV9-specific monoclonal cell line, 68A62 was also generated.				
RT (309–317)	Pol (464–472)	ILKEPVHGV	Vaccine	transgenic mouse (A*0201)	Daftarian2003
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* CpG immunostimulatory sequence (ISS) **Epitope name** I9V. **Assay type** cytokine production, Tetramer binding, Intracellular cytokine staining, Chromium-release assay. **Donor HLA** H-A2/Kb. • HLA-A*0201 transgenic mice were immunized with a Th-CTL-fusion peptide composed of the I9V CTL epitope linked to the promiscuous PADRE Th epitope. The peptide only when given in combination with CpG elicited strong I9V-CTL responses. • The peptide-CpG vaccinated mice, when challenged with pol embedded in vaccinia (pol-vv), could clear the virus from the ovaries. Additionally, intranasal immunized mice given an intranasal pol-vv challenge had reduced virus in the lungs.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A*0201)	Shacklett2003
	Keywords genital and mucosal immunity. **Epitope name** IV9.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type Tetramer binding. • Lymphocytes from rectal biopsies were used to characterize the CD8+ T cell response to HIV in GALT, Gut-associated lymphoid tissues. Patients were selected on the basis of being HLA-A2+ and having detectable SLYNTVATL and ILKEPVHGV tetramer responses in PBMC. SLYNTVATL frequency was increased in GALT relative to PBMC in 6/7 patients studied, while a control response to a CMV-peptide was diminished in GALT. Only two patients had ILKEPVHGV CD8+ T cell responses, and both had slightly higher frequencies in GALT than PBMC. • HIV may perturb lymphocyte retention in GALT, suggested by an overall reduction of GALT CD8+ cells expressing alphaEbeta7. GALT HIV-specific CD8+ T cells expressed alphaEbeta7, suggesting mucosal priming.				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A*0201, A*0205)	Mollet2000
	Keywords HAART. **Epitope name** P1. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
RT (309–317)		ILKEPVHGV	HIV-1 infection	human (A02)	Sabbaj2002b
	Epitope name Pol-IV9. • Among HIV+ individuals who carried HLA A02, 9/29 (31%) recognized this epitope.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2. • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice. • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost. • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested. • ILKEPVHGV was recognized by 2 of the patients.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Kolowos1999
	Keywords inter-clade comparisons, TCR usage. • TCR usage in CTL specific for this epitope was examined in three patients and identical Vβ6.1 and Valpha2.5 gene segments were used and two of the patients had very similar complementarity-determining regions – clonal expansion of RT-HIV-specific CTL can contribute to the skewed TCR repertoire in HIV-1 infected patients.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL clones from all three patients showed similar sensitivity to mutation in the epitope, ilkepvhEv was well recognized (the sequence from SF2), ilkDpvhgv was not (the common A clade form)				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Collins1998
	• Nef down-regulates MHC class I molecules, which inhibits CTL killing of HIV-infected targets. • The anti-RT CTL clone killed Nef- cells less efficiently than anti-gag clones, correlated with the reduced expression of RT.				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A2)	Fan1997
	Keywords dendritic cells. • The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied.				
RT (309–317)	RT (464–472)	ILKEPVHGV	HIV-1 infection	human (A2)	Kundu1998b
	Keywords dendritic cells. • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients. • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated. • ILKEPVHGV is a conserved HLA-A2 epitope included in this study – 5/6 patients had this sequence as their HIV direct sequence, and these had a detectable CTL response– one person carried the form ILREPVHGV and had no detectable CTL.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Tsomides1994
	• CTL clones recognize naturally processed peptide – peptide abundance corresponded to level of CTL killing.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is ILKDPVHGV. • The D subtype consensus is identical to the epitope ILKEPVHGV.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Cao1997a, Menendez-Arias1998
	Keywords inter-clade comparisons. • The consensus peptides of B and D clade viruses and some As have the sequence ILKEPVHGV. • The consensus peptide of a subset of A clade viruses, ILKDPVHGV, is not cross-reactive.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Yang1996
	• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL. • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones. • The distinction was thought to be due to lower expression of RT relative to Env and Gag. • CTL can lyse infected cells early after infection, possibly prior to viral production.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Yang1997a
	Assay type CTL suppression of replication. • CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*. • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL suppress HIV replication more efficiently in HLA-matched cells.				
RT (309–317)	RT (309–317) **Keywords** TCR usage. • Two clones were obtained with different TCR usage, $V_\beta 1$ and $V_\beta 21$.	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Moss1995
RT (309–317)	RT (476–484) • Cervical CTL clones from an HIV-infected woman recognized this epitope.	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Musey1997
RT (309–317)	RT (476–484 LAI) • Precise identification of the nonamer that binds to A2.	ILKEPVHGV	HIV-1 infection	human (A2)	Menendez-Arias1998, Tsomides1991
RT (309–317)	RT (476–484 LAI) • Promotes assembly of HLA-A2 molecules in T2 cell lysates.	ILKEPVHGV	Peptide-HLA interaction	human (A2)	Connan1994, Menendez-Arias1998
RT (309–317)	RT (510–518) • Studied in the context of HLA-A2 peptide binding.	ILKEPVHGV	in vitro stimulation or selectio	human (A2)	Parker1992
RT (309–317)	Pol (476–484) • CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective. • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.	ILKEPVHGV	HIV-1 infection	human (A2)	Dyer1999
RT (309–317)	RT (476–484) **Keywords** dendritic cells. • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses. • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA. • A weak response to KLTPLCVSL was stimulated using macrophages as the APC. • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.	ILKEPVHGV	in vitro stimulation or selectio	human (A2)	Zarling1999
RT (309–317)	RT (480–) **Keywords** inter-clade comparisons. • This study uses EpiMatrix for T cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV. • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule. • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV. • This sequence is not conserved between clades, but is found only in a small number of B clade isolates.	ILKEPVHGV	computer prediction	(A2)	Schafer1998
RT (309–317)	RT **Keywords** binding affinity, inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** RT IV9.	ILKEPVHGV	HIV-1 infection	human (A2)	Altfeld2001c

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • This peptide binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802. • RT IV9 was recognized in 7/22 patients with chronic HIV-1 infection. • 1/13 patients with acute HIV-1 infection recognized RT IV9.				
RT (309–317)	Pol (subtype A)	ILKDPVHGV	HIV-1 infection	human (A2)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS), escape. • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • ILKDPVHGV or ILKEPVHGV was recognized in 1 of the 6 women (ML1760), and the response was present in the last available sample prior to seroconversion, 12 months. • 20/20 sequences of the infecting strain had no substitutions in this epitope, all were ILKDPVHGV, so there was no evidence for escape. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized by 4/22 HEPS control sex workers: ML887, ML1192, ML1250, and ML1749.				
RT (309–317)	RT (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** ILK. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • One of the 2/8 HLA-A2+ study subjects recognized this CTL epitope. • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIY-HTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent.				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A2)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load. • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional. • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival.				
RT (309–317)	Pol	ILKEPVHGV	HIV-1 infection	human (A2)	Seth2001
	Keywords HAART, immunodominance. • CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized. • 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy. • 3/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV.				
RT (309–317)	RT (476–484 SF2)	ILKEPVHGV	HIV-1 infection	human (A2)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 3/4 group 3.				
RT (309–317)	Pol (476–484)	ILKDPVHGV	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS), immunodominance. • Variants ILK(D/E)PVHGV are A/B clade specific. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-A2 women, 7/10 HEPS and 14/26 HIV-1 infected women recognized this epitope, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women. • The dominant response to this HLA allele was to this epitope in all 7/10 HEPS cases but in only 5 of the 14/26 HIV-1 infected women. • Four epitopes were considered to be "resistant epitopes", as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILK(D/E)PVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLN(M/T)LN(I/V)V in p24 and B18 FRDYVDRF(Y/F)K also in p24. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort. • Subject ML 1250 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, which switched to SL(F/Y)NTVATL post-seroconversion. • Subject ML 1760 had an A2 response to ILK(D/E)PVHGV prior to seroconversion, and gained responses to epitopes A2 SL(F/Y)NTVATL and B27 KRWII(L/M)GLNK post-seroconversion.				
RT (309–317)	Pol (93TH253 subtype CRF01)	ILRIPVHGV	HIV-1 infection	human (A2)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P464-472. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–317)	Pol (93TH253 subtype CRF01)	ILRIPVHGV	HIV-1 infection	human (A2)	Bond2001
	Keywords inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids: ILKEPVHGV. • This epitope was not conserved in many subtypes, and exact matches were very rare.				
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	human (A2)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
RT (309–317)	Pol (476–484 LAI)	ILKEPVHGV	HIV-1 infection	human (A2)	Kelleher2001a
	Keywords HAART, epitope processing. • Ritonavir (RTV) inhibits chymotryptic activity in the 20S proteasome *in vitro*, as does Saquinavir (SQV) to a lesser extent; Indinavir (IDV) does not. Thus there is concern protease inhibitors may adversely effect CTL epitope processing, but this paper indicates that processing is not inhibited at therapeutically relevant concentrations of RTV when the proteasome is functioning in in an intracellular context. • RTV did not alter the presentation two RT A2 epitopes processed by distinct pathways: ILKEPVHGV, generated by the constitutive proteasome containing the MB1 beta subunit, and VIYQYMDDL which is dependent on IFNgamma induction of LMP7 which replaces MB1 in the immunoproteasome, and is destroyed by MB1 in the constitutive proteasome. • RTV did not inhibit the processing and assembly of HLA-B35 or -A2, which are assembled with a rapid and moderate time course, respectively, or of HLA-A3, -B27 and -B39.				
RT (309–317)	Pol	ILKDPVHGV	HIV-1 infection	human (A2)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
RT (309–317)	RT (476–484 NL43)	ILKEPVHGV	HIV-1 infection	human (A2)	Yang2002
	Keywords class I down-regulation by Nef. • Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL-43 infected cells. The CTL clone 68A62, specific for the class I A2 presented ILKEPVHGV epitope, was one of four used in this study.				
RT (309–317)	RT (476–484 BRU)	ILKEPVHGV	HIV-1 infection	human (A2)	Cohen2002
	Keywords epitope processing. **Donor HLA** A2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The antigen presentation of two A2-restricted epitopes was compared, SLYNTVATL (p17) and ILKEPVHGV (RT). HIV-1 infected cells were more sensitive to lysis by SLYNTVATL-specific CTL than by ILKEPVHGV-specific CTL, because of a higher density of SLYNTVATL-A2 resulting from differences in processing. • Incubation with a T1-cell proteolytic extract showed that by four hours, 25% of a p17 peptide had a C-term Leu-85 and were SLYNTVATL-precursors, while ILKEPVHGV-precursors were far less frequent (6.8%) even with four times more proteolytic extract after 30 hours. • p17 was preferentially cleaved between Leu85 and Tyr86, while appropriate Val484 and Tyr485 cleavage was minor for RT. • In a competition experiment, RSLYNTVATL bound TAP 3.7-fold more efficiently than RT peptides. • No difference in CTL avidity was detected in six patients with HLA-A2-restricted responses to these epitopes. • No significant difference in HLA-A2 binding of to p17 or RT epitopes was observed.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	Vaccine	mouse (A2)	De Lucca2002
	Vaccine *Vector/Type:* peptide *Adjuvant:* Complete Freund's Adjuvant (CFA) **Epitope name** p9. • BALB/c mice immunized with the p9 peptide, ILKEPVHGV, elicited specific lymphocyte proliferation activity. • Exposure of lymphocytes from HIV-negative, HLA-A2 positive people to p9-RNA stimulated lymphocyte proliferation activity to p9. Anti-p9 CTL activity in human lymphocytes incubated with RNA extracted from lymphoid organs of p9-vaccinated mice could be more intensely stimulated. • This murine RNA also mediated RNA-dependent protein kinase (PKR) and NFkappaB activation in the human lymphocytes, which may be driving the enhanced CTL stimulation in the human cells.				
RT (309–317)	RT	ILKEPVHGV	HIV-1 infection	human (A2)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** ILK. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
RT (309–317)	p51 (476–484)	ILKEPVHGV	Vaccine	mouse (A2)	Kmieciak2001
	Vaccine *Strain:* B clade IIIB *HIV component:* Gag, Pol *Adjuvant:* IL-12 **Donor HLA** H2/Kb. • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with either a p17-p24-p51 fusion protein (vG/P-92) or the Gag-Pol precursor protein (vVK1). • Compared to vVK1, vG/P-92 induced a significant increase in Gag and Pol induced IFNgamma production and CTL responses, and to the epitopes SLYNTVATL and ILKEPVHGV, as determined by Elispot and 51Cr-release assays.				
RT (309–317)	RT (309–317 NL-43)	ILKEPVHGV	HIV-1 infection	human (A2)	Ali2003
	Keywords class I down-regulation by Nef, escape. • NL43 was passaged in the presencNL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days. • Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNVATL in p17 Gag.				
RT (309–317)	Pol (476–)	ILKEPVHGV	HIV-1 infection	human (A2)	Corbet2003
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol476. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • 9/17 HIV-infected HLA-A2+ people recognized this epitope.				
RT (309–317)	RT (309–317)	ILKEPVHGV	Vaccine, in vitro stimulation or selectio	transgenic mouse (A2)	Domingo2003
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Epitope name** RT2. • A virus-like protein scaffold, called E2DISP, derived from pyruvate dehydrogenase multienzyme from Bacillus stearothermophilus has been engineered to display 60 copies of one or more epitopes on a single molecule. • The E2DISP scaffold displaying pep23 is able to stimulate a Th responses, and peptide RT2, which is a CTL epitope from HIV-1 RT, was able to elicit a CD8+ T cell response *in vitro* and in a vaccinated HLA-A2 transgenic mouse. Thus the E2DISP scaffold allows cell-entry and access to the class I and class II processing pathways.				
RT (309–317)	Pol (476–484)	ILKEPVHGV	HIV-1 infection	human (A2)	Sandberg2003
	Keywords responses in children. **Assay type** CD8 T-cell Elispot - IFNγ, Tetramer binding, Flow cytometric CTL assay. • 65 vertically HIV-1 infected children, ages 1-16, the majority undergoing ART, were analyzed in regard to their plasma viremia and CD4+ and CD8+ T cell counts, and CD8+ T cell responses. • Using vaccina expressed Gag, Pol, Env, Rev, Nef in target cells in an Elispot assay, 85% of the children recognized at least one HIV antigen. The strong CD8+ T cell responses were directed against Pol, followed by Gag and Nef. Children younger than 4 had significantly weaker responses (7/14 had no reponse) than older children (only 1/32 had no response, and responses were greater in magnitude). • SLYNTVATL and ILKEPVHGV tetramers were used to quantitate specific responses. 49 chlidren in an expanded cohort carried HLA-A2. 1/11 children under 3 years of age had detectable CD8+ T-cell responses to SLYNTVATL, 2/11 to ILKEPVHGV. Among children over 3, 11/38 recognized SLYNTVATL and 9/38 recognized ILKEPVHGV. • Older children that maintained a CD4 count greater than 400 cells/ul tended to have stronger CTL reponses.				
RT (309–317)	RT (309–317)	ILKEPVHGV	HIV-1 infection	(A2)	Sun2003
	Keywords assay standardization, memory cells. **Assay type** cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding, Intracellular cytokine staining. **Donor HLA** A2, A3, B27, B51; A2, A3, B27, B57; A2, A23, B57. • This study compares assay methods for testing CTL responses using samples from 20 HIV+ patients. The study compares ELISpot, tetramer-binding, and intracellular IFNγ. Tetramer-bidning analysis was performed with Gag (SLYNTVATL) or Pol (ILKEPVHGV) tetramers. Antigen presentation using recombinant vaccinia viruses (rVVs) encoding HIV-LAI Gag, Pol, Env, Nef, Tat and Vif proteins was compared to peptide panels. HIV antigen recognition in memory CTLs was measured by chronium release assay and compared to effector/memory CD8+ T cells in an IFN-γ ELISpot assay.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Results: IFNγ Elispot and flow cytometry gave similar frequencies of HIV specific CD8+ Tcells. Tetramer-binding analysis was most sensitive. Pools of peptides and the sum of frequencies of individual peptides were comparable. Elispot assays using peptides were more sensitive than assays using vaccinia expressed proteins. Cr release and Elispot against rVVs gave comparable memory cell responses 2/3s of the time. • 3/7 HLA-A2+ patients recognized this epitope.				
RT (309–317)	RT (309–317 NL43) **Keywords** escape. **Epitope name** IV9. **Assay type** Chromium-release assay, CTL suppression of replication. • Virus was cultured in the presence of CTL lines specific for 4 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts. • There was one cloned cell line that recognized ILKEPVHGV, 68A62. After 2 weeks of passaging HIV-1 in the presence of 68A62, the mutated epitope ilkeLvhgv was found in 6/12 sequences.	ILKEPVHGV	HIV-1 infection	human (A2)	Yang2003
RT (309–317)	Pol (476–484) **Keywords** supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).	ILKEPVHGV	HIV-1 infection	human (A2 supertype)	Propato2001
RT (309–317)	Pol (464–472) • One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.	ILKEPVHGV	HIV-1 infection	human (A2, A*0201)	Ferrari2000
RT (309–317)	Pol (subtype B) **Keywords** inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among B and D clade viruses. • Clade A version of the epitope, ILKDPVHGV, was preferentially recognized by CTL.	ILKEPVHGV	HIV-1 exposed seronegative	human (A2, A*0202)	Rowland-Jones1998b
RT (309–317)	RT (309–317) **Vaccine** *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT **Keywords** epitope processing. **Epitope name** RT2.	ILKEPVHGV	Vaccine, in vitro stimulation or selectio	human, mouse (A2, A2 transgenic)	De Berardinis2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses *in vitro* in PBMC from HIV negative individuals in and *in vivo* in immunization of HLA-A2 transgenic mice. • Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors.				
RT (309–317)	Pol	ILKEPVHGV	Vaccine	transgenic mouse (A2.1)	Ishioka1999
	Vaccine *Vector/Type:* DNA • A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed. • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans. • HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection.				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR22. • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
RT (309–317)	RT (476–484 LAI)	ILKEPVHGV	Vaccine	mouse (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30 **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR22. • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
RT (309–318)	RT (476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human (B*1501)	Frahm2004
	• C. Brander notes this is a B*1501 epitope.				
RT (309–318)	RT (309–318)	IKLEPVHGVY	HIV-1 infection	human (B62)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to four B62-restricted epitopes tested.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (309–318)	RT (476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human (Bw62)	McMichael1994, Menendez-Arias1998
	Keywords review. • Review of HIV CTL epitopes.				
RT (309–318)	Pol	ILKEPVHGVY	HIV-1 infection, Vaccine	human (Bw62)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
RT (328–352)	RT (495–515 LAI)	EIQKQGQGQWTYQIYQEPF-KNLKTG	HIV-1 infection	human (A11)	Menendez-Arias1998, Walker1989
	• One of five epitopes defined for RT-specific CTL clones in this study.				
RT (340–350)	RT (507–516)	QIYQEPFKNLK	HIV-1 infection	human	Menendez-Arias1998, Price1995
	• Study of cytokines released by HIV-1 specific activated CTL.				
RT (340–350)	Pol (487–497 93TH253 subtype CRF01)	QIYQEPFKNLK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P495-505. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33. • This epitope was reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.				
RT (340–350)	Pol (487–497 93TH253 subtype CRF01)	QIYQEPFKNLK	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 5/8 tested FSWs recognized this epitope. • This epitope was highly conserved in other subtypes, although exact matches were not very common.				
RT (340–352)	RT (507–519 LAI)	QIYQEPFKNLKTG	HIV-1 infection	human (A11)	Johnson1994c, Menendez-Arias1998
	Keywords review. • This epitope was listed in a review.				
RT (340–352)	Pol (495–507)	QIYQEPFKNLKTG	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (341–350)	RT (508–516)	IYQEPFKNLK	HIV-1 infection	human (A*1101)	Culmann1998
	• C. Brander notes that this is an A*1101 epitope in the 1999 database.				
RT (341–350)	RT (508–517 LAI)	IYQEPFKNLK	HIV-1 infection	human (A*1101)	Frahm2004
	• C. Brander notes this is an A*1101 epitope.				
RT (341–350)	RT (508–517 SF2)	IYQEPFKNLK	HIV-1 infection	human (A11)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3.				
RT (341–350)	Pol (508–516)	IYQEPFKNLK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
RT (356–365)		RMRGAHTNDV	HIV-1 infection	human (A*3002)	Sabbaj2002b
	Epitope name Pol-RV10. **Donor HLA** A*2904 A*3002 B*1503 B*5802 Cw*0202 Cw*0602. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 01RCH50 also recognized the epitope WRFDSRLAF, Nef(183-191), B*1503. • Among HIV+ individuals who carried HLA A30, 5/16 (31%) recognized this epitope.				
RT (356–365)	RT (356–365)	RMRGAHTNDV	HIV-1 infection	human (A*3002)	Frahm2004
RT (356–366)	RT (356–366)	RMRGAHTNDVK	HIV-1 infection	human (A*03)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (356–366)	RT (15–26)	RMRGAHTNDVK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-RK11. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 5/7 individuals began to have detectable responses to this epitope after STI.			
RT (364–372)	RT (518–526 U455)	DVKQLTEVV		human (A28, A*6802)	Dong1998a, Menendez-Arias1998
	Keywords inter-clade comparisons. • Predicted on binding motif, no truncations analyzed. • Reacts with clade A consensus (U455), and with the peptide DVKQLAEAV, from the D clade.				
RT (364–372)	RT (470–478 subtype A)	DVKQLTEVV	HIV-1 infection	human (B70)	Dorrell1999
	Keywords inter-clade comparisons. • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa. • This CTL response was defined in a patient with an A subtype infection. • Bulk cultures from this patient gave a CTL response that could recognize the subtype D form of this epitope, with two substitutions (DVKQLAEAV), though a CTL line from these cultures didn't recognize the B clade variant (DVKQLTEAV)				
RT (366–385)	Pol (521–540)	KQLTEAVOKIAMESIVIWGK	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
RT (373–390)	RT (373–390 HXB2)	QKIATESIVIWGKTPKFK	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 21% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
RT (374–383)	RT (LAI)	KITTESIVIW	HIV-1 infection	human (B*5701)	Menendez-Arias1998, vanderBurg1997
	Keywords rate of progression. • Patients studied were from the Amsterdam cohort. • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS); no differences could be found in the degree of conservation between them. • Epitope recognized by LTS and by a progressor.				
RT (374–383)	RT (LAI)	KITTESIVIW	HIV-1 infection	human (B*5701)	vanderBurg1997
	• Recognized by CTL from a progressor and a long-term survivor, PIVLPEKDSW was also recognized.				
RT (375–383)	RT (375–383 LAI)	ITTESIVIW	HIV-1 infection	human (B*5701 B*5801)	Klein1998
	Keywords rate of progression. • Another patient recognized the ten-mer version of this epitope, KITTESIVIW [vanderBurg1997] • B57 has been associated with long-term non-progression in the Amsterdam cohort. • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag. • The patient that recognized ITTESIVIW also recognized IVLPEKDSW.				
RT (375–383)	RT (375–383)	IAMESIVIW		human (B*5801)	Frahm2004
RT (375–383)	RT (375–383 SF2)	ITTESIVIW	HIV-1 infection	human (B57)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3.				
RT (392–401)	RT (559–568 LAI)	PIQKETWETW		human (A*3201)	Harrer1996b, Menendez-Arias1998
	• Reviewed in [Menendez-Arias1998], suggest the epitope is HLA B53/Cw2. • C. Brander notes that this is an A*3201 epitope in the 1999 database.				
RT (392–401)	RT (559–568 LAI)	PIQKETWETW		human (A*3201)	Frahm2004
	• C. Brander notes this is an A*3201 epitope.				
RT (392–401)		PIQKETWETW	HIV-1 infection	human (A*3201)	Sabbaj2002b
	Keywords HAART. **Epitope name** Pol-PW10. **Donor HLA** 01RCH59 A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This study monitored epitope responses in HIV-1 infected minority women living in the United. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previou. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated. • Subject 01RCH59 was Hispanic, was not on HAART, viral load 5100, CD4 count 349, and she also recognized QASQEVKNW, p24(176-184), B*5301. • Among HIV+ individuals who carried HLA A32, 1/2 (50%) recognized this epitope.				
RT (392–401)	RT (559–568 SF2)	PIQKETWETW	HIV-1 infection	human (A32)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A32+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3.				
RT (392–401)	RT	PIQKETWETW	HIV-1 infection	human (A32)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** A32-PW10(RT). **Donor HLA** A32,A?,B7,B14; A32,A?,B44,B?; A30,A32,B18,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT). Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
RT (397–406)	RT (LAI)	TWETWWTEYW	HIV-1 infection	human (B44)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from two progressors, EILKEPVGHGV and EELRQHLLRW were also recognized by one, and RETKLGKAGY was also recognized by the other.				
RT (416–423)	Pol (571–)	FVNTPPLV	HIV-1 infection, Vaccine	transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol571.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced a CTL responses 1/6 transgenic mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.				
RT (416–424)	Pol (563–571 93TH253 subtype CRF01)	FVNTPPLVK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P571-579. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33.				
RT (416–424)	Pol (563–571 93TH253 subtype CRF01)	FVNTPPLVK	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 1/8 tested FSWs recognized it. • This epitope was conserved many subtypes (but not subtype H), but exact matches were not very common.				
RT (421–429)	RT (421–429)	PLVKLWYQL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules.				
RT (432–440)	RT (587–597 SF2)	EPIVGAETF	HIV-1 infection	human (B*3501)	Menendez-Arias1998, Tomiyama1997
	Keywords review. • A CTL clone responsive to this epitope was obtained. • 5/7 B35-positive individuals had a CTL response to this epitope. • An E to D substitution at position 1, and V to I at position 4, reduces activity but not binding to B*3501. • [Menendez-Arias1998] note in their review that this epitope is near the protease cleavage site and conservation of this region is important for proper viral maturation.				
RT (432–440)	Pol (587–595)	EPIVGAETF	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A. • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm. • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
RT (432–440)		EPIVGAETF	HIV-1 infection	human (B35)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
RT (432–440)	Pol (587–595)	EPIVGAETF	HIV-1 infection	human (B35)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective. • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.				
RT (432–440)	RT (587–596 SF2)	EPIVGAETF	HIV-1 infection	human (B35, B51)	Shiga1996
	• Binds HLA-B*3501, and is also presented by B51 – but CTL could not kill RT-vaccinia virus infected cells that expressed B51.				
RT (432–440)	Pol (587–595)	EPIVGAETF	HIV-1 infection	human (B35, B51)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (432–441)	Pol (587–596)	EPIVGAETFY	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A. • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals. • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm. • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
RT (432–441)	RT (587–597 SF2)	EPIVGAETFY	HIV-1 infection	mouse (B35)	Menendez-Arias1998, Shiga1996
	Keywords review. • Binds HLA-B*3501, but not presented by B51, in contrast to the peptide EPIVGAETF. • [Menendez-Arias1998] note in their review that this epitope is located near the protease cleavage site and conservation of this region is important for viral maturation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain.				
RT (432–441)	RT (587–597 SF2)	EPIVGAETFY	HIV-1 infection	human (B35)	Kawana1999
	Keywords rate of progression. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.				
RT (434–447)	RT (LAI)	IVGAETFYVDGAAS	HIV-1 infection	human (A*6802)	Menendez-Arias1998, vanderBurg1997
	• Recognized by CTL from a long-term survivor that recognized a set of 5 overlapping peptides spanning IVGAETFYVDGAAS as well as PIVLPEKDSW and KITTESIVIW. • A*6802 is a subset of HLA-A28. • This epitope spans the Pol p66 RT – p15 (RNAse) domain.				
RT (436–445)	RT (591–600 IIIB)	GAETFYVDGA	HIV-1 infection	human (B45)	Menendez-Arias1998
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain.				
RT (436–445)	Pol (591–600 IIIB)	GVETFYVDGA	HIV-1 infection	human (B45)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • No variants of this epitope were found in a non-transmitting mother who had a CTL response to it. • This epitope spans the Pol p66 RT – p15 (RNAse) domain.				
RT (437–445)		AETFYVDGA	HIV-1 infection	human (B*4501)	Sabbaj2002b
	Keywords HAART. **Epitope name** Pol-AA9. **Donor HLA** A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; RSLYNTVATLY, p17(76-86), HLA A*3002; and HIGPGRAFY, gp160(310-318), HLA A*3002. • Among HIV+ individuals who carried HLA B45, 3/9 (33%) recognized this epitope.				
RT (437–447)	RT (592–602 LAI)	AETFYVDGAAN		human (A28)	Brander1996b, Menendez-Arias1998
	• P. Johnson, pers. comm. • This epitope spans the Pol p66 RT – p15 (RNAse) domain.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (437–447)	Pol (592–602)	AETFYVDGAAN	HIV-1 infection	human (A28)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
RT (438–448)	RT (593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human (A26)	Menendez-Arias1998
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain.				
RT (438–448)	Pol (593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human (A26)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • One other variant was found that gave a positive, though reduced, CTL response: ETYYVNGAANR. • This epitope spans the Pol p66 RT – p15 (RNAse) domain.				
RT (440–448)	Pol (594–602 SF2)	FYVDGAANR	HIV-1 infection, computer prediction	human (A*3303)	Hossain2003
	Keywords binding affinity, computational epitope prediction. **Assay type** Chromium-release assay. • HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing. • This epitope is one of the 4 that are properly processed.				
RT (448–457)	RT	RETKLGKAGY	HIV-1 infection	human (A29)	vanderBurg1997
	Keywords rate of progression. • Patients studied were from the Amsterdam cohort. • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS) and no differences could be found in the degree of conservation between them. • Epitope recognized by a LTS. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (449–457)		ETKLGKAGY	HIV-1 infection	human (A*2601)	Sabbaj2002b
	Keywords HAART. **Epitope name** Pol-EY9. **Donor HLA** A*3303 A*2601 B*5801 B*8201 Cw*0302 Cw*0701. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 03RCH40 was African American, had a viral load of 2500, CD4 count of 372, was not on HAART, and also recognized the epitope DILDLWIY, Nef(108-115), HLA Cw*0701. • Among HIV+ individuals who carried HLA A26, 2/8 (25%) recognized this epitope.				
RT (449–457)	Pol (604–612)	ETKLGKAGY	HIV-1 infection	human (A*2601)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (451–459)	Pol (606–)	KLGKAGYVT	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol606. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that did not induce CTL or CD8+ T-cell IFN gamma responses in transgenic mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.			
RT (481–505)	RT (648–672)	AIYLALQDSGLEVNIVTDS-QYALGI	HIV-1 infection	human	Menendez-Arias1998, Price1995
	• Study of cytokines released by HIV-1 specific activated CTL. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (481–505)	RT (648–672 PV22)	AIYLALQDSGLEVNIVTDS-QYALGI	HIV-1 infection	human (B14)	Kalams1994, Menendez-Arias1998
	• A CTL response used to study gene usage in HLA-B14 response. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (485–493)	Pol (649–659 BH10, LAI)	ALQDSGLEV	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is IYLALQDSGLE) has similarity with the epidermal growth factor receptor kinase substrate EPS8, fragment ISAAASDSGVE.				
RT (485–493)	RT (640–648 HXB2R)	ALQDSGLEV	Vaccine	human (A2)	Brander1995a
	Vaccine *Strain:* B clade HXB2 *HIV component:* RT • Epitope studied in the context of inclusion in a synthetic vaccine. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (485–493)	RT (640–648 HXB2R)	ALQDSGLEV	HIV-1 infection	human (A2.1)	Brander1995a, Brander1996a
	• This epitope was recognized by PBMC from 3/14 HIV+ asymptomatic patients. • This epitope was used along with Env CTL epitope TLTSCNTSV and a tetanus toxin T helper epitope for a synthetic vaccine. • This vaccine failed to induce a CTL response, although a helper response was evident. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (485–505)	RT (648–672)	ALQDSGLEVVTDSQYALGI	HIV-1 infection	human (B14)	Brander1995b
	• Unpublished, S. Kalams. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (496–505)		VTDSQYALGI	HIV-1 infection	human (B*1503)	Sabbaj2002b
	Keywords HAART. **Epitope name** Pol-VI10.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA A*3002 A*6801 B*0801 B*1503 Cw*0701 Cw*08(02,05). • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 01RCH51 was an African American on HAART, viral load 980, CD4 count 811. • Among HIV+ individuals who carried HLA B15, 1/17 (6%) recognized this epitope.				
RT (496–505)	Pol (651–660)	VTDSQYALGI	HIV-1 infection	human (B*1503)	Frahm2004
RT (496–505)	Pol (subtype B)	VTDSQYALGI	HIV-1 exposed seronegative	human (B14, B*1402)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B and D clade viruses.				
RT (496–505)	RT (663–672 IIIB)	VTDSQYALGI	HIV-1 infection	human (Cw8)	Brander1996b
	• Unpublished, P. Johnson. • Published in this database in 1995 as B14, but B14 transfected cells did not present the peptide and it is thought to be presented by the genetically linked Cw8 molecule instead [Brander1996b] • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (496–505)	RT	VTDSQYALGI	HIV-1 exposed seronegative	human (Cw8)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A and D subtype consensus are identical to the B clade epitope. • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication) • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (509–518)	Pol	QPDKSESELV		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay. • QPDKSESELV was newly identified as an HLA-B7 epitope in this study.				
RT (516–525)	RT (516–525)	ELVNQIIEQL	HIV-1 infection	human (A2)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				
RT (520–528)	Pol (520–528 LAI)	QIIEQLIKK		human (A*1101)	Frahm2004, Fukada1999
	• C. Brander notes this is an A*1101 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (520–528)	Pol (675–683)	QIIEQLIKK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons, TCR usage. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • QIIEQLIKK was found to elicit clade-specific responses in clade B (QIIEQLIKK is most common) and clade E (qiieElikk is most common). QIIEQLIKK was strongly recognized by CTL from 1/5 B clade infected Japanese subjects, and qiieElikk from 3/7 E clade infected Thai subjects. The variant qiieKliEk, common in the A subtype, was also recognized in 2/7 E clade infected Thai subjects. • The binding of QIIEQLIKK, qiieElikk and qiieKliEk to HLA A*1101 was similar, but CTL clones from individuals did not cross-react with the cross-clade peptides indicating that the substitutions inhibited TCR interaction.			
RT (520–528)	RT (80–88)	QIIEQLIKK	HIV-1 infection	human (A*1101)	Frahm2004
RT (530–538)	Pol (680–691 BH10, LAI)	KVYLAWVPA	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is IKKEKVYLAWV) has similarity with B-cell growth factor precursor, fragment IKKERLWLGPV.				
RT (530–538)		KVYLAWVPA	HIV-1 infection	human (A*0301)	Sabbaj2002b
	Keywords HAART. **Epitope name** Pol-KA9. **Donor HLA** A*0202 A*0301 B*4501 B*5301 Cw*0401 Cw*1502. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Patient 04RCH86 was Hispanic, not on HAART, and had a viral load of 7600 and CD4 count of i774. • Among HIV+ individuals who carried HLA A*03, 2/21 (10%) recognized this epitope.				
RT (532–540)	Pol (687–)	YLAWVPAHK	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Pol687. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.				
RT (532–540)	Pol (714–722)	YLAWVPAHK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
RT (532–540)	RT (532–540)	YLAWVPAHK	HIV-1 infection	human (B7)	Haas1998
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules. • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT.				

II-B-11 RT-Integrase CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT-Integrase (560–8)	Pol (715–723)	LFLDGIDKA		human (B*81)	Frahm2004

II-B-12 Integrase CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (20–28)	Pol (762–770)	RAMASDFNL	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
Integrase (22–31)	Pol (764–773)	MASDFNLPPV	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)				
Integrase (28–36)	Pol (743–751 SF2)	LPPVVAKEI	HIV-1 infection	human (B*5101)	Tomiyama1999
	Keywords inter-clade comparisons, rate of progression. • HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed. • Four of the six epitopes were highly conserved among B subtype sequences – LPPVVAKEI is highly conserved.				
Integrase (82–89)	RT (797–804 SF2)	GYIEAEVI	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • GYIEAEVI bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
Integrase (89–98)	Pol (805–814 BH10, LAI)	IPAETGQETA	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is PAETGQETAY) has similarity with Integrin beta-4 precursor (GP150)(CD104), fragment PAETNGEITAY.				
Integrase (89–98)	Pol	IPAETGQETA		human (B56)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay. • IPAETGQETA was newly identified as an HLA-B56 epitope in this study.				
Integrase (96–104)	Integrase (823–831)	ETAYFILKL		human (A*6802)	Dong1998b
	Keywords inter-clade comparisons. • Epitope found in clade A, B, and D – pers. comm. S. Rowland-Jones and T. Dong.				
Integrase (96–104)	Pol (subtype A)	ETAYFILKL	HIV-1 exposed seronegative	human (A*6802)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
Integrase (96–104)	Pol	ETAYFILKL	HIV-1 infection	human (A*6802)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls (ML1671)				
Integrase (96–104)	Pol (744–752)	ETAYFYILKL	HIV-1 infection, HIV-1 exposed seronegative	human (A*6802)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • ETAYFYILKL cross-reacts with clades A, B and D. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-A*6802 women, 3/12 HEPS and 9/11 HIV-1 infected women recognized this epitope likelihood ratio 7.9, p value 0.01, and HEPS women tended to respond to DTVLEDINL, while infected women to ETAYFYILKL. • The dominant response to this HLA allele was to this epitope in 2 of the 3/12 HEPS cases and in all 9/11 HIV-1 infected women that responded to the epitope. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort. • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV. • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Subject ML 1830 made no detectable response prior to seroconversion, but responded to A*6802 DTVLEDINL and A*6802 ETAYFILKL post-seroconversion.				
Integrase (96–104)	Pol (744–752)	ETAYFILKL	HIV-1 infection	human (A*6802)	Appay2000
	• This epitope is newly defined in this study. • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Integrase (123–132)	Integrase (123–132)	STTVKAACWW		human (B*57)	Frahm2004
Integrase (127–135)	Pol (869–877)	KAACWWAGI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
Integrase (173–181)	Pol (888–896)	KTAVQMAVF		human (B*5701)	Frahm2004
	• C. Brander notes this is a B*5701 epitope. • Epitope is motif based, personal communication from C. Hay. • Subtype of B57 not determined.				
Integrase (173–181)	Pol (888–896)	KTAVQMAVF		human (B57)	Hay1999a
	• Epitope is motif based, personal communication from C. Hay.				
Integrase (177–186)	Pol (919–928)	QMAVFIHNFK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
Integrase (178–186)	Pol (920–928)	MAVFIHNFK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
Integrase (179–187)	Pol (921–929)	AVFIHNFKR	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
Integrase (179–188)	Integrase (179–188)	AVFIHNFKRK	HIV-1 infection	human (A*03)	Frahm2004
Integrase (179–188)	Integrase (179–188 LAI)	AVFIHNFKRK		human (A*1101)	Frahm2004, Fukada1999
	• C. Brander notes this is an A*1101 epitope.				
Integrase (179–188)	Pol (894–903)	AVFIHNFKRK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • AVFIHNFKRK is commonly found in viruses representing subtypes A-E. It was strongly recognized by CTL from 4/7 E clade infected Thai subjects.				
Integrase (179–188)	Pol (894–903 93TH253 subtype CRF01)	AVFIHNFKRK	HIV-1 exposed seronegative	human (A11)	Bond2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** P894-903. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and had been predicted to be a possible A11 epitope using Epimer in [Bond2001]				
Integrase (179–188)	Integrase (894–904)	AVFIHNFKRK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-AK10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (179–196)	Pol (894–911)	AVFIHNFKRKGGIGGYSA	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Integrase (185–194)	Integrase (185–194)	FKRKGGIGGY	HIV-1 infection	human (B*1503)	Frahm2004
Integrase (210–227)	Pol (925–942)	TKELQKQIIKIQNFRVYY	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Integrase (218–235)	RT-Integrase (218–235 HXB2)	TKIQNFRVYYRDSRDPLW	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 21% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
Integrase (219–227)		KIQNFRVYY	HIV-1 infection	human (A*3002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Pol-KY9. **Donor HLA** A*0205 A*3002 B*1402 B*5301 Cw*0401 Cw*0802. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Patient 00RCH28 was African American, not on HAART, had a viral load of 5900 and CD4 count of 889, and she also recognized RIRQGLERA, gp160(846-854), A*0205. • Among HIV+ individuals who carried HLA A30, 6/16 (38%) recognized this epitope.				
Integrase (219–227)	Integrase (219–227)	KIQNFRVYY	HIV-1 infection	human (A*3002)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (219–228)	Pol (934–943 SF2)	KIQNFRVYYR	HIV-1 infection, computer prediction	human (A*3303)	Hossain2003
	Keywords binding affinity, computational epitope prediction. **Assay type** Chromium-release assay. • HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individual, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing. • This epitope is one of the 4 that are properly processed.				
Integrase (219–228)	Pol (919–928)	KIQNFRVYYR	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
Integrase (241–249)	Pol (576–584)	LLWKGEGAV	in vitro stimulation or selectio	human (A*0201)	vanderBurg1996
	• Slow dissociation rate, associated with immunogenicity in transgenic HLA-A*0201/K^b mice. • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual.				
Integrase (241–249)	Pol (956–964)	LLWKGEGAV	HIV-1 infection	human (A2)	Kundu1998b
	Keywords dendritic cells. • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients. • 1/6 showed increased Env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated. • LLWKGEGAV is a conserved HLA-A2 epitope included in this study – 6/6 patients had this sequence as their HIV direct sequence, but only four of these had a detectable CTL response.				
Integrase (241–249)	Pol (956–964 HXB2R)	LLWKGEGAV	Peptide-HLA interaction	human (A2)	Parker1992, Parker1994
	• Studied in the context of HLA-A2 peptide binding.				
Integrase (241–249)	Pol (956–964 HXB2R)	LLWKGEGAV	Peptide-HLA interaction	human (A2)	Brander1995a
	• No CTL activity found in HIV-infected subjects, epitope studied in the context of inclusion in a synthetic vaccine.				
Integrase (241–249)	Pol (956–964)	LLWKGEGAW	HIV-1 infection	human (A2, A*0201)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Integrase (241–249)	RT (956–964 HXB2R)	LLWKGEGAV	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR28.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
Integrase (241–249)	RT (956–964 HXB2R)	LLWKGEGAV	Vaccine	mouse (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30 **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR28. • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
Integrase (260–268)	Integrase (260–268)	VPRRKAKII		human (B*42)	Frahm2004
Integrase (263–271)	Integrase (263–271)	RKAKIIRDY	HIV-1 infection	human (B*1503)	Frahm2004
Integrase (263–271)	Integrase (263–271)	RKAKIIRDY	HIV-1 infection	human (B*1503)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*2301, B*3501, B*1503 (B72), Cw2, Cw7. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				

II-B-13 Pol CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	RT (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.				
Pol	p66 (LAV)		HIV-1 infection	human	Zheng1999
	Keywords epitope processing, dendritic cells.				
	• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone.				
	• Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway.				
Pol	Pol (IIIB)		HIV-1 infection	human	Wasik2000
	Keywords rate of progression, Th1.				
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants.				
	• No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors.				
	• CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.				
Pol	Pol (LAI)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp41, Protease, V3				
	• The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36))				
	• Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36.				
	• Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160.				
Pol	Pol (172–219 subtype B)		Vaccine	human	Gorse1999b
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade SF2 *HIV component:* Env, Gag, Nef, Protease				
	• The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120.				
	• In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients.				
	• The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity.				
Pol	Pol (IIIB)		HIV-1 infection	human	Betts1999
	Keywords rate of progression.				
	• This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection.				
Pol	Pol (BRU)		HIV-1 infection	human	Aladdin1999
	Keywords rate of progression.				
	• In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	RT (LAI)		HIV-1 infection	human	Buseyne1998b
	Keywords inter-clade comparisons.				
	• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.				
Pol	RT		Vaccine	mouse	Kim1997c
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12				
	• A gag/pol, vif or gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice.				
	• When IL-12 was present, CTL response could be detected even without *in vitro* stimulation.				
Pol	RT		HIV-1 infection	human	Trickett1998
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection.				
	• Improvement in CD4+ and CD8+ T cells were seen in 7/12, and an increase in the CTL response to Pol was seen in one patient.				
Pol	RT		HIV-1 infection	human	Froebel1997
	Keywords rate of progression.				
	• Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor.				
	• Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells.				
	• The child who progressed consistently had CTL against Pol and Tat.				
	• The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression.				
Pol	Pol (IIIB)		HIV-1 infection	human	Betts1997
	Keywords inter-clade comparisons.				
	• 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins.				
	• A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients.				
Pol	RT		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function.				
	• Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.				
Pol	Pol (LAI, MN)		HIV-1 exposed seronegative	human	Goh1999
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype.				
	• In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins.				
Pol	Pol (LAI)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT				
	• A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86				
	• The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.				
Pol	Pol (IIIB)		HIV-1 infection	human	Jin1998a
	• CTL precursor frequencies were determined in HIV-1 infected pregnant women, and significantly higher CTLp frequencies to Pol and Nef were found in non-transmitting mothers than in transmitting mothers;				
Pol	Pol		HIV-1 infection	human	Young2001
	• Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500.				
	• 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12.				
Pol	RT (subtype A, B, D)		HIV-1 infection	human	Cao2000
	Keywords inter-clade comparisons.				
	• HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.				
	• Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.				
Pol	Pol		HIV-1 infection	human	White2001
	• HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women.				
Pol	Pol (IIIB)		HIV-1 infection	human	Jin2000a
	Keywords rate of progression.				
	• The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets.				
	• LTNPs have high memory CTL numbers and low viral load.				
Pol	Pol		HIV-1 exposed seronegative	human	Rowland-Jones2001
	Keywords review, HIV exposed persistently seronegative (HEPS).				
	• This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population.				
	• The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays.				
	• CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases.				
	• CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people.				
Pol			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env. • Reviewed in [Kuhn2002].				
Pol			HIV-1 infection	human	Kuhn2002, Wasik1999
	Keywords HAART, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission, rate of progression. • In HIV-infected infants HIV-specific, CTL responses were not detectable in icord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied. • The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies. • Stronger responses were detected after initiation of the antiretroviral therapy. • Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth. • Reviewed in [Kuhn2002].				
Pol			HIV-1 infection	human	Aldhous1994, Kuhn2002
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Pol			HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed, however, epitopes were not found that span the invariant, most highly conserved regions of RT and Protease. This might be due to the virus evolving conserved features that disallow the CTL responses in these most conserved regions, as functional constraints for enzyme function would not tolerate change and normal capacity for immune escape by rapid evolution is lost in these domains.				
Pol			HIV-1 infection	human	Loemba2002
	Keywords HAART, inter-clade comparisons. • Therapeutic RT inhibitors were used to select *in vitro* for resistance mutations in subtype C viruses. Many of the resistance mutations were located within analogs to CTL epitopes that had been defined for the B subtype,				
Pol	(IIIB) **Keywords** HAART, acute infection.		HIV-1 infection	human	Ortiz2002

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Subjects treated with HAART early in HIV-infection showed a correlation between the number of viremic episodes and the total as well as the Pol-specific CD8 T-cell activity as measured by Elispot SFC per million PBMC summed across Pol, Env, Nef and Gag. The subjects treated early after infection had higher levels of CD8+ T-cell activity (N = 31) than those treated later (N = 23), and a greater capacity to enhance CD8+ T-cell responses to viremic episodes.				
Pol	(MN)		HIV-1 infection	human	Edwards2002
	Keywords rate of progression. • 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag. • Nef and/or Pol CTL responses were detected in 86% of the subjects. • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load. • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count. • Nef and Env responses did not correlate with either CD4 counts or viral load.				
Pol			HIV-1 infection	human	Larsson2002b
	Keywords HAART, dendritic cells. • Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.				
Pol	(IIIB)		HIV-1 infection	human	Trickett2002
	Keywords immunotherapy. • Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.				
Pol	(IIIB)		HIV-1 and HCV co-infection	human	Lauer2002
	Keywords rate of progression. • HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins. • All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load. • Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted. • HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.				
Pol			HIV-1 infection	human	Scott2001
	Keywords HAART, responses in children. • CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age. • Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses. • One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol. • Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	(IIIB, MN)		HIV-1 infection	human	Larsson2002a
	Keywords dendritic cells.				
	• Dendritic cells acquire and present HIV-1 antigens derived from dead, apoptotic cells or from non-infectious, fusion-competent HIV-1 virions, and these DC cells could stimulate CD4+ and CD8+ T-cells resulting in IFNgamma production in an Elispot assay. Both HLA Class I and class II molecules were used for presentation. This may be an important aspect of the initial immune response to HIV-1 infection of CD4+ cells in the mucosal subepithelia.				
Pol	(IIIB)		HIV-1 infection	human	Ortiz2001
	Keywords HAART, supervised treatment interruptions (STI).				
	• Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.				
Pol	Pol		HIV-1 infection	human (A*0201 and Cw*08)	Shacklett2000
	• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples.				
Pol			computer prediction	(A*0201, B*3501)	Schönbach2002
	Keywords inter-clade comparisons, computational epitope prediction.				
	• Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.				
Pol	RT (IIIB)		HIV-1 infection	human (A2)	Moore2002b
	Keywords epitope processing, escape.				
	• HIV polymorphisms in the RT protein were examined relation to HLA alleles found in a population of 473 participants in the Western Australian HIV Cohort Study. 64 significant associations between polymorphisms at particular positions and HLA alleles were detected, for HLA-B7, -B12, -B35 and -B15. Fifteen of these were in positions with known epitopes, 4 in anchor residues, 11 in other positions. Six additional polymorphic sites associated with particular HLA molecules flanked known epitopes and may relate to processing.				
	• 25 negative associations were also found between polymorphism and HLA alleles. The authors propose this is due to escape mutations in epitopes presented by common HLA types dominating in the population, and give examples of five amino acids which are in the consensus and tend to be stable in those with the most common HLA allele, HLA-A2.				
Pol	Pol		HIV-1 infection	human (B*35)	Jin2002
	Keywords rate of progression.				
	• Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501.				
	• Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env.				
	• The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Pol	Pol		Vaccine	mouse (H-2^d)	Huang2001
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB2, B clade NL43 *HIV component:* Gag, Pol				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Different HIV strains were used for different regions: gag HXB2, pol NL43 • Mice were immunized with four humanized DNA constructs: GagPol, that would form a pseudoparticle carrying Gag and Pol, Gag, Pol or a GagPol fusion construct. • The GagPol pseudoparticle, Gag and GagPol fusion construct all elicited strong anti-Gag CTL, but only the GagPol fusion construct elicited strong anti -Pol CTL.				

II-B-14 Vif CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (17–26)		RIRTWKSLVK	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Vif (17–26)	Vif (17–26 SF2)	RIRTWKSLVK	HIV-1 infection	human (A*0301)	Altfeld2001a
	Epitope name RK10. • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • 10/29 (35%) individuals tested responded to Vif. • This epitope was recognized by 3/15 individuals expressing A*0301 allele. • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • Overlapping Vif peptides QVDRMRIRTWKSLVK and RIRTWKSLVKHHMYI both reacted with T-cells from AC-06 and contained epitope RIRTWK-SLVK.			
Vif (17–26)	Vif (17–26)	RIRTWKSLVK	HIV-1 infection	human (A*0301)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (17–26)		RIRTWKSLVK	HIV-1 infection	human (A03)	Sabbaj2002b
	Epitope name Vif-RK10. • Among HIV+ individuals who carried HLA A03, 3/21 (14%) recognized this epitope.				
Vif (17–26)	(LAI)	RIRTWKSLVK		(A3)	Altfeld2000a, Frahm2004
Vif (17–26)	Vif (17–26)	RIRTWKSLVK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-RK10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals had detectable responses to this epitope after STI.				
Vif (23–31)	Vif (23–)	SLVKHHMYV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Vif *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Vif23(9V). **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. A response was detected in 1/17 HIV+ HLA-A2 subjects. • The variant slvkhhmyI was an intermediate A2 binder, and was able to stimulate immune reponses in fewer A2 transgenic mice. The same person recognized both variants.				
Vif (27–41)	Vif	HHMYISKKAKGWGWFYR	HIV-1 infection	human	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 33% (23/70) targeted one or more Vif peptides, and this peptide was the most frequently recognized epitope in Vif (25%). • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Vif (28–36)	Vif (28–36)	HMYISKKAK	HIV-1 infection	human (A*03)	Frahm2004
Vif (28–36)	Vif (28–36)	HMYISKKAK	HIV-1 infection	human (A*0301)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (28–36)	Vif (28–36)	HMYISKKAK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-HK9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 2/7 individuals had detectable responses to this epitope after STI.				
Vif (31–39)		ISKKAKGWF	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vif (31–39)	Vif (31–39 SF2)	ISKKAKGWF	HIV-1 infection	human (B*5701)	Altfeld2001a
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • 10/29 (35%) individuals tested responded to Vif. • This epitope was recognized by 2/6 individuals expressing B*5701 allele.				
Vif (31–39)	Vif (31–39)	ISKKAKGWF	HIV-1 infection	human (B*5701)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (31–39)	Vif (31–39)	ISKKAKGWF		human (B*5701)	Frahm2004
Vif (48–57)		HPRVSSEVHI	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (48–57)	Vif (48–57 SF2)	HPRVSSEVHI	HIV-1 infection	human (B*0702)	Altfeld2001a
	Epitope name HI10. • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • 10/29 (35%) individuals tested responded to Vif. • This epitope was recognized by 3/8 individuals expressing B*0702 allele. • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • Overlapping Vif peptides HHYESTHPRVSSEVH and THPRVSSEVHIPLG both reacted with T-cells from AC-06 and contained epitope HPRVSSEVHI.				
Vif (48–57)	Vif (48–57)	HPRVSSVHI	HIV-1 infection	human (B*0702)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (48–57)	Vif (48–57)	HPRVSSEVHI	HIV-1 infection	human (B*0702)	Frahm2004
Vif (48–57)	Vif (48–57)	HPRVSSEVHI	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-HI10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.				
Vif (57–66)	Vif (57–66)	IPLGDAKLII		human (B*51)	Frahm2004
Vif (61–80)	Vif (61–80)	EARLVIKTYWGLOTGERDWH	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Vif (71–90)	Vif (71–90)	GLQTGERDWHLGHGVSIEWR	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Vif (79–87)	Vif (79–87)	WHLGHVSI	HIV-1 infection	human (B*1510)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (79–87)	Vif (79–87)	WHLGQGVSI	HIV-1 infection	human (B*3801)	Frahm2004
Vif (101–109)	Vif (101–)	GLADQLIHL	HIV-1 infection, Vaccine, computer prediction	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Vif101(9L). **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 3/17 HIV+ HLA-A2 subjects. • The variant gladqlihM was an intermediate A2 binder, but still could stimulate a response in HLA-A2 transgenic mice. It was not recognized by the 3 people who recognized with GLADQLIHL.			
Vif (102–111)		LADQLIHLHY	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Vif (102–111)	Vif (102–111 SF2)	LADQLIHLHY	HIV-1 infection	human (B*1801)	Altfeld2001a
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • 10/29 (35%) individuals tested responded to Vif. • This epitope was recognized by 2/5 individuals expressing B*1801 allele.				
Vif (102–111)	Vif (102–111)	LADQLIHLHY	HIV-1 infection	human (B*1801)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vif (102–111)	Vif (102–111)	LADQLIHLHY	HIV-1 infection	human (B*1801)	Frahm2004
Vif (127–135)	Vif (125–135)	HIVSPRCEY	HIV-1 infection	human	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A29, B58, B62, Cw*0301, Cw*1601. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
Vif (149–157)	Vif (149–)	ALAALITPK	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Vif *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Vif149. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects.				
Vif (158–166)	Vif (158–)	KIKPPLPSV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Vif *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Vif158(2I). **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects. • The substitution kTkpplpsv was also a good binder, but did not elicit a response in transgenic mice, and no reponse to this variant was detected among the 17 HIV+ people tested.				
Vif (158–168)	Vif (158–168)	KTKPPLPSVKK	HIV-1 infection	human (A*03)	Frahm2004
Vif (158–168)	Vif (158–168)	KTKPPLPSVKK	HIV-1 infection	human (A*0301)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (158–168)	Vif (158–168)	KTKPPLPSVKK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-KK11. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 2/7 individuals had detectable responses to this epitope after STI.			
Vif (160–169)	Vif	KPPLPSVKKL		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay. • KPPLPSVKKL was newly identified as an HLA-B7 epitope in this study.				
Vif	Vif		Vaccine	mouse	Kim1997c
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12 • A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice. • When IL-12 was present, CTL response could be detected even without *in vitro* stimulation.				
Vif	Vif		Vaccine	mouse (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Vif, Vpu **Keywords** inter-clade comparisons, Th1. • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels. • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response. • IL-4 production was not significantly changed after antigen stimulation compared to control levels. • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.				
Vif	Vif		Vaccine	mouse (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Vif, Vpu **Keywords** inter-clade comparisons, Th1. • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels. • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response. • IL-4 production was not significantly changed after antigen stimulation compared to control levels. • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.				

II-B-15 Vpr CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (12–20)		REPHNEWTL	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Vpr (12–20)	Vpr (12–20 SF2)	REPHNEWTL	HIV-1 infection	human (B*4002)	Altfeld2001a
	Keywords acute infection. • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection. • Only one B*4002+ individual was tested, and had a CTL response against REPHNEWTL. • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.			
Vpr (12–20)	Vpr (12–20)	REPHNEWTL	HIV-1 infection	human (B*4002)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.			
Vpr (25–40)	Vpr (25–40 HXB2)	ELKNEAVRHFPRIWLH	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 17% of the study subjects, and it was one of the 25 most frequently recognized peptides.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (29–37)	Vpr (29–37)	EAVRHFPRI		human (B*51)	Frahm2004
Vpr (29–37)	Vpr (29–37 B)	EAVRHFPRI	HIV-1 infection	human (B51)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins.				
	Assay type CD8 T-cell Elispot - IFNγ.				
	Donor HLA A*0201, A*2501, B18, B51, Cw*0102, Cw*1203.				
	• CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.				
	• All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				
	• More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
Vpr (30–38)		AVRHFRPIW	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape.				
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.				
	• While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.				
	• In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.				
	• What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vpr (30–38)	Vpr (29–38 SF2)	AVRHFPRIW	HIV-1 infection	human (B*5701)	Altfeld2001a
	Keywords acute infection.				
	• CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals.				
	• This epitope was recognized by 4/6 individuals expressing B*5701 allele.				
	• Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection.				
	• Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.				
Vpr (30–38)	Vpr (29–38)	AVRHFPRIW	HIV-1 infection	human (B*5701)	Addo2002b
	Keywords early-expressed proteins.				
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.				
	• 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.				
	• All known optimally defined epitopes were summarized for the five proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (30–38)	Vpr (30–38)	AVRHFPRIW		human (B*5701)	Frahm2004
Vpr (30–38)		AVRHFPRIW	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Vpr-AW9. • Among HIV+ individuals who carried HLA B57, 1/7 (14%) recognized this epitope.				
Vpr (31–39)	Vpr (31–39)	VRHFPRIWL	HIV-1 infection	human (B*27)	Frahm2004
Vpr (31–50)	Vpr (31–50)	VRHFPRPWLHSLGQYIYETY	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Vpr (34–42)		FPRIWLHGL	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vpr (34–42)	Vpr (34–)	FPRPWLHGL	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Vpr *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Vpr34. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 3/17 HIV+ HLA-A2 subjects.				
Vpr (34–42)	Vpr (34–42 SF2)	FPRIWLHGL	HIV-1 infection	human (B*0702)	Altfeld2001a
	Keywords acute infection. **Epitope name** FL9. • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • This epitope was recognized by 2/2 individuals expressing B*8101 allele and 4/8 individuals expressing B*0702 allele.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection. • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells. • HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • FPRIWLHGL was the only epitope identified in Vpr for AC-06.				
Vpr (34–42)	Vpr (34–42) **Keywords** early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.	FPRIWLHGL	HIV-1 infection	human (B*0702)	Addo2002b
Vpr (34–42)	Vpr (34–42)	FPRIWLHGL	HIV-1 infection	human (B*0702)	Frahm2004
Vpr (34–42)	Vpr (34–42 SF2) **Keywords** acute infection. **Epitope name** FL9. • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • This epitope was recognized by 2/2 individuals expressing B*8101 allele and 4/8 individuals expressing B*0702 allele. • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection. • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells.	FPRIWLHGL	HIV-1 infection	human (B*8101)	Altfeld2001a
Vpr (34–42)	Vpr (34–42) **Keywords** early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.	FPRIWLHGL	HIV-1 infection	human (B*8101)	Addo2002b
Vpr (34–42)	Vpr (34–42)	FPRIWLHGL		human (B*8101)	Frahm2004
Vpr (34–42)	Vpr (34–42) **Keywords** dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-FL9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 1/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.	FPRIWLHGL	HIV-1 infection	human (B7)	Yu2002a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (41–49)	Vpr	SLGQHIYET	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003

Vaccine *Vector/Type:* peptide *HIV component:* anchored gp120, Vpr *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Keywords binding affinity, inter-clade comparisons, computational epitope prediction.
Epitope name Vpr41.
Assay type T-cell Elispot, Chromium-release assay, Flow cytometric CTL assay.

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.

Vpr (52–62)	Vpr (52–62)	DTWAGVEAIIR	HIV-1 infection	human (A*6801)	Frahm2004
Vpr (53–63)	Vpr (53–63)	TWAVEAIIRI	HIV-1 infection	human	Cao2003

Keywords acute infection, early-expressed proteins.
Assay type CD8 T-cell Elispot - IFNγ.
Donor HLA A1, A3, B7, B14, cw*0702, Cw*0802.

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

Vpr (55–70)	Vpr	AGVEAIIRILQQLLFI	HIV-1 infection	human	Addo2002b

Keywords early-expressed proteins.

- CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 40% (28/70) targeted one or more Vpr peptides, and this peptide was the most frequently recognized epitope in Vpr (41%).
- The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.

Vpr (59–67)		AIIRILQQL	HIV-1 infection	human	Yusim2002

Keywords epitope processing, escape.

- Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.
- While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Vpr (59–67)	Vpr (58–66 LAI)	AIIRILQQL		human (A*0201)	Altfeld2001c, Frahm2004
	• C. Brander notes this is an A*0201 epitope.				
Vpr (59–67)	Vpr (58–66 SF2)	AIIRILQQL	HIV-1 infection	human (A*0201)	Altfeld2001a
	Keywords acute infection. **Epitope name** AL9. • CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals. • This epitope was recognized by 8/24 individuals expressing A*0201 allele. • Epitope is located within a highly conserved alpha helix in Vpr. • Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection. • Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells. • The A2 epitopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded.				
Vpr (59–67)	Vpr (59–)	AIIRILQQL	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction, immunodominance. **Epitope name** Vpr-59. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • AIIRILQQL binds to four HLA-A2 supertype alleles: A*0203, A*0201, A*0206 and A*6802 (highest affinity), but not A*0202. • 5/22 individuals with chronic HIV-1 infection recognized this epitope, but with low magnitude responses in ELISPOT. • 2/12 HLA-A2 patients with acute HIV-1 infection responded strongly to this peptide, but during chronic infection SL9 and Gag-386 tended to be immunodominant while Vpr-59 was weak and sub-dominant. • One of the the acutely infected individuals, AC13, was HLA A*0201/68 B44/14 and also had a strong acute response to gp41 epitope SV10 SLLNATDIAV. • This peptide was shown to be properly processed and presented in TAP-competent B-cell lines *in vitro*.				
Vpr (59–67)	Vpr (58–66)	AIIRILQQL	HIV-1 infection	human (A*0201)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (59–67)	Vpr (59–67)	AIIRILQQL	HIV-1 infection	human (A*0201)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA A*0201, A32, B49, B51, Cw1, Cw7. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
Vpr (59–67)		AIIRILQQL	HIV-1 infection	human (A02)	Sabbaj2002b
	Epitope name Vpr-AL9. • Among HIV+ individuals who carried HLA A02, 4/35 (11%) recognized this epitope.				
Vpr (59–67)	Vpr (59–)	AIIRILQQL	HIV-1 infection	human (A2)	Goulder2001a
	Keywords acute infection. **Epitope name** AL9. • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia. • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.				
Vpr (59–67)	Vpr (59–67 SF2)	AIIRILQQL	HIV-1 infection	human (A2)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 0/4 group 3.				
Vpr (59–67)	Vpr (59–67)	AIIRILQQL	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
Vpr (62–70)	Vpr (62–)	RILQQLLFI	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** Vpr-62.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • This epitope binds to three HLA-A2 supertype alleles: A*0202, A*6802 (strongest affinity) and A*0203. • 3/22 chronically infected patients had a weak ELISPOT response to this epitope. • 0/12 HLA-A2 patients with acute HIV-1 infection responded to this peptide.				
Vpr (62–70)	Vpr (62–70)	RILQQLLFI	HIV-1 infection	human (A*0201)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Vpr (62–70)	Vpr (62–70)	RILQQLLFI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
Vpr			Vaccine	mouse	Muthumani2002
	Vaccine *Vector/Type:* adenovirus *HIV component:* Gag-Pol, Nef, Vpr • Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens. • Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol. • In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.				

II-B-16 Tat CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Tat (2–11)		WPVDPRLEPW	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.			
Tat (2–11)		EPVDPRLEPW	HIV-1 infection	human (B*5301)	Sabbaj2002b
	Epitope name Tat-EW10. • Among HIV+ individuals who carried HLA B*5301, 3/15 (20%) recognized this epitope.				
Tat (2–11)	(LAI)	EPVDPRLEPW		(B53)	Addo2001, Frahm2004
Tat (2–11)	Tat (2–11 BRU)	EPVDPRLEPW	HIV-1 infection	human (B53)	Addo2001
	Epitope name Tat 1. • Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides. • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide. • EPVDPRLEPW was recognized by four individuals, but only two were B53, thus this epitope can probably be presented by other HLA alleles.				
Tat (2–11)	Tat (2–11)	EPVDPRLEPW	HIV-1 infection	human (B53)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Tat (2–11)	Tat	EPVDPRLEPW	HIV-1 infection	human (B53)	Bobbitt2003
	Keywords class I down-regulation by Nef. **Epitope name** EW10. **Assay type** Chromium-release assay, Flow cytometric CTL assay.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Nef, through Nef-mediated MHC-1 down-regulation, is not the only viral protein to influence levels of HIV-specific CTL recognition. The Rev L60F mutation, a common natural variant, can decrease CTL recognition of late gene products. The Rev mutation impacts the early to late gene switch, reducing late gene product production (Gag, Pol, Env, Vpu, Vpr and Vif), while increasing Nef production, both of which reduce the impact CTL recognition of late gene products. As expected, Rev L60F rendered HIV infected cells more resistant to CTL that recognized epitopes from the late proteins Env and Gag. Gag expression is more profoundly reduced than Env, and Gag-specific CTL were more profoundly affected. Conversely CTL against an epitope in an early gene product, Tat, were more effeciently recognized when infected with viruses carrying the Rev L60F mutation. • Patients in the asymptomic phase with active immune responses had more CTL resistant viruses, with lower Rev activity, lower Gag expression and greater resistance to Gag-specific CTL killing, while viruses isolated from people with AIDS were more sensitive to CTL killing.				
Tat (16–30)	Tat (16–30)	SQPKTACNKCYCKRC	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Tat (17–26)		QPKTACTTCY	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Tat (17–26)	Tat (17–26)	QPKTACTTCY	HIV-1 infection	human (B35)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Tat (30–37)	Tat (30–37)	CCFHCQVC		human (Cw*12)	Frahm2004
Tat (30–37)	Tat (30–37)	CCFHCQVC	HIV-1 infection	human (Cw*1203)	Cao2003
	Keywords acute infection, early treatment. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A3, A26, B7, B*3801, Cw*0702, Cw*1203; A*0201, A*2501, B18, B51, Cw*0102, Cw*1203.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • Two individuals recognized this epitope both presented by Cw*1203. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				
Tat (30–37)	Tat (30–37)	CCFHCQVC	HIV-1 infection	human (Cw*1203)	Cao2003
	Keywords acute infection, early treatment. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A3, A26, B7, B*3801, Cw*0702, Cw*1203; A*0201, A*2501, B18, B51, Cw*0102, Cw*1203. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • Two individuals recognized this epitope both presented by Cw*1203. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				
Tat (36–50)	(subtype C)	VCFQTKGLGISYGRK		human	Novitsky2001
	Keywords immunodominance, escape. • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 17 of 46 patient reacted with Tat immunodominant peptide VCFQTKGLGISYGRK. • Most of the CTL responses occurred despite a mismatch between the autologous viral sequence and peptide – complete matches were seen only in 4 of 19 cases (21%) and the mismatched CTL tended not to respond to the autologous viral peptide indicative of immune escape.				
Tat (36–50)	Tat (36–50)	VCFQTKGLGISYGRK	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Tat (36–52)	Tat	VCFTTKALGISYGRKKR	HIV-1 infection	human	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 28% (19/70) targeted one or more Tat peptides, and this peptide was the most frequently recognized epitope in Tat (27%).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Tat (38–47)	(subtype C) **Keywords** immunodominance. **Epitope name** T38-FY10. • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 17 of 46 patient reacted with Tat immunodominant peptide VCFQTKGLGISYGRK. • FQTKGLGISY was the optimal epitope in the peptide VCFQTKGLGISYGRK among B*1503+ individuals.	FQTKGLGISY		human (B*1503)	Novitsky2001
Tat (38–47)	Tat (38–47)	FQTKGLGISY	HIV-1 infection	human (B*1503)	Frahm2004
Tat (39–49)	Tat (38–48) **Keywords** assay standardization. **Epitope name** Tat-4.8. • This epitope and HLA-A*6801 presenting molecule were rapidly defined using a modified Elispot assay. • The 11-mer is the optimal epitope but A*6801 epitopes tolerate length variation.	ITKGLGISYGR	HIV-1 infection	human (A*6801)	Oxenius2002a
Tat (39–49)	Tat (39–49)	ITKGLGISYGR	HIV-1 infection	human (A*6801)	Frahm2004
Tat (39–49)	Tat (38–48) **Keywords** early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.	ITKGLGISYGR	HIV-1 infection	human (A68)	Addo2002b
Tat (40–49)	**Keywords** epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.	TKALGISYGR	HIV-1 infection	human	Yusim2002
Tat (49–57)	Tat (49–57) • The Tat peptide RKKRRQRRR when conjugated to a protein can cause that protein to be taken up by APCs and presented to CTL. • The system was demonstrated by vaccinating mice with an OVA-Tat peptide conjugate and immunizing H-2 K^b mice. • The CTL response to the H-2 K^b specific OVA peptide SIINFEKL was stimulated.	RKKRRQRRR		mouse	Kim1997a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Tat (49–57)	Tat (49–57)	RKKRRQRRR	Vaccine	mouse (H-2^{d})	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18 **Keywords** Th1. • DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization. • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost. • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma) • Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.				
Tat (83–92)	Tat	GPKESKKKVE		human (B58)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay. • GPKESKKKVE was newly identified as an HLA-B58 epitope in this study.				
Tat	Tat		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat **Keywords** HAART. • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated. • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses. • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.				
Tat	Tat		HIV-1 infection	human	Froebel1997
	Keywords rate of progression. • Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long-term non-progressor. • Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells. • The child who progressed consistently had CTL against Pol and Tat. • The long-term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression.				
Tat	Tat		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS) **Keywords** review. • This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals.				
Tat	Tat		Vaccine	macaque	Cafaro2001
	Vaccine *Vector/Type:* DNA *Strain:* B clade BH10 *HIV component:* Tat *Adjuvant:* Immune stimulating complexes (ISCOM), CpG immunostimulatory sequence (ISS) • Macaques (macaca fascicularis) were immunized with HIV-1 Tat on an adenovirus major late promotor in a plasmid with 23 CpG sequences, 12 unmethylated.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The vaccinated animals contained a primary infection challenge with SHIV89.6P, preventing CD4+ T-cell decline in the animals, suggesting Tat may be useful at blocking viral replication at its early stage.				
Tat			HIV-1 infection	human	Aldhous1994, Kuhn2002
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses to Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Tat	Tat		HIV-1 infection, Vaccine	human	Gruters2002
	Keywords review, escape, early-expressed proteins. • This paper is a review that makes a case for using Tat and Rev as part of a vaccine strategy. • CTL against Tat and Rev were found preferentially in long term non-progressors. • Tat/Rev vaccinations of macaques provided protection or reduction in viremia, with high levels of CTL providing protection from challenge, lower levels of CTL having lower viremia, while Gag/Pol vaccinations with did not result in decreased viremia. • Early expression of Tat/Rev may in part explain the enhanced benefit of a CTL response directed at these proteins, and CTL escape is more prominent in these proteins.				
Tat	Tat (BH10)		Vaccine	mouse	Caputo2003
	Vaccine *Vector/Type:* DNA *Strain:* B clade BH10 *HIV component:* Tat *Adjuvant:* cationic block copolymer K2 **Assay type** proliferation, Chromium-release assay. **Donor HLA** H-2d. • Mice were immunized intramuscularly with a plasmid DNA vaccine (HIV-1 pCV-tat DNA) alone or complexed with a cationic block polymer K1, K2, or K5, which block digestion by DNAase I and enhance DNA delivery to APC. • CTL responses to low dose Tat DNA vaccination with K2 were greatly enhanced relative to responses to DNA alone.				
Tat	Tat		Vaccine	macaque	Fanales-Belasio2002a
	Vaccine *Vector/Type:* DNA, protein *HIV component:* Tat *Adjuvant:* aluminum hydroxide, Ribi adjuvant (MPL+TDM) (RIBI) **Keywords** review, early-expressed proteins. • HIV-1 Tat protein is efficiently taken up by monocyte-derived dendritic cells (MDDCs) and promotes Th1 immune responses. A Tat based vaccine can elicit an immune response that can control primary infection in monkeys that are in early stage of in infection with SHIV89.6P. • Tat-specific CTL activity was detected in four monkeys inoculated with i.m. with pCV-tat.				
Tat	Tat		Vaccine	mouse (H-2^d)	Xin2001
	Vaccine *Vector/Type:* adeno-associated virus (AAV) *HIV component:* Env, Rev, Tat *Adjuvant:* IL-2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice. • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL. • Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.				
Tat	Tat (IIIB)		Vaccine	mouse (H-2d)	Borsutzky2003
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide (MALP) **Assay type** T-cell Elispot.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• BALB/c mice that were vaccinated intranasally with Tat protein plus mucosal adjuvant macrophage-activating lipopeptide-2 (MALP-2) had increased proliferative, antibody, and IFN-gamma producing T-cell responses than did with Tat+IFA delivered by the i.p. route. • IFA as adjuvant stimulated a Th2-dominant response pattern, and MALP-2 as adjuvant shifted to a Th1 response. Anti-Tat IgG1 dominated the Ab response with IFA, IgG2b dominated with MALP-2. In animals vaccinated with Tat+MALP-2, IFN-gamma and IL-2 were the most prominent cytokines, with some IL-6. In contrast, in mice vaccinated with Tat+IFA, IL-6 was the dominant cytokine. Secreted IL-4, IL-5 and IL-10 were below the detection limit in both cases.				
Tat	Tat		Vaccine	mouse (H-2d)	Dominici2003
	Vaccine *Vector/Type:* protein *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA), red blood cells **Keywords** dendritic cells, Th1, Th2, immunotherapy. **Assay type** Chromium-release assay. • BALB/c mice were immunized with Tat protein bound to red blood cells via biotin-avidin conjugation. This antigen delivery system was successfully internalized by dendritic cells, and induced more consistent anti-Tat Abs responses and sightly increased Tat-specific CTL responses relative to Tat with CFA.				

II-B-17 Rev CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (9–23)	Rev (9–23 HXB2)	DEELIRTVRLIKLLY	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities, no HLA restriction analysis performed.				
Rev (11–23)	Rev (14–23)	KAVRRLIKFLY	HIV-1 infection	human (B*5701)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (11–23)	Rev (14–23)	KAVRRLIKFLY	HIV-1 infection	human (B*5801)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (12–31)	Rev (11–30 SF2)	LLKAVRLIKFLYQSNPPPNF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Only one subject had CTL that could recognize vaccinia-expressed LAI Rev. • This subject had a CTL response to this peptide, and was HLA-A2, A24, B13, B35.				
Rev (14–23)		KAVRLIKFLY	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Rev (14–23)	Rev (14–23 subtype B)	KAVRLIKFLY		human (B*5701)	Addo2001, Frahm2004
	• C. Brander notes this is a B*5701 epitope.				
Rev (14–23)	Rev (14–23 BRU)	KAVRIKLFLY	HIV-1 infection	human (B*5701)	Addo2001
	Keywords cross-presentation by different HLA. • Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides. • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was also recognized by another individual in whom it was restricted by HLA*B5801, an allele closely related to HLA*B5701, suggesting cross-presentation by the two HLA alleles.				
Rev (14–23)	Rev (14–23 subtype B)	KAVRLIKFLY		human (B*5801)	Addo2001, Frahm2004
	• C. Brander notes this is a B*5801 epitope.				
Rev (14–23)	Rev (14–23 BRU)	KAVRIKLFLY	HIV-1 infection	human (B*5801)	Addo2001
	Keywords cross-presentation by different HLA.				
	• Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides.				
	• 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide.				
	• This epitope was also recognized by another individual in whom it was restricted by HLA*B5701, an allele closely related to HLA*B5801, suggesting cross-presentation by the two HLA alleles.				
Rev (25–39)	Rev (25–39 HXB2)	SNPPPNPEGTRQARR	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities, no HLA restriction analysis performed.				
Rev (33–48)	Rev (33–48 HXB2)	GTRQARRNRRRRWRER	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities, no HLA restriction analysis performed.				
Rev (41–56)	Rev (41–56 HXB2)	RRRRWRERQRQIHSIS	HIV-1 infection	human	Blazevic1995
	• Induces both Th and CTL activities.				
Rev (55–63)	Rev (55–63 LAI)	ISERILSTY	HIV-1 infection	human (A1)	vanBaalen1997
	Keywords rate of progression.				
	• Predicted to be an HLA-A1 epitope based on anchor residues 2S and 9Y.				
	• Both forms LSGWL(L or I)STY, with intact anchors, were found in an HLA-A1+ individual with Rev-responsive CTL.				
	• An HLA-A1 individual who did not make a Rev response had lost the C-term anchor, ISGWILS(T or N)S.				
	• 3/7 long-term non-progressors and 0/5 progressors were positive for HLA-B57 (associated with prolonged survival)				
	• CTLp frequencies to Rev and Tat were inversely correlated with rapid progression to AIDS, but not Gag, RT or Nef.				
Rev (55–63)	Rev (55–63)	ISERILSTY	HIV-1 infection, HIV-1 exposed seronegative	human (A1)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS).				
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Rev (57–66)		ERILSTYLGR	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape.				
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17.				
	• While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Rev (57–66)	Rev (57–66)	ERILSTYLGR	HIV-1 infection	human (A*03)	Frahm2004
Rev (57–66)	Rev (57–66)	ERILSTYLGR	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-ER10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals had detectable responses to this epitope after STI.				
Rev (58–66)	Rev (58–66)	RILSTYLGR	HIV-1 infection	human (A*0301)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (66–73)	Rev (66–)	RSAEPVPL	HIV-1 infection, Vaccine	transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Rev *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, computational epitope prediction. **Epitope name** Rev66. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a low A2-binder that induced a CTL responses in 1/6 A2 transgenic mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.				
Rev (66–81)	Rev	RSAEPVPLQLPPLERL	HIV-1 infection	human	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – 36% (25/70) targeted one or more Rev peptides, and this peptide was the most frequently recognized epitope in Rev (32%). • The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Rev (67–75)		SAEPVPLQL	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed. • What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Rev (67–75)	Rev (65–77 BH10, LAI)	SAEPVPLQL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is GRSAEPVPLQLPP) has similarity with transforming growth factor beta binding protein protein I, fragment ARSAEPEVATAPP. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is EPVPLQLPPL) also has similarity with the epidermal growth factor receptor substrate 15, fragment EPVPMSLPPA.				
Rev (67–75)	(LAI)	SAEPVPLQL		(B14)	vanBaalen2000
Rev (67–75)	Rev **Keywords** escape.	SAEPVPLQL	HIV-1 infection	human (B14)	Schutten2001
	• Molecularly cloned primary NSI macrophage tropic strain 2.1 and SI non-macrophage tropic strain 1.2 were isolated from study participant ACH320 and use to infect irradiated XID mice that had been reconstituted with human PBMC from B14+ seronegative donors – results indicate CTL may favor selective outgrowth of macrophage tropic strains. • The CTL clone TCC108 specific for SAEPVPLQL, previously described by van Baalen 1997, and van Baalen 1998, was stimulated *in vitro* and given to the mice to apply specific CTL pressure. • The macrophage-tropic HIV-1 strain #2.1 escaped CTL pressure more efficiently (7/14 animals) than its non-macrophage-tropic counterpart #1.2(SI) – the latter isolate was suppressed in 13/14 animals – macrophage may serve as a CTL sanctuary and reduced pressure on macrophage tropic HIV strains may allow additional replication to assist with acquisition of escape. • Specific HIV-1 variants selectively induced by TCC108 were for strain 1.2: SEEPVPLQL, and for strain 2.1: SAEHVPLQL, SAESVPLQL, SVEPVPLQL, SLEPVPLQL, SAEPVPFQL, and SAEPVPFQL.				
Rev (67–75)	Rev (67–75) **Keywords** acute infection, early-expressed proteins, kinetics.	SAEPVPLQL	HIV-1 infection	human (B14)	vanBaalen2002
	• Tat, Rev and Nef are the first HIV proteins expressed upon acute infection of T-cells (< 6 hours), and RT is not expressed until after 24 hours. The B14-restricted Rev-SAEPVPLQL specific CD8 T-cell clone TCC108, and the B57-restricted RT-IVLPEKDSW specific CD8 T-cell clone TCL1C11 were co-incubated with CD4+ cultures innoculated with HIV-1 at low MOI. Co-incubation with the Rev-specific CTL resulted in two logs less HIV-1 production in ten days of culture. When the RT epitope was cloned into the Nef gene of the infecting strain, another early expressed protein, it proved as effective as the Rev epitope at inhibiting viral production. A mathematical model of CTL-target interactions suggest early proteins are important for vaccine design.				
Rev (67–75)	Rev (67–75) **Keywords** early-expressed proteins.	SAEPVPLQL	HIV-1 infection	human (B14)	Addo2002b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (67–75)	Rev (67–75 IIIB)	SAEPVPLQL	HIV-1 infection	human (B14, Cw8)	vanBaalen1998
	• The Rev-specific CTL response studied here was from an individual infected with HIV-1 for more than 12 years without developing symptoms – Rev and Tat are expressed early and CTL activity against these proteins has been correlated with long-term survival. • The CTL clone TCC108 specific for this epitope was studied *in vitro*. • CTLs added immediately after infection suppressed viral production, indicative of CTL interference with viral production prior to lysis – CTL-mediated lysis occurred after the onset of progeny viral release, but prior to peak viral production. • Rapid selection of a E69K mutation, which abolished CTL, recognition was observed. • The epitope was originally listed as B14, but Cw8 and B14 are in linkage disequilibrium, and in this case were not distinguished (pers. comm., Christian Brander, 1999)				
Rev (67–75)	(LAI)	SAEPVPLQL		human (Cw*0501)	Addo2001, Frahm2004
Rev (67–75)	Rev (SF2)	SAEPVPLQL	HIV-1 infection	human (Cw5)	Goulder2001a
	Keywords acute infection. **Epitope name** SL9. • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia. • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.				
Rev (67–75)	Rev (67–75 SF2)	SAEPVPLQL	HIV-1 infection	human (Cw5)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-Cw5+ individuals that had a CTL response to this epitope broken down by group: 2/6 group 1, 0/1 group 2, and 0/2 group 3.				
Rev (67–75)	Rev (67–75)	SAEPVPLQL	HIV-1 infection	human (Cw5)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A*0201, B44, B57, Cw5, Cw6. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
Rev (67–75)	Rev (67–75)	SAEPVPLQL	HIV-1 infection	human (Cw5/Cw8)	Addo2002b
	Keywords early-expressed proteins. • CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot. • 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides. • All known optimally defined epitopes were summarized for the five proteins.				
Rev (67–75)	Rev (69–77 BRU)	SAEPVPLQL	HIV-1 infection	human (Cw8)	Addo2001
	Keywords HAART, supervised treatment interruptions (STI), acute infection. **Epitope name** Rev SL9. • Rev and Tat are expressed early in the virus life cycle and thus may be important targets for CTL against HIV early in infection and for vaccines – therefore CTL responses against Tat and Rev were screened using overlapping peptides. • 11/57 (19.3%) HIV-1+ individuals recognized at least 1 Tat peptide, and 21/57 (37%) responded to at least 1 Rev peptide. • This epitope is the first HIV-specific CTL epitope resticted by HLA-Cw5. • This epitope was recognized by 2/5 individuals expressing HLA-Cw8 and by 5/11 individuals expressing Cw5 allele, which differs from Cw8 by 4 amino acids, suggesting promiscuous presentation of the epitope between those HLA molecules. • Longitudinal data was available for 6 Rev-SL9 responders, who were treated during acute infection, and the response was stable 2 and 12 months after initiaion of HAART, measurements by ELISPOT and flow-based intracellular cytokine staining (ICS) were concordant – in two subjects the response was heightened by transient reexposure to antigen with treatment interruption at 12 to 14 months.				
Rev (73–81)	Rev (73–)	LQLPPIERL	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Rev *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Rev73. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL responses in mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.				
Rev (75–83)		LPPLERLTL	HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• What was learned from proteins where many epitopes have been defined (Gag, Pol, Env and Nef) was used to develop an algorithm to predict where epitopes would be localized in Rev, Tat, Vif, and Vpr. Predictions were made blinded, and then compared to the first 15 epitopes defined in these proteins; the epitopes were concentrated in the predicted regions.				
Rev (96–104)	Rev (96–)	GMGSPQILV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Rev *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Rev96(2M). **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects. • The variant gVgspqilv did not elicit a CD8+ T-cell IFN gamma response in transgenic mice, and bound to A2 with low affinity.				
Rev (102–110)	Rev (102–)	ILVESPAVL	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Rev *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Rev102. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that did not induce CTL or CD8+ T-cell IFN gamma responses in mice, but responses were detected in 2/17 HIV+ HLA-A2 subjects.				
Rev	Rev		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat **Keywords** HAART. • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated. • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses. • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.				
Rev	(subtype C)			human	Novitsky2001
	• This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • Anti-Rev CTL responses were distributed throughout the protein and 27 of 47 subjects (57%) demonstrated HIV-1C Rev-specific ELISPOT CTL responses of more than 100 SFC/106 PBMC.				
Rev	Rev		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Keywords review. • This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals.				
Rev	Rev		HIV-1 infection, Vaccine	human	Gruters2002
	Keywords review, escape, early-expressed proteins. • This paper is a review that makes a case for using Tat and Rev as part of a vaccine strategy. • CTL against Tat and Rev were found preferentially in long term non-progressors. • Tat/Rev vaccinations of macaques provided protection or reduction in viremia, with high levels of CTL providing protection from challenge, lower levels of CTL having lower viremia, while Gag/Pol vaccinations with did not result in decreased viremia. • Early expression of Tat/Rev may in part explain the enhanced benefit of a CTL response directed at these proteins, and CTL escape is more prominent in these proteins.				
Rev	Rev		Vaccine	mouse (H-2^d)	Ishii1997
	Vaccine *Vector/Type:* DNA with CMV promotor with cationic liposome *HIV component:* gp160, Rev • pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor) • pCMV160/Rev given in conjunction with a cationic liposome gave enhanced DTH, Ab and CTL responses.				
Rev	Rev		Vaccine	mouse (H-2^d)	Ihata1999
	Vaccine *Vector/Type:* DNA *HIV component:* Rev *Adjuvant:* CD40 **Keywords** Th1, Th2. • pcRev DNA i.m. vaccination in BALB/c mice induced Th1, Th2 and IgG responses, and enhanced the CTL response to Rev, but did not induce mucosal IgA.				
Rev	Rev		Vaccine	mouse (H-2^d)	Xin2001
	Vaccine *Vector/Type:* adeno-associated virus (AAV) *HIV component:* Env, Rev, Tat *Adjuvant:* IL-2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice. • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL. • Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.				

II-B-18 Vpu CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpu (4–13)	Vpu	LVILAIVALV		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes.				
	• A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay.				
	• LVILAIVALV was newly identified as an HLA-B7 epitope in this study using ELISPOT, but could not be shown to bind to B7.				
Vpu (13–21)	Vpu (13–)	VVAAIIAIV	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Vpu *Adjuvant:* Incomplete Freund's Adjuvant (IFA)				
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction.				
	Epitope name Vpu13.				
	Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay.				
	• HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.				
	• This peptide was an intermediate A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.				
Vpu (25–40)	Vpu	IVFIEYRKLRQRKID	HIV-1 infection	human	Addo2002b
	Keywords early-expressed proteins.				
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot – only 2% (2/70) targeted one or more Vpu peptides, including this peptide.				
	• The regulatory proteins Rev and Tat combined contributed to 3%, and the accessory proteins Vif, Vpr and Vpu to 7%, of the total magnitude of HIV-1 specific CTL responses in a subset of 22 HIV-1 infected individuals in whom all HIV-1 proteins were studied.				
Vpu (29–37)	Vpu (29–37)	EYRLKILRQR	HIV-1 infection	human (A*3303)	Addo2002b
	Keywords early-expressed proteins.				
	• CTL responses against regulatory and accessory proteins in 70 HIV-1 infected patients were studied using overlapping peptides and Elispot.				
	• 28% targeted one or more overlapping Tat peptides; 36%, Rev peptides; 33%, Vif peptides; 40%, Vpr peptides; and 2%, Vpu peptides.				
	• All known optimally defined epitopes were summarized for the five proteins.				
Vpu (29–37)	Vpu (29–37)	EYRLKILRQR	HIV-1 infection	human (A*3303)	Addo2002a
	Keywords early-expressed proteins.				
	• Detection of HIV CTL epitopes is rare in Vpu, and this is the first optimally defined Vpu epitope.				
	• This CTL response was first detected in a long term non-progressor, and 3/6 HLA A*3303 positive individuals were found to have a CTL response to this epitope.				
	• HLA A*3303 is common in West Africa and Asia.				
Vpu (29–37)	Vpu (29–37)	EYRKILRQR	HIV-1 infection	human (A*3303)	Frahm2004
Vpu	Vpu		Vaccine	mouse (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Vif, Vpu				
	Keywords inter-clade comparisons, Th1.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-gamma levels. • Antigen stimulation increased IFN-gamma production in pVVN-P immunized mice, indicating a Th1 response. • IL-4 production was not significantly changed after antigen stimulation compared to control levels. • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization-stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.				

II-B-19 gp160 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (2–10)	gp160 (2–10 IIIB) • C. Brander notes this is a B*0801 epitope.	RVKEKYQHL	HIV-1 infection	human (B*0801)	Frahm2004
gp160 (2–10)	gp160 (2–10 IIIB) **Keywords** inter-clade comparisons. • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • Type-specific epitope, unique to the LAI and IIIB because of a deletion of three amino acids that are present in all other subtype B HIV-1s. • RVKGIRKNYQHL, a variant found in JRCSF, was not recognized. • This epitope is in the signal sequence of gp120.	RVKEKYQHL	HIV-1 infection	human (B8)	Sipsas1997
gp160 (2–10)	gp120 (2–10) • B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.	RVKEKYQHL	HIV-1 infection	human (B8)	Day2001
gp160 (6–12)	gp120 (6–15 CM243 subtype CRF01) **Keywords** HIV exposed persistently seronegative (HEPS). **Epitope name** E6-15. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11.	TQMNWPNLWK	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
gp160 (6–12)	gp120 (6–15 CM243 subtype CRF01) **Keywords** inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it. • This epitope was not conserved in other subtypes, and exact matches were rare.	TQMNWPNLWK	HIV-1 infection	human (A11)	Bond2001
gp160 (30–49)	gp120 **Keywords** TCR usage. • Peptide 7035.1: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population. • HIV CTL responses to 3 Env and 2 Gag peptides were studied. • The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ6.	AAEQLWVTVYYGVPVWKEAT	HIV-1 infection	human (A11)	Weekes1999b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (31–39)	gp120 (30–38 SF2)	AENLWVTVY	HIV-1 infection	human (B44)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B44+ individuals that had a CTL response to this epitope broken down by group: 1/8 group 1, 2/3 group 2, and 3/4 group 3.			
gp160 (31–39)	gp120 (30–38)	AENLWVTVY	HIV-1 infection	human (B44)	Day2001
gp160 (31–39)	gp120	AENLWVTVY	HIV-1 infection	human (B44)	Cao2002
	Keywords epitope processing. • AC2 is a B44 restricted CTL clone that recognizes AENLWVTVY. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
gp160 (31–40)	gp160 (30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human (B*4402)	Frahm2004
	• C. Brander notes this is a B*4402 epitope.				
gp160 (31–40)	gp160 (30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human (B44)	Borrow1997, Borrow1998, Goulder1997a
	Keywords immunodominance, escape. • Two CTL lines from the patient WEAU were studied – one had an optimal peptide of (A)AENLWVTVYY, and the other (A)AENLWVTVY, and both responded equally well with one or two N-term Alanines. • Rapidly post-infection, a strong immunodominant response was observed against this epitope. • The naturally occurring forms of the peptide found in WEAU were tested as targets for early WEAU CTLs – the form TENLWVTVY was as reactive as the wild type AENLWVTVY – but the forms AKNLWVTVY, AGNLWVTVY, AANLWVTVY did not serve as targets. • The glutamic acid in the second position is a B44 anchor residue. • [Goulder1997a] and [Borrow1998] are reviews of immune escape that summarizes this study in the context of CTL escape to fixation.				
gp160 (31–55)	gp120 (32–56 LAI)	TEKLWVTVYYGVPVWKEAT-TTLFCA	Vaccine	human (B18)	Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees.				
gp160 (31–55)	gp120 (32–56 LAI)	TEKLWVTVYYGVPVWKEAT-TTLFCA	Vaccine	human (B18)	Ferris1999, Hammond1995
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • This peptide can be processed for HLA-B18 presentation by both TAP-1/2 independent and dependent pathways.				
gp160 (33–42)	gp120 (32–41 LAI)	KLWVTVYYGV	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL from HLA-A2 positive subject react with this peptide.				
gp160 (33–42)	Env (32–41 subtype B)	KLWVTVYYGV	HIV-1 infection, Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period. • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual. • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.				
gp160 (34–42)		LWVTVYYGV	HIV-1 infection	human (A*0201)	Dagarag2003
	Assay type cytokine production, proliferation, Tetramer binding, Intracellular cytokine staining, Chromium-release assay. • Telomer length is short in the CD8+ T-cell compartment of HIV-1 infected people, indicating excessive CTL activation and premature senescense. Here human telomerase RT (hTERT) transduction of HIV-1-specific CTL was used to study the functional impact of telomerase. Telomerase expression enhanced proliferative capacity, as well as cytolytic and antiviral capabilities; cytokine production was unchanged. hTERT transduced CTLs were 10-fold more efficient in controlling HIV-1 replication in culture. Thus telomerase transduction can restore CTL mediated cytolysis, and may have therapeutic potential. • Three polyclonal CD8+ T-cell lines derived from an HIV-1, HLA A*0201 positive patient were used in this study, including one specific for this epitope.				
gp160 (34–55)	gp120 (25–46 BRU)	LWVTVYYGVPVWKEATTTL-FCA	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through peptide blocking of CTL activity, and Env deletions.				
gp160 (36–44)	Env (35–)	VTVYYGVPV	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Env *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Env35. **Assay type** CD4 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced a CD8+ T-cell IFN gamma response in 1/6 mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.				
gp160 (36–46)	gp120 (36–46 CM243 subtype CRF01)	VTVYYGVPVWR	HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** E36-4. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope after a second stimulation *in vitro* gave a weak response in HEPS study subject 186 who was HLA A2/A11.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (36–46)	gp120 (36–46 CM243 subtype CRF01)	VTVYYGVPVWR	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined. • 1/8 tested FSWs recognized this epitope. • This epitope was only conserved in CRF01 and subtypes B and C, and exact matches were uncommon.				
gp160 (36–46)	gp120	VTVYYGVPVWK	HIV-1 infection	human (A11 and A*6801)	Threlkeld1997
	• Study of the fine specificity of an A3-like-HLA-super-type epitope (the A3-super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801) • The A3 super-type is characterized as a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position. • While most lines were specific, a promiscuous cloned CTL line was derived from an HIV+ donor that could recognize this epitope presented by either A11 or A*6801.				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	Vaccine	human (A*0301)	Johnson1994b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • Multiple CTL clones obtained from two vaccinees. • C. Brander notes that this is an A*0301 epitope in the 1999 database.				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	Vaccine	human (A*0301)	Frahm2004
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • C. Brander notes this is an A*0301 epitope.				
gp160 (37–46)	gp120	TVYYGVPVWK	HIV-1 infection, Vaccine	human (A*0301)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
gp160 (37–46)		TVYYGVPVWK	HIV-1 infection	human (A03)	Sabbaj2002b
	Epitope name Env-VK9. • Among HIV+ individuals who carried HLA A03, 0/20 (0%) recognized this epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (37–46)	Env	TVYYGVPVWK	Vaccine	transgenic mouse (A11)	Ishioka1999
	Vaccine *Vector/Type:* DNA • A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed. • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans. • HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes.				
gp160 (37–46)	gp120 (37–46)	TVYYGVPVWK	Vaccine	human (A3)	Carruth1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease • The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease) • CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination. • CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls. • The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen.				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human (A3)	Goulder1997e, Goulder1997a
	Keywords review, escape. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. • One had a response to this epitope, the other did not. • [Goulder1997a] is a review of immune escape that summarizes this study.				
gp160 (37–46)	gp120 (36–45)	TVYYGVPVWK	HIV-1 infection	human (A3)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
gp160 (37–46)	gp120 (37–46)	TVYYGVPVWK	HIV-1 infection	human (A3)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.				
gp160 (37–46)	Env (49–58)	TVYYGVPVWK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
gp160 (37–46)	gp120 (38–41 LAI)	TVYYGVPVWK	Vaccine	human (A3.1)	Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Highly conserved epitope recognized by multiple CTL clones from vaccinee.				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	Vaccine	human (A3.1)	Ferris1999, Hammond1995
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• This peptide can be processed for HLA-A3.1 presentation by TAP-1/2 independent and dependent pathways.				
gp160 (37–46)	gp120 (37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human (B*0301)	Wilson2000a
	Keywords acute infection.				
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found.				
	• All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39.				
	• ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK.				
	• The subject with A*0201 had a moderately strong response to SLYNTVATL.				
	• Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705.				
	• No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.				
gp160 (38–48)	gp120 (45–55)	VYYGVPVWKEA	HIV-1 infection	human (Cw7)	Nehete1998a
	• Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one.				
	• HLA-C antigens are expressed on lymphoid cells to a lesser extent than either HLA-A or -B.				
	• HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing.				
gp160 (42–51)	gp120 (42–51 PV22)	VPVWKEATTT	HIV-1 infection	human (B*5501)	Frahm2004
	• C. Brander notes this is a B*5501 epitope.				
gp160 (42–51)	gp120 (42–51 PV22)	VPVWKEATTT	HIV-1 infection	human (B55)	Brander1995b
	• P. Johnson, unpublished.				
gp160 (42–51)	gp120 (41–55)	VPVWKEATTT	HIV-1 infection	human (B55)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
gp160 (42–52)	Env (43–52 BH10, LAI)	VPVWKEATTTL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins.				
	• This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this peptide is PVWKEATTTL) has similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta-3) (CD61): PLYKEATSTF.				
gp160 (42–52)	gp120 (42–52)	VPVWKEATTTL	HIV-1 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (42–52)	gp120 (42–52 PV22)	VPVWKEATTTL	HIV-1 infection	human (B35)	Cao1997a
	Keywords inter-clade comparisons. • VPVWKEATTTL is the consensus sequence for clades B and D. • VPVWKDAETTL is the consensus sequence for clade A and it is cross-reactive. • VPVWKEADTTL is the consensus sequence for clade C and it is cross-reactive. • VPVWKEADTTL is the consensus sequence for clade E and even with three substitutions still retains some cross-reactivity.				
gp160 (42–52)	gp120 (41–51)	VPVWKEATTTL	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
gp160 (42–61)	gp120 (49–68)	VPVWKEATTTLFCASDAKAY	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (42–61)	gp120 (49–68 SF2)	VPVWKEATTTLFCASDAKAY	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • Three of these 11 had CTL response to this peptide. • The responding subjects were HLA-A2, A3, B8, B62; HLA-A3, A24, B7, B38.				
gp160 (42–61)	gp120 (49–68 SF2)	VPVWKEATTTLFCASDAKAY	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
gp160 (50–59)	Env (62–71)	TTLFCASDAK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
gp160 (51–59)	Env (63–71)	TLFCASDAK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
gp160 (52–61)	gp120 (59–68 HXB2)	LFCASDAKAY	HIV-1 infection	human (A*2402)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping. • C. Brander notes that this is an A*2402 epitope in the 1999 database.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (52–61)	gp120 (53–62 LAI)	LFCASDAKAY	HIV-1 infection	human (A*2402)	Frahm2004
	• C. Brander notes this is an A*2402 epitope.				
gp160 (52–61)	gp120 (53–62)	LFCASDAKAY	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (52–61)	gp120 (53–62 LAI)	LFCASCAKAY	HIV-1 infection	human (B38)	Shankar1996
	• Uncertain whether optimal, binds A24 as well.				
gp160 (52–71)	gp120 (59–78)	LFCASDAKAYDTEVHINVW-AT	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (52–71)	gp120 (59–78 SF2)	LFCASDAKAYDTEVHINVW-AT	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A2 and B-21.				
gp160 (62–80)	gp120 (69–88 SF2)	DTEVHNVWATHACVPTDPN	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A2 and B-21.				
gp160 (67–75)	Env (67–)	NIWATHACV	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* gp120 *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Env67(2I). **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 1/17 HIV+ HLA-A2 subjects. • The variant nVwathacv was also immunogenic in transgenic mice, but was not recognized in the 17 people tested.				
gp160 (75–84)	gp120	VPTDPNPPEV	HIV-1 infection	human (A2)	Höhn2003
	Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Tetramer binding.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The M. tuberculosis HLA-A2 restricted epitope VLTDGNPPEV and this HLA-A2 HIV-1 gp120 VPTDPNPPEV epitope are cross-recognized. HLA-A2+ patients with pulmonary tuberculosis exhibit cross-reactivity with the HIV gp160 epitope, and those with HIV-1 infection have cross-reactive responses to M.tuberculosis antigen.				
gp160 (78–86)	gp120 (77–85)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Ogg1998b
	• This epitope was included to illustrate the specificity of HIV-tetrameric staining, in a cross-sectional study correlating HLA A*0201 CTL effector cells and low viral load.				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained. • 2/7 B35-positive individuals have a CTL response to this epitope. • This epitope is highly variable. • The substitutions: 1N, 3S and 7I, 7L and 9M, 8I, 8K all abrogate specific CTL lysis, while only 8K reduces binding to B*3501. • The substitution 8V to 8E does not reduce specific CTL activity.				
gp160 (78–86)	Env (77–85)	DPNPQEVVL	HIV-1 infection	human (B*3501)	Ogg1999
	Keywords HAART. • CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVANTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient. • Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy. • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days.				
gp160 (78–86)	Env (77–85)	DPNPQEVVL	HIV-1 infection	human (B35)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective. • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.				
gp160 (78–86)		DPNPQEVVL	HIV-1 infection	human (B35)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T cells and viral load. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.				
gp160 (78–86)	(SF2)	DPNPQEVVL	HIV-1 infection	human (B35)	Kawana1999
	Keywords rate of progression.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3.				
gp160 (78–86)		DPNPQEVVL	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Env-DL9. • Among HIV+ individuals who carried HLA B35, 3/20 (15%) recognized this epitope.				
gp160 (78–86)	gp120 (78–86)	DPNPQEVVL	HIV-1 infection	human (B35)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A3, A33, B14, B35, Cw*0401, Cw*0802. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
gp160 (78–86)	gp120 (77–85 SF2)	DPNPQEVVL	HIV-1 infection	human (B35, B51)	Shiga1996
	• Binds HLA-B*3501 and B*5101 – binds and kills gp120-vaccinia virus infected cells carrying B35 or B51.				
gp160 (78–86)	gp120 (77–85)	DPNPQEVVL	HIV-1 infection, HIV-1 exposed seronegative	human (B51)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (103–111)	Env (102–110)	QMHEDIISL	HIV-1 infection	human (A*0201)	Kmieciak1998a
	Keywords binding affinity, TCR usage.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues. • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*. • Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity. • Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire.				
gp160 (104–112)	gp160 (104–112)	MHEDIISLW	HIV-1 infection	human (B*3801)	Frahm2004
gp160 (104–112)	gp120 (104–112) **Keywords** binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A3, A26, B7, B*3801, Cw*0702, Cw*1203. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.	MHEDIISLW	HIV-1 infection	human (B*3801)	Cao2003
gp160 (104–119)	gp120 (111–126 IIIB) • Primary CTL response with cells from non-infected donors stimulated by the peptide.	MQEDIISLWDQSLKPC	in vitro stimulation or selectio	human	Macatonia1991
gp160 (105–117)	gp120 (MN) • No epitope-specific CTL were detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant despite a response to peptides P18 and T1. • Helper and cytotoxic T cells have been found to be stimulated by this peptide (T2)	HEDIISLWDQSLK	HIV-1 infection	chimpanzee	Lubeck1997
gp160 (105–117)	gp120 (112–124 IIIB) • CTL and T helper cell reactivity in healthcare workers exposed to HIV.	HEDIISLWDQSLK	HIV-1 exposed seronegative	human	Pinto1995
gp160 (105–117)	gp120 (112–124 IIIB) • Helper and cytotoxic T cells can be stimulated by this peptide (T2)	HEDIISLWDQSLK	HIV-1 infection	human (A2)	Clerici1991a
gp160 (108–116)	Env (107–115 subtype B) **Vaccine** *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period. • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.	IISLWDQSL	Vaccine	human (A2.1)	Kundu1998a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.				
gp160 (109–117)	Env (109–117 CM243 subtype CRF01) **Keywords** HIV exposed persistently seronegative (HEPS). **Epitope name** E109-117. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11, and had been predicted to be a possible A11 epitope using Epimer in [Bond2001]	ISLWDQSLK	HIV-1 exposed seronegative	human (A11)	Bond2001
gp160 (112–130)	gp120 (119–139 SF2) • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A2 and B-21.	WDQSLKPCVKLTPLCVSLK	HIV-1 infection	human	Lieberman1997a
gp160 (112–131)	gp120 (MN) **Keywords** assay standardization, HAART. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2. • 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.	WDQSLKPCVKLTPLCVTLNC	HIV-1 infection	human	Chitnis2003
gp160 (117–126)	Env (72–81) • This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor. • A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing.	KPCVKLTPLC	HIV-1 infection	human (B7)	Jin2000b
gp160 (121–129)	Env (120–128) **Keywords** binding affinity, TCR usage. • CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL—all have A2 anchor residues. • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*. • Peptides 4.3 and D1 bound HLA-A*0201 molecules with high affinity. • Peptides 4.3 and D1 stimulated CTL with a relatively limited TCR Vβ repertoire. • In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher over time.	KLTPLCVTL	HIV-1 infection	human (A*0201)	Kmieciak1998a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (121–129)	Env (134–)	KLTPLCVTL	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** Env-134. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT. • 0/12 acutely infected individuals recognized this epitope. • KLTPLCVTL binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0203 and A*6802 (highest affinity).			
gp160 (121–129)	gp120 (120–128 LAI)	KLTPLCVTL	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 • CTL from HLA-A2 positive subject react with this peptide.				
gp160 (121–129)	gp120 (120–128)	KLTPLCVTL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2. • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice. • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost. • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested. • KLTPLCVTL was recognized by 3 of the patients.			
gp160 (121–129)	gp120 (120–128)	KLTPLCVTL	HIV-1 infection	human (A2)	Kundu1998b
	Keywords dendritic cells. • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients. • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated. • KLTPLCVTL is a conserved HLA-A2 epitope included in this study – all six patients had this sequence as their HIV direct sequence, and a detectable CTL response. • CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine.			
gp160 (121–129)	gp120 (120–128)	KLTPLCVTL	HIV-1 infection	human (A2)	Kmieciak1998b
	• Increased CTL response to cells expressing a VV construct Δv3 mutant compared with a full-length env gene product.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (121–129)	gp120 (121–129)	KLTPLCVSL	in vitro stimulation or selectio	human (A2)	Zarling1999
	Keywords dendritic cells. • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses. • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA. • A weak response to KLTPLCVSL was stimulated using macrophages as the APC. • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL.				
gp160 (121–129)	gp120 (120–128)	KTLPLCVTL	HIV-1 infection	human (A2)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
gp160 (121–129)	gp120 (121–129 IIIB)	KLTPLCVTL	Vaccine	mouse (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160, gp160ΔV3 *Adjuvant:* IL-12 **Keywords** vaccine-specific epitope characteristics. **Epitope name** D1. • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.				
gp160 (121–129)	Env (121–)	KLTPLCVTL	HIV-1 infection	human (A2)	Corbet2003
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Env121. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • 3/17 HIV-infected HLA-A2+ people recognized this epitope.				
gp160 (121–129)	Env (134–142)	KLTPLCVTL	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
gp160 (121–129)	Env	KLTPLCVTL	Vaccine	transgenic mouse (A2.1)	Ishioka1999
	Vaccine *Vector/Type:* DNA				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed. • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans. • HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection.				
gp160 (121–129)	Env (120–128 subtype B) **Vaccine** *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period. • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual. • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.	KLTPLCVTL	Vaccine	human (A2.1)	Kundu1998a
gp160 (156–165)	Env (162–171 BH10, LAI) • This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is STSIRGKVQK) has similarity with the macrophage colony stimulating factor I receptor fragment SISIRLKVQK.	NCSFNISTSI	HIV-1 infection	human	Maksiutov2002
gp160 (156–165)	gp120 (156–165) **Keywords** epitope processing. • Recognized by CTL clone LWF A5, isolated from a lab worker exposed to HIV-1 in 1985. • The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains two N-linked glycosylation sites that are glycosylated in Env. • Only peptide that has been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) was recognized: the aspartic acid at position 5 was critical, position 1 could be either D or N. • This peptide also contains a Cys involved in a disulfide linkage but reducing conditions did not effect recognition by CTL clone LWF A5. • The HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules. • The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively.	NCSFNISTSI	HIV-1 infection	human (Cw*08)	Ferris1999
gp160 (156–165)	gp120 (156–165 IIIB) • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • NCSFNITTSI, a variant found in HIV-1 MN, was not recognized, thus this epitope was type-specific. • NCSFNISTSI contains two potential N-linked glycosylation sites and cysteine residue, possibly related to the requirement for a high sensitizing dose of peptide for CTL activity.	NCSFNISTSI	HIV-1 infection	human (Cw8)	Sipsas1997
gp160 (188–207)	gp120 (193–212 BRU) • Defined through blocking CTL activity, and Env deletions.	TTSYTLTSCNTSVITQACPK	HIV-1 infection	human (A2)	Dadaglio1991

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (191–200)	gp120 (194–202 CM243 subtype CRF01)	YRLINCNTSV	HIV-1 infection	human (A2)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** E191-200. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.				
gp160 (191–200)	gp120 (194–202 CM243 subtype CRF01)	YRLINCNTSV	HIV-1 infection	human (A2)	Bond2001
	Keywords inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by four amino acids, KLTSCNTSV. • This epitope was somewhat conserved in 4/8 subtypes: CRF01 (E), B, C, and D.				
gp160 (192–200)	gp120 (192–199)	KLTSCNTSV	HIV-1 infection	human (A*02)	Rinaldo2000
	Keywords HAART. **Epitope name** SL9. • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection.				
gp160 (192–200)	gp120 (192–199 HXB2R)	KLTSCNTSV	HIV-1 infection	human (A2)	Brander1995a
	• Epitope predicted on HLA binding motif, and studied in the context of inclusion in a synthetic vaccine.				
gp160 (192–200)	gp120 (192–199)	KLTSCNTSV	HIV-1 infection	human (A2)	Huang2000
	Keywords HAART. • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed. • Increases in gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-gamma-production ELISPOT.				
gp160 (192–200)	gp120 (197–205)	TLTSCNTSV	Peptide-HLA interaction	human (A2)	Garboczi1992
	• Crystallization of HLA-A2 molecules complexed with antigenic peptides – refers to Dadaglio *et al.* 1991.				
gp160 (192–200)	gp120 (199–207)	TLTSCNTSV	HIV-1 infection	human (A2.1)	Brander1996a
	• This epitope was recognized by PBMC from 6/14 HIV+ asymptomatic patients. • This epitope was used along with pol CTL epitope ALQDSGLEV and a tetanus toxin T helper epitope for a synthetic vaccine. • This vaccine failed to induce a CTL response, although a helper response was evident.				
gp160 (192–211)	gp120 (199–219 SF2)	SLTSCNTSVITQACPKVSFE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The responding subject was HLA-A2, -B21.				
gp160 (199–207)	Env (202–210)	SVITQACPK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons, TCR usage. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • SVITQACPK was found to elicit clade-specific responses in clade B (SVITQACPK is most common, sAitqacpk is most common variant in clade A, C and D) and clade E (saiKqacpk is most common). SVITQACPK was recognized by CTL from 3/5 B clade infected Japanese subjects, and aiKqacpk by CTL from 0/7 E clade infected Thai subjects, so this seems to be a B clade exclusive epitope. • The binding of the three variant peptides to HLA A*1101 was comparable, implicating TCR interaction differences.				
gp160 (199–207)	gp160 (199–207)	SVITQACPK	HIV-1 infection	human (A*1101)	Frahm2004
gp160 (201–225)	gp120 (201–225 LAI)	ITQACPKVSFEPIPHYCAP-AGFAI	Vaccine	human (CD4+ CTL)	Johnson1994b, Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • CD4+ CTL isolated from LAI IIIB gp160 vaccinees.				
gp160 (202–221)	gp120 (209–228)	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (202–221)	gp120	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Weekes1999b
	Keywords TCR usage. • Peptide 740.18: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population. • HIV CTL responses to 3 Env and 2 Gag peptides were studied. • The clonal composition of the TCR Vβ responses were studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.1.				
gp160 (202–221)	gp120	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Weekes1999a
	• Peptide 740.18: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.				
gp160 (202–221)	gp120 (209–228 SF2)	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide.				
gp160 (202–221)	gp120 (209–228 SF2)	TQACPKVSFEPIPIHYCAPA	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
gp160 (207–216)	gp120 (subtype A)	KMTFEPIPIH	HIV-1 infection	human (A29)	Cao2000
	Keywords inter-clade comparisons. • HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype. • CTL derived from subtype A clade infection (patient SP 528), recognized the subtype A version of the peptide (KMSFEPIPIH), had a slightly reduced specific lysis using the B clade version of the peptide (KVSFEPIPIH), and no lysis using the D clade version of the epitope (KVTFEPIPIH) • Patient SP 528 is HLA A1, A29, B57, B81, Bw4, Bw6.				
gp160 (208–217)	gp120 (subtype B)	VSFEPIPIHY	HIV-1 exposed seronegative	human (A29)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
gp160 (208–217)	gp120 (263–272)	VSFEPIPHY	HIV-1 infection, HIV-1 exposed seronegative	human (A29)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (208–217)	gp120	VSFEPIPIHY	HIV-1 infection	human (A29)	Kaul2003
	Keywords immunodominance, genital and mucosal immunity. **Assay type** Intracellular cytokine staining. • Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher. • The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).				
gp160 (208–219)	Env	VSFEPIPPHYCA	HIV-1 infection	human (A2)	Cao2002
	Keywords epitope processing. • SP 511 is an A2 restricted CTL clone generated from a Ugandan subject that recognizes VSFEPIPPHYCA. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
gp160 (209–217)	(LAI)	SFEPIPIHY		(A29)	Altfeld2000a, Frahm2004
gp160 (209–217)	gp120 (213–221 SF2)	SFEPIPIHY	HIV-1 infection	human (A29)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Number of HLA-A29+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/0 group 3.				
gp160 (209–217)	gp120 (209–217)	SFEPIPIHY	HIV-1 infection	human (A29)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A29, B58, B62, Cw*0301, Cw*1601; A*0201, A29, B44, B60, Cw3, Cw16. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • Two subjects recognized this epitope during primary infection, both in the context of A29. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
gp160 (212–231)	gp120	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human	Weekes1999a
	• Peptide 740.19: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations.				
gp160 (212–231)	gp120 (219–238 HXB2)	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping.				
gp160 (212–231)	gp120 (219–238)	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (212–231)	gp120	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human (A2)	Weekes1999b
	Keywords TCR usage. • Peptide 740.19: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population. • HIV CTL responses to 3 Env and 2 Gag peptides were studied. • The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.6.				
gp160 (212–231)	gp120	PIPIHYCAPAGFAILKCNNK	HIV-1 infection	human (B57)	Jin1998b
	• Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction. • Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK.				
gp160 (237–246)	Env	GPCKNVSTVQ		human (B56)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• GPCKNVSTVQ was newly defined as an epitope in this study, was shown to stimulate an ELISPOT response, and to bind to HLA-B7.				
gp160 (239–247)	gp120 (241–249 LAI)	CTNVSTVQC	HIV-1 infection	human (Cw8)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • CTNVSTVQC contains a potential N-linked glycosylation site and cysteine residues, possibly related to a requirement for a high sensitizing dose of peptide for CTL activity.				
gp160 (242–261)	gp120 (249–268)	VSTVQCTHGIRPVVSTQLLL	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (242–261)	gp120 (249–268 SF2)	VSTVQCTHGIRPVVSTQLLL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-2, -B21.				
gp160 (242–261)	gp120 (249–268)	VSTVQCTHGIRPVVSTQLLL	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
gp160 (252–260)	gp120 (255–263 SF2)	RPIVSTQLL	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained. • Only 1/7 B35-positive individuals had a CTL response to this epitope. • An I to V substitution at position 3 reduces specific lysis, but not binding to B*3501. • A Q to H substitution at position 7 abrogates specific lysis, but not binding to B*3501.				
gp160 (252–260)	gp120 (255–263 SF2)	RPIVSTQLL	HIV-1 infection	human (B35)	Shiga1996
	• Binds HLA-B*3501.				
gp160 (252–260)	(SF2)	RPIVSTQLL	HIV-1 infection	human (B35)	Kawana1999
	Keywords rate of progression. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.				
gp160 (252–261)	Env	RPVVSTQLLL		human (B7)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay. • RPVVSTQLLL was one of the 15, and had been previously identified as an HLA-B7 epitope, and was confirmed in this study.				
gp160 (252–271)	Env (256–268 BH10, LAI)	RPVVSTQLLLNGSLAEEEVV	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is STQLLLNGSLAEE) has similarity with the lymphatic endothelium-specific hyaluronan receptor LYVE-1 fragment TTRLLVQGSLRAEE.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (252–271)	gp120 (256–275 LAI)	RPVVSTQLLLNGSLAEEEVV	HIV-1 infection	human (B7)	Shankar1996
gp160 (291–307)	Env (292–301 BH10, LAI)	SVEINCTRPNNNTRKSI	HIV-1 infection	human	Maksiutov2002
• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is VEINCTRPNN) has similarity with the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO-1 antigen) (CD95 antigen) fragment VEINCTRQN.					
gp160 (291–307)	gp120 (295–312 BRU)	SVEINCTRPNNNTRKSI	HIV-1 infection	human (A2)	Dadaglio1991
• Defined through blocking CTL activity, and Env deletions.					
gp160 (291–307)	gp120 (291–307 IIIB)	SVEINCTRPNNNTRKRI	Vaccine	mouse (A2)	Kiszka2002
Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-12 **Keywords** vaccine-specific epitope characteristics. • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells. • The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.					
gp160 (297–322)	gp120 (297–322 IIIB)	TRPNNNTRKRIRIQRGPGR-AFVTIGK	Vaccine	mouse (H-2D^{d})	Chang1999
Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* liposome • Induction of peptide-specific CTLs in BALB/c mice was dependent on immunization with peptide encapsulated liposomes containing MPL as adjuvant. • T26K (26mer) elicited a stronger AB and CTL response than R15K (a V3 15mer, RIQRGPGRAFVTIGK)					
gp160 (297–330)	Env (303–335 BX08)	TRPNNNTRKSIHIGPGRAF-YATGEIIGDIRQAH	Vaccine	human	Gahery-Segard2000
Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide. • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees. • None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed.					
gp160 (298–307)	gp120 (298–307)	RPNNNTRKSI	HIV-1 infection	human (B*07)	Ferris1999, Hammond1995
Keywords epitope processing, TCR usage. • The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains an N-linked glycosylation site that is glycosylated in Env. • Peptide that had been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) (RPNDNTRKSI) was recognized a 100-fold more efficiently than either glycosylated or non-glycosylated RPNNNTRKSI. • Position 5 is not involved with HLA B*07 binding, so is probably important for TCR recognition.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules. • The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively.				
gp160 (298–307)	gp120 (302–312 HXB2) • C. Brander notes this is a B*0702 epitope.	RPNNNTRKSI	HIV-1 infection	human (B*0702)	Frahm2004
gp160 (298–307)	gp120 (302–312 HXB2) • CTL from two acute seroconversion cases.	RPNNNTRKSI	HIV-1 infection	human (B7)	Safrit1994b
gp160 (298–307)	gp120 (302–312 HXB2) • Peptide processed by a TAP-1/2-dependent pathway only. • CTL from an acute seroconverter.	RPNNNTRKSI	HIV-1 infection	human (B7)	Hammond1995
gp160 (298–307)	gp120 (302–312 HXB2) • Longitudinal study of epitope variation *in vivo*.	RPNNNTRKSI	HIV-1 infection	human (B7)	Wolinsky1996
gp160 (298–307)	gp120 (302–311 subtype B) **Keywords** inter-clade comparisons, immunodominance. • The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed. • Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope RPNNNTRKSI is immunodominant, conserved between the LAI and clade A and C strains, but is very divergent in MN (RPNYNKRKRI), and that this epitope might be dominating the specificity of the response in the HLA B7 individuals.	RPNNNTRKSI	HIV-1 infection	human (B7)	Wilson1998b
gp160 (298–307)	gp120 (303–312 SF2) **Keywords** HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 1/3 group 2, and 1/1 group 3.	RPNNNTRKSI	HIV-1 infection	human (B7)	Altfeld2001b
gp160 (298–307)	gp120 (298–307) **Keywords** rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.	RPNNNTRKSI	HIV-1 infection	human (B7)	Day2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.				
gp160 (298–307)	gp120 (298–307)	RPNNNTRKSI	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-RI10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 4/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 1/4 individuals had detectable responses to this epitope after STI.				
gp160 (298–307)	gp120	RPNNNTRKSI	HIV-1 infection	human (B7)	Appay2002
	Keywords HAART. **Donor HLA** A2,A3,B7,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
gp160 (298–307)	gp120 (303–312 IIIB)	RPNNNTRKSI	HIV-1 infection	human (B7?)	Wilson1996
	Keywords responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • RPNNNTRKDI and RPNNNTRKGI, naturally occurring variants, were found in non-transmitting mother – ability to recognize these variants has not yet been determined.				
gp160 (299–319)	Env (299–319)	PNNNTRKSIRIGPGQTFYA	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (303–322)	gp120	TRKSIHIGPGRAFYTTGE	Vaccine	mouse	Luo1998
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade consensus *HIV component:* Gag, V3 • Intramuscular injection of chimeric gag-env virus-like particles (VLPs) containing V3 loop sequences into BALB/c mice induce V3 specific CTL – TRKSIHIGPGRAFYTTGE is a B subtype consensus that stimulated a cross-reactive CTL response.				
gp160 (304–318)	gp120 (304–318 IIIB)	RKSIRIQRGPGRAFV	Vaccine	mouse (H-2^d)	Kang1999
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade IIIB, B clade MN, B clade RF, B clade SF2, HIV-2 VLP *HIV component:* Gag, V3 • Virus-like particles could be formed from HIV-2 gag after deleting 143 amino acids at the C-terminal end – a proline rich region in positions 373-377 was critical to VLP formation. • CTL responses in BALB/c mice were induced by chimeric gag-V3 particles against the V3 region of HIV-1 clade B isolates IIIB (SIRIQRGRAFVTI), MN (KRIHIGPGRAFYTTK), RF (SITKGPGRVIYATGQ), and SF2 (SIYIGPGRAFHTTGR)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The vaccine induced CTL were cross-reactive with a broad spectrum of B clade isolates, with the exception of the RF V3 which did not induce CTL.				
gp160 (305–321)	gp120 (MN)	KRIHIGPGRAFYTTK	HIV-1 infection	human	Chitnis2003
	Keywords assay standardization, HAART. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2. • 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.				
gp160 (306–322)	gp160 (LAI)	SIRIQGPGRAFVTIGI	Vaccine	mouse (H-2D^d)	Deml1999
	Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 *Adjuvant:* aluminum hydroxide, CpG immunostimulatory sequence (ISS) **Keywords** immunodominance, Th1, Th2. • Addition of CpG oligodeoxynucleotide to a gp160/alum vaccine given to BALB/c mice shifted the response to Th0/Th1 from Th2, but no still CTL response to this immunodominant epitope was induced.				
gp160 (308–321)	Env (gp160)	RIQRGPGRAFVTIK	Vaccine	mouse	Sakaue2003
	Vaccine *Vector/Type:* hemagglutinating virus of Japan (HVJ)-liposome *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** genital and mucosal immunity. **Epitope name** P18IIIB. **Assay type** cytokine production, Chromium-release assay. **Donor HLA** H-2d. • BALB/c mice were immunized nasally with HIVgp160-encapsulated hemagglutininating virus of Japan (HVJ)-liposome. Vaccination induced IgG in serum and IgA in nasal wash, saliva, fecal extract, and vaginal wash, with some ability to neutralize the primary field isolate HIV-MNp. • Th1 and Th2-type responses were stimulated, as well as gp160 V3-specific MHC class I-restricted CTL responses.				
gp160 (308–321)	Env (IIIB)	RIQRGPGRAFVTIG	Vaccine	mouse (Dd)	Ahlers2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 **Keywords** binding affinity, Th1. **Epitope name** P18IIIB. • BALB/c and A.AL were immunized with an Env-peptide vaccine construct containing the CTL epitope P18IIIB and the T helper epitope T1, KQIIN-MWQEVGKAMYA. • Substitution of Glu (wt) to Ala in T1, kqiinmwqAvgkamya, caused increased affinity for MHC class II Ek, resulting in the upregulation of CD40L in the responding Th cells, and shifting the response towards Th1. Increased Th responses stimulated DCs to produce higher levels of IL-12, and B7-1 and B7-2, and enhanced CTL responses to P18. • The modified epitope, T1A, elicited stronger protection against increasing doses of viral challenge with vaccinia expressing HIV-1 IIIB gp120 compared to the wt epitope T1.				
gp160 (308–322)	gp160 (MN)	RIHIGPGRAFYTTKN	Vaccine	human	Pinto1999
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 *Adjuvant:* Montanide (ISA 51) • Peptide P18: Eight HIV+ individuals were vaccinated with peptides containing specific T helper, CTL and Ab epitopes in Montanide ISA 51 in a Phase I trial. • Four displayed a 4-fold increase in PCLUS 3-18 MN-specific T helper responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• One patient developed a new, sustained P18MN-peptide-specific CTL response – the patient's HLA haplotype was A2,30; B53,7; Cw2,4, and anti-HLA A2 antibody did not inhibit the response, suggesting it was not A2. • Patients with low baseline Ab levels developed an increase of neutralizing Ab titers. • No significant change was observed in plasma HIV viral loads and CD4 cell counts.				
gp160 (308–322)	gp120 (MN)	RIHIGPGRAFYTTKN	HIV-1 infection	chimpanzee	Lubeck1997
	• Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant. • CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV.				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV.				
gp160 (308–322)	gp120 (110–122)	RIQRGPGRAFVTIGK	Vaccine	mouse	Moore2002a
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *Adjuvant:* FLt3 ligand (FL), GM-CSF, IL-12, IL-15, IL-2 **Keywords** vaccine-specific epitope characteristics. • Intramuscular immunization of BALB/c mice with DNA vaccines carrying either gp160 or Nef in the expression vector plasmid pNGVL gave different responses – gp160 induced strong gp160-specific CTL and IFN-responses and low-titer humoral responses, and Nef generated humoral (IgG1, IgG2a) responses and IFN-responses but little CTL activity. • Co-injection of DNA plasmids encoding cytokines and/or hematopoietic growth factors, IL2, IL-12, IL-15, Flt3 ligand (FL), and GMCSF tended to give responses that were enhanced quantitatively, but not altered qualitatively. • Co-administration of GMCSF most strongly enhanced CTL and IFN-responses against pNGVL-gp160. • Repeated immunization with pNGVL-Nef failed to induce CTL responses. Co-administration of IL-12 most strongly enhanced humoral and IFNgamma responses. • FL, which enhances innate immune responses, in combination with IL-2, IL-12 or IL-15 generated with most potent Nef responses.				
gp160 (308–322)	Env (315–329)	RIQRGPGRAFVTIGK	Vaccine	mouse (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 **Keywords** epitope processing, vaccine-specific epitope characteristics, immunodominance. **Epitope name** P18. • C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome. • A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members. • Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN-responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen. • The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	human (A11)	Achour1994
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 • One of 3 HLA type restrictions associated with this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp120 (315–329 BRU)	RIQRGPGRAFVTIGK	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (P18)				
gp160 (308–322)	gp120 (308–322 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-12				
	Keywords vaccine-specific epitope characteristics.				
	• Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.				
	• Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.				
	• The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	human (A2, A3)	Achour1993
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• Two of 3 HLA type restrictions associated with this peptide.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (D^d)	Takahashi1989a
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3				
	• Positions R(8) and F(10) are important for MHC/peptide interaction.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (D^d)	Sastry1992
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3				
	• Free peptide injected into the footpad of a mouse could stimulate specific CTL.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (D^d)	Ahlers1997b
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3				
	• PCLUS 3-18MN synthetic peptide vaccine construct contained T1 helper epitope covalently linked to truncated P18 CTL epitope.				
	• A substitution in the T1 peptide stimulated an enhanced Th response and class II binding specificity, which in turn enhanced CTL induction by vaccine.				
	• Construct PCLUS 3-18MN is currently in a phase I vaccine clinical trial.				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	mouse (D^d)	Takahashi1989b
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB, B clade MN *HIV component:* gp160				
	• Y(11 MN) exchange with V(11 IIIB) interchanges specificities.				
gp160 (308–322)	gp120 (313–327 IIIB, MN, RF)	SITKGPGRVIYATGQ	Vaccine	mouse (D^d)	Takahashi1992
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade RF *HIV component:* gp160				
	• Comparison of MN, IIIB, and RF specificities, position 11 is critical.				
gp160 (308–322)	gp160 (315–329 IIIB)	RIQRGPGRAFVTIGK	in vitro stimulation or selectio	mouse (Dd)	Yokosuka2002
	Keywords TCR usage.				
	Epitope name P18.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA H-2d. • The TCR repertoire and its specificity was studied through analyzing the spectrum of TCR-alpha and beta chains able to reconstitute a reaction to the H-2 Dd-restricted P18 peptide. The RT-1 TCR alpha chain was able to react with 1/3 of the tested TCR beta chains to create a specific response. Experiments in transgenic mice also supported the observation that a single TCR alpha chain would confer the specificity of the response and could interact with a large variety of TCR beta chains.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-$2^{d, p, u, q}$)	Shirai1992, Shirai1993
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 • In a murine system multiple class I molecules can present this peptide, called P18, to CTL, including H-$2D^d$, H-$2D^p$, H-$2D^q$, H-$2L^q$ • The MHC class I molecule D^d as well as H-$2^{u,p,q}$, were found to present peptides P18 and HP53. • The V-β usage in T cells showing cross-reaction between these two peptides was conserved for H-$2^{d,u,p}$, but not in H-2^q				
gp160 (308–322)	gp120 (HXB2)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2^d)	Griffiths1993
	Vaccine *Vector/Type:* protein *HIV component:* Gag, V3 • Gag-V3 fusion protein immunization elicited V3 CTL response in mice.				
gp160 (308–322)	gp120 (HXB2)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2^d)	Deml1997
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* Env, Gag • Env bound to virus-like particles (VLPs) can elicit a CTL response that is dependent on the amount of Env presented on the VLP.				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	mouse (H-2^d)	Fomsgaard1998a
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* gp160, V3 • Enhanced B and CTL responses to the V3 region occur following epidermal immunization by gene gun with a chimeric DNA vaccine of V3-hepatitis B surface antigen relative to a gp160 plasmid vaccine.				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	mouse (H-2^d)	Ahlers1996, Ahlers1997a
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 *Adjuvant:* GM-CSF, IL-12 **Keywords** Th1. • Vaccine constructs containing helper, antibody and CTL peptide epitopes induce strong Th1, CTL and NAb responses against the autologous HIV-1 virus. • The peptide CTL response was as cross-reactive as one elicited by a vaccinia construct expressing rgp160 MN. • GM-CSF and IL-12 were the two cytokines most effective for inducing and boosting CTLs.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2^d)	Layton1993
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade IIIB *HIV component:* Gag, V3 • V3-Ty-Virus-like particles can induce type-specific CTL in mice in the absence of adjuvant.				
gp160 (308–322)	gp120 (IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2^d)	Barouch1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* IL-2, IL2/Ig • A discistronic IL-2 gp120 expression vector gave a weaker CTL response than gp120 alone in the expression vector, however co-administration of an Il-2/IgG fusion protein enhanced the immune response and administration of a Il-2/IgG plasmid had a response that depended on the timing of administration. • This study showed that a response to an HIV-1 DNA vaccine could be either augmented or suppressed by plasmid Cytokine/Ig administration.				
gp160 (308–322)	Env (308–322 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2^d)	Uno-Furuta2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* B7, CpG immunostimulatory sequence (ISS), in vivo electroporation **Keywords** Th1. **Epitope name** P18.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peptide immunization usually doesn't elicit a good CTL response because epitopes are not internalized and processed and presented, so vaccination with electric pulsing was tried (i.m. injection followed by 8 electric pulses), to enhance peptide uptake through electroporation. • BALB/c immunized with HIV P18 or hepatitis C P17 peptides with an electric pulse elicited a CTL response, those that did not receive the pulse did not. • The CTL response was enhanced by addition of immunostimulatory sequences ISS in the plasmid pCMV-LacZ, that contains hexamers GACGTC, AGCGCT, AACGCT, sequences common in prokaryotic genomes but rare in eukaryotic genomes that elicit Th1 cytokines and result in B cell and T-cell proliferation. • The CTL response was also enhanced by addition of B7-1 cDNA – the B7 family of proteins transduce co-stimulatory signals through interaction with CD28.				
gp160 (308–322)	gp160 (MN)	RIHIGPGRAFYTTKN	Vaccine	mouse (H-2^{d}, H-2^{b})	Fomsgaard1998b
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* gp160 • CTL responses to a primary gene gun vaccination were rapid and strong for several methods of vaccinations: i.m., bupivacaine pretreatment, cardiotoxin pretreatment or gene gun – the CTL response was more rapid and consistent than the antibody response.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-$2D^{d, p, q}$, H-2^{u})	Shirai1996b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 • Multiple murine MHC can cross-present this epitope (P18) and HP53, DRVIEVVQGAYRAIR, to specific CTL.				
gp160 (308–322)	gp160 (IIIB)	GIHIGPGRAFYAARK	Vaccine	mouse (H-$2D^{d}$)	Morris2000
	Vaccine *Vector/Type:* peptide, protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** Th1, Th2. • LT(R192G) induces gp160-specific serum and mucosal IgG1 and IgG2a, systemic CTL activity and Th1 and Th2 cytokine responses upon internasal immunization.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-$2D^{d}$)	Porgador1997
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* Cholera toxin (CT) • A intranasal peptide vaccine with cholera toxin as a mucosal adjuvant was given. • IIIB peptide referred to as R15K. • Peptide-specific CTLs were induced after *in vitro* restimulation with peptide-pulsed targets. • R15K was superior at inducing CTL compared to the RGPGRAFVTI, in contrast to the findings of Nehete *et al.* • Memory CTL responses were induced.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	(H-$2D^{d}$)	Chiba1999
	Vaccine *Vector/Type:* vaccinia with H1 influenza HA gene cassette *Strain:* B clade IIIB *HIV component:* p18 Gag • Vaccine was capable of priming P18IIIB specific CTL in BALB/c mice, but could not induce a P18IIIB-specific antibody response.				
gp160 (308–322)	gp120 (multiple)	RIHIGPGRAFYTTKN	Vaccine	mouse (H-$2D^{d}$)	Casement1995
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN, B clade SC *HIV component:* V3 • V3 peptides from MN and SC induce murine CTL that are cross-reactive with diverse strains.				
gp160 (308–322)	gp120 (313–327 MN)	RIHIGPGRAFYTTKN	Vaccine	mouse (H-$2D^{d}$)	Newman1997
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* QS21 • MN vaccine induced CTL reactive with MN, IIIB and RF vaccinia-expressed Env, but not this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2D^d)	Newman1997
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* QS21				
	• IIIB vaccine induced IIIB type-specific CTL to this peptide (P18), and an additional Env CTL response that was cross-reactive.				
gp160 (308–322)	gp120 (315–329)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2D^d)	Takahashi1988
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160				
	• V3 loop CTL response in mice vaccinated with gp160.				
gp160 (308–322)	gp120 (315–329)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2D^d)	Fukasawa1998
	Vaccine *Vector/Type:* liposome *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* oligomannose				
	• The peptide RIQRGPGRAFVTIGK was incorporated into liposomes and given as a subcutaneous injection, which induces a MHC class I restricted CTL response in mice.				
	• Liposomes coated with oligomannose show no toxicity and can elicit a potent CTL response upon a single subcutaneous infection, while non-coated liposomes do not, suggesting that oligomannose may be a good adjuvant for CTL responses.				
gp160 (308–322)		RIQRGPGRAFVTIGK	Vaccine	mouse (H-2D^d)	Lu2000a
	Vaccine *Vector/Type:* fusion protein with anthrax delivery domain *HIV component:* V3 *Adjuvant:* B. anthracia lethal toxin LF component				
	Keywords epitope processing, vaccine-specific epitope characteristics.				
	Epitope name P18.				
	• Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs *in vitro*.				
gp160 (308–322)	gp120 (V3 loop) (MN)	RIHIGPGRAFYTTKN	Vaccine	mouse (H-2D^d)	Staats2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* Cholera toxin (CT), GM-CSF, IL-12, IL-18, IL-1alpha				
	• Cholera toxin (CT) is a potent adjuvant used in animal studies that is not safe in humans, so combinations of cytokins were used in nasal immunization of BALB/c mice V3 peptides to attempt to replace CT as a potent adjuvant.				
	• Peptide vaccine induced CTL activity was significantly increased by IL-1alpha , IL-18, and GMCSF given alone as adjuvant, but CT gave more potent CTL activity than any single cytokine.				
	• Combinations of cytokins could be more potent that CT as an adjuvant. The highest tetramer binding of H-2Dd peptide-specific PBMC after nasal immunization was observed with IL-1alpha plus IL-18 as adjuvant.				
	• Nasal immunization with HIV peptide in the presence of IL-1alpha, IL-12 and GM- CSF induced IFN-gamma-secreting cells in the cervical lymph node, the lung and the spleen, and was associated with upregulation of MHC class II and B7.1 on nonlymphocytes in NALT/nasal mucosal cells.				
	• Consistent results were obtained for the IIIB and the MN peptides.				
gp160 (308–322)	gp160 (315–329 MN)	RIHIGPGRAFYTTKN	in vitro stimulation or selectio	mouse (H-2D^d)	Yokosuka2002
	Keywords TCR usage.				
	Epitope name P18.				
	Donor HLA H-2d.				
	• The TCR repertoire and its specificity was studied through analyzing the spectrum of TCR-alpha and beta chains able to reconstitute a reaction to the H-2 Dd-restricted P18 peptide. The RT-1 TCR alpha chain was able to react with 1/3 of the tested TCR beta chains to create a specific response. Experiments in transgenic mice also supported the observation that a single TCR alpha chain would confer the specificity of the response and could interact with a large variety of TCR beta chains.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (309–317)	gp120 (310–318 SF2)	IYIGPGRAF	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • IYIGPGRAF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – no specific CTL clones were obtained.				
gp160 (309–318)	gp120 (314–323 CM243 subtype CRF01)	ITVGPGQVFY	HIV-1 infection	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** E309-318. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was strongly reactive in HIV+ control study subject 184 who carried HLA-A11.				
gp160 (309–318)	gp120 (314–323 CM243 subtype CRF01)	ITVGPGQVFY	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it. • This epitope was not conserved in other subtypes, and exact matches were rare.				
gp160 (310–318)		HIGPGRAFY	HIV-1 infection	human (A*3002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Env-HY9. **Donor HLA** A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes YPLTFGWCY, Nef(135-143), HLA B*5301; AETFYVDGA, RT(437-445), HLA B*4501; and RSLYNTVATLY, p17(76-86), HLA A*3002. • Among HIV+ individuals who carried HLA A30, 3/16 (19%) recognized this epitope.				
gp160 (310–318)	gp120 (310–318)	HIGPGRAFY	HIV-1 infection	human (A*3002)	Frahm2004
gp160 (310–318)		HIGPGRAFY	HIV-1 infection	human (A02)	Sabbaj2002b
	Epitope name Env-HY9. • Among HIV+ individuals who carried HLA A02, 6/29 (21%) recognized this epitope.				
gp160 (310–323)	gp120 (315–328 MN)	HIGPGRAFYTTKNI	Vaccine	mouse (H-2D^{d})	Arp1999
	Vaccine *Vector/Type:* canarypox prime with pseudovirion boost *Strain:* B clade IIIB, B clade MN *HIV component:* Gag, gp120, Protease				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name p97. • The vaccine vCP205, canarypox vector, MN gp120 + Gag/Pro IIIB, with a HIV-1 pseudovirion boost was given to mice;) • HIV-1 pseudovirion boost enhanced the CTL to this epitope in immunized BALB/ c mice as measured by CTL lysis and IFN gamma production.				
gp160 (311–318)	(MN)	IGPGRAFY	Vaccine	mouse (H-2D^{d})	Golding2002a
	Vaccine *Vector/Type:* B. abortus complex *Strain:* B clade MN *HIV component:* V3 • Intranasal immunization of B. abortus conjugated to V3 peptides induces mucosal IFN-gamma producing T-cell responses in BALB/c mice.				
gp160 (311–319)	gp120 (311–320 IIIB)	RGPGRAFVT	Vaccine	mouse (A2)	Kiszka2002
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-12 **Keywords** vaccine-specific epitope characteristics. • Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV. • Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells. • The most intense CTL responses to the intact gp160 vaccine were directed at three V3 peptides.				
gp160 (311–319)	gp120 (312–320 SF2)	IGPGRAFHT	Vaccine	mouse (D^{d})	Selby1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade SF2 *HIV component:* gp120 • Murine CTL response to peptide observed after immunization with DNA plasmid containing HIV-1 (SF2) gp120 gene regulated by bacteriophage T7 promoter. • CTL response required coadministration of rec vaccinia virus expressing T7 RNA polymerase or T7 RNA polymerase soluble protein.				
gp160 (311–319)	gp120 (SF2)	IGPGRAFHT	Vaccine	mouse (H-2D^{d})	Barnett1997
	Vaccine *Vector/Type:* DNA prime with gp120 boost *Strain:* B clade SF2 *HIV component:* gp120 • CTL were induced by vaccine, and restimulated *in vitro* with V3 peptide. • DNA vaccine with protein boost stimulated both CTL and antibodies. • Strains SF2 (IGPGRAFHT), US4 (IGPGRAFYA), and CM235 (IGPGQVFYR) were tested.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	macaque	Okuda1997
	Vaccine *Vector/Type:* DNA prime with peptide boost *Strain:* B clade IIIB *HIV component:* CD4BS, gp160, HPG30, V3 • Murine BALB/c (H-2^{d}) and macaque both showed highest level of CTL vaccine response when a DNA vaccine was boosted with a peptide including four peptide subtypes of the V3 region, HPG-30 and a fragment of the CD4 binding region.				
gp160 (311–320)	gp120 (318–327)	RGPGRAFVTI	HIV-1 infection	human	Kmieciak1998b
	• Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product. • This epitope doesn't have A2 anchors, but has features that confer promiscuous A2 binding, which may relate to the inhibitory effect seen in this paper.				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	mouse	Lu1999
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* MIP-1alpha • MIP-1alpha co-inoculation increased IgG1/IgG2a ratio T-helper type 1 response. • A MIP-1 alpha expression plasmid increased the CTL response to this DNA vaccine, as well as the T help response, presumably by the MIP-1 alpha interacting with T lymphocytes and macrophages.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (311–320)		RGPGRAFVTI	Vaccine	mouse	Barouch2002
Vaccine *Vector/Type:* DNA *Strain:* B clade BH10 *HIV component:* gp120 *Adjuvant:* GM-CSF **Epitope name** P18. • gp120 encoding DNA co-injected with a plasmid carrying GMCSF gave meager CD4+ T-cell responses in BALB/c mice relative to the enhanced response to bicistronic gp120 and GMCSF cloned into the same vector and expressed from the same promoter. • Both mono and bicistronic DNA vaccines induced similar CTL responses directed against the H-2Dd restricted P18 peptide RGPGRAFTVTI in murine splenocytes despite the greatly enhanced proliferative responses.					
gp160 (311–320)	gp120 (313–322 BRU)	RGPGRAFVTI	Vaccine	mouse	Arora2001
Vaccine *Vector/Type:* DNA *Strain:* B clade BRU *HIV component:* gp160, Rev, Tat **Keywords** inter-clade comparisons, Th1. **Epitope name** Pep 09. • Plasmid DNA encoding gp160, tat, rev was given i.m. to immunize BALB/c mice. • Vaccine-induced CTL activity produced a low degree of cell lysis of V3-peptide pulsed target cells, using a B (RGPGRAFVTI) or C (RIGGPGQTFYATG) clade V3 peptides. Th1 proliferative T-cell responses were observed, and weak Ab responses.					
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	mouse	Gherardi2003
Vaccine *Vector/Type:* influenza prime with vaccinia boost *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** Th1, Th2, genital and mucosal immunity. **Epitope name** 10 Env. **Assay type** cytokine production, proliferation, CD8 T-cell Elispot - IFNγ. **Donor HLA** H-2d. • Mice were intranasally primed with a recombinant influenza virus A vector that carries HIV-1 Env inserted into its hemagglutinin protein. Boosting was performed intranasally with either influenza-Env or intraperitoneally with two vaccinia virus recombinants expressing the Env protein, VVenv and MVAenv. • Peritoneal heterologous immunization with VVenv induced a 60-fold higher CD8+ IFN-gamma T cell responses than homologous influenza prime-boost. The intraperitoneal MVAenv boost response was greater than the VVenv boost in the spleen and genital lymph nodes, while the VVenv response gave the highest boost with the intranasal route. • Mice with increased CD8+-T-cell responses also had a higher Th1/Th2 ratio, indicated by the cytokine secretion profile and the IgG2a/IgG1 ratio.					
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	in vitro stimulation or selectio	human (A*0201)	Alexander-Miller1996
• This epitope stimulates a CTL line derived from an HIV negative donor. • This immunogenic peptide does not have the known binding motif for A2.1. • The same optimal peptide for this human HLA-A2.1 epitope was observed for a murine H-2 D^d epitope.					
gp160 (311–320)	gp120 (311–320 IIIB)	RGPGRAFVTI		human (A*0201)	Frahm2004
• C. Brander notes this is an A*0201 epitope.					
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	human (A2)	Achour1996
Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 • Individual was immunized with rec vaccinia gp160 IIIB and boosted with purified gp160. • Lysis only occurs with IIIB P18 peptide pulsed onto autologous targets; MN, RF, SIMI P18 peptides fail to stimulate CTL. • Restimulating immune cells from gp160 IIIB vaccinees with MN, RF, or SIMI P18 did not enhance the MN, RF, or SIMI specific CTL response.					
gp160 (311–320)	gp160 (318–327 SIMI)	MGPKRAFYAT	Vaccine	human (A2)	Achour1996
Vaccine *Vector/Type:* vaccinia prime with gp160 boost *Strain:* B clade SIMI *HIV component:* gp160					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Individual was immunized with rec vaccinia gp160 SIMI and boosted with purified recombinant gp160 SIMI. • P18 MN and RF peptides were able to stimulate the HIV-specific CTL that arose in response to the SIMI vaccination, thus the P18 MN peptide (IGPGRAFYTT) and the P18 RF peptide (KGPGRVIYAT) could cross-react. • The P18 IIIB peptide does not cross-react (RGPGRAFVTI in the epitope region) • gp160 SIMI primed immune cells could generate a significantly broader specificity when stimulated with P18 MN or P18RF peptides, but not P18 IIIB.				
gp160 (311–320)	gp120 (311–320)	RGPGRAFVTI	HIV-1 infection	human (A2)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR25. • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (D)	Nehete1995
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 • RGPGRAFVTI was defined as the optimal peptide for vaccination, out of RIQRGPGRAFVTIGK. • This peptide, in a carrier-free form in Freund's adjuvant, could stimulate Env specific CTL in BALB/c mice.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (D^d)	Takahashi1993
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 **Keywords** dendritic cells. • Successful priming with vaccination of peptide pulsed splenic dendritic cells.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (D^d)	Takahashi1996
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 • Exposure of CD8+ CTL to free peptide corresponding to the epitope results in strong inhibition of the CTL response to targets presensitized with the same peptide. • The authors propose this is due to a "self-veto", where the CTL is inactivated by a CD8+ cell carrying the appropriate peptide-MHC complex.				
gp160 (311–320)	gp120 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse ($H\text{-}2^{d, p, u}$)	Shirai1997
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Three class I MHC, H-$2^{d,p,u}$, that differ in sequence and serology, cross-present this peptide to T cells of each of the other haplotypes. • The amino acids R, F, and I are each critical for strong CTL activity with all three MHC molecules.				
gp160 (311–320)	gp160	RGPGRAFVTI	Vaccine	mouse (H-2^{d17})	Hanke1998a
	Vaccine *Vector/Type:* vaccinia • MVA is an attenuated vaccinia that can not replicate in mammalian cells – strings of CTL epitopes were delivered and expressed in a MVA DNA vector. • INFγ and CTL activity were induced after a single vaccination. • An MVA boost enhanced the response.				
gp160 (311–320)	gp160	RGPGRAFVTI	Vaccine	mouse (H-2^{d})	Gherardi2000
	Vaccine *Vector/Type:* DNA, vaccinia *HIV component:* Env *Adjuvant:* IL-12 • Induction of HIV-1 specific CD8 gamma IFN secreting cells was enhanced when IL-12 and Env were given together in a prime, followed by a VV expressing Env boost. • If IL-12 was also delivered as a boost from the viral vector, impairment of the IL-12 effects was noted, indicating that the vaccination schedule can be a critical parameter for success with DNA and vaccinia vectors used in combination with immunomodulators. • The negative effect observed when IL-12 was delivered with the boost involved nitric oxide.				
gp160 (311–320)	Env	RGPGRAFVTI	Vaccine	mouse (H-2^{d})	Xin1999
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* IL-12, IL-15, IL-2 **Keywords** Th1. • A study of the DNA vaccine pCMV160IIIB/REV with IL-15 and IL-2 or IL-12 expression plasmids. • Intranasal immunization of BALB/c mice with HIV DNA and IL-15 plasmid induced increased Th1 and CTL responses. • Co-administration of IL-15 with IL-12 or IL-2 plasmids did not alter the effect of IL-15. • Both the CTL (peptide pulsed targets) and DTH response (injection of peptide into footpad) to this peptide was monitored. • The Ab response to NNTRKSIRIQRGPGRAFVTIGKIGN was monitored, and IL-15 co-administration resulted in a decrease in the IgG1/IgG2a ratio.				
gp160 (311–320)	Env	RGPGRAFVTI	Vaccine	mouse (H-2^{d})	Villacres1999
	Vaccine *Vector/Type:* vaccinia, Sindbis *HIV component:* V3 • HIV-1 epitope p18 was expressed in two different vaccine vectors and the CTL response was compared in BALB/c mice. • Class I tetramer staining showed that up to 13% of the CD8+ splenocytes were p18 specific in the acute response using vaccinia, only 4% using Sindbis. • vp18 had more gamma IFN secreting splenocytes and activated CD4+ and CD8+ T cells. • The overall decline in CD8+ T cells in the transition into memory was 2-3 fold for both vectors. • Sindbis virus recombinants induced protective memory cytotoxic T cells, although reduced quantitatively, without vaccinia associated inflamation and replication.				
gp160 (311–320)	Env (318–327)	RGPGRAFVTI		mouse (H-2^{d})	Lopez2000
	Keywords epitope processing, immunodominance. • A series of protease and proteasome inhibitors was used to identify elements of the processing pathway of this epitope, called p18, both from within Env and from within a chimeric hepatitis B protein which allows proper processing. • Lactacystin, a proteasome inhibitor, partially inhibits endogenous processing of p18 epitope suggesting both a proteasome pathway and an additional pathway can be used. • Both TAP dependent and TAP-independent pathways can be used. • 1,10-phenanthrolin (metallopeptidases inhibitor) blocks epitope presentation demonstrating metalloproteinase processing in the Tap-dependent pathway. • The Tap-independent pathway does not involve processing by metalloproteinases.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope is immunodominant in mice, and is presented by multiple human HLA alleles – it as been suggested that the high processing efficiency of this epitope might result in poor presentation of co-expressed epitopes.				
gp160 (311–320)	gp120	RGPGRAFVTI	Vaccine	mouse (H-2^d)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia • This murine epitope was incorporated into a vaccine of CTL epitopes expressed together including 20 HIV epitopes recognized by humans from 12 HLA types, one murine HIV epitope and three macaque HIV epitopes, delivered in a vaccinia virus Ankara (VVA) construct. • The murine vaccination was more effective at generating CTL when given i.v. rather than i.m.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2^d)	Hamajima1997
	Vaccine *Vector/Type:* peptide *HIV component:* CD4BS, HPG30, V3 *Adjuvant:* IL-12 • B cell epitope HGP-30 also serves as a CTL epitope. • Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide. • IL-12 expression plasmid included with the vaccination enhanced the CTL response.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2^d)	Arai2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** Th1, Th2. • Low-dosage 8 Br-cAMP given in combination with a DNA vaccine to BALB/c mice increased IgG and sIgA levels, and enhanced Th1, Th2 and CTL activity – the adjuvant activity may be mediated by activation of the CMV promotor in the DNA vaccine.				
gp160 (311–320)	gp120 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2^d)	Goletz1997
	Vaccine *Vector/Type:* fusion protein with anthrax delivery domain *HIV component:* gp120 • Anthrax lethal toxin can deliver proteins to the cytosol of eukaryotic cells. • A fusion protein linking the delivery domain of the anthrax protein to gp120 achieved cellular uptake, and gp120 was processed allowing presentation of this V3 epitope to CTL *in vitro*.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	in vitro stimulation or selectio	mouse (H-2^d)	Takahashi2001
	Epitope name I-10. • Pre-incubation of HIV-1 (IIIB) gp160 specific CTL with peptide without APCs reduced cytolytic activity 3.5 fold and induced peptide concentration dependent IL-2 unresponsiveness that might be due to IL-2Rbeta down regulation. • An enhanced cytolytic activity was observed by addition of anti-IFN-gamma, TNF-alpha or MIP-1beta to I-10 suppressed CTLs.				
gp160 (311–320)	gp160 (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2^d)	Shirai2001
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** Th1, Th2. • Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori.				
gp160 (311–320)	Env (89.6)	IGPGRARYAR	Vaccine	mouse (H-2D)	Belyakov1998b
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade 89.6 *HIV component:* gp160 • Recombinant modified vaccinia virus Ankara (MVA), an attenuated vaccina which has lost the ability to replicate in mammalian cells, was used as the live vector for this vaccine study. • A single intrarectal mucosal immunization resulted in long lasting mucosal CTL responses and production of proinflammatory cytokines in mucosal sites, indicating that MVA was as effective in inducing mucosal CTL as replicating recombinant vaccinia.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (311–320)	Env (IIIB)	IGPGRARYAR	Vaccine	mouse (H-2D)	Belyakov1998a
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3				
	• HIV protection and mucosal CTL response was studied – an HIV peptide immunogen could protect against gp160 expressing vaccinia in a murine intrarectal challenge system in which neutralizing Abs did not play a role, demonstrating mucosal CTL at the site of exposure can be protective.				
gp160 (311–320)	gp120 (MN)	IGPGRAFYTT	Vaccine	mouse (H-2D^d)	Lapham1996
	Vaccine *Vector/Type:* B. abortus complex				
	• B. abortus-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice.				
gp160 (311–320)	gp160 (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2D^d)	Bruce1999
	Vaccine *Vector/Type:* non-replicating adenovirus *Strain:* B clade IIIB *HIV component:* Env, Rev				
	• A good HIV-1 Env immune response using non-replicating adenovirus vectors in BALB/c mice is dependent upon the presence of the stimulatory tat/rev 5'splice-donor site sequence and the presence of Rev.				
	• Administration of monocistronic RAd501 expressing env and RAd46 expressing rev resulted in a positive CTL response, but required two immunizations for a CTL response comparable to that induced by the bicistronic virus RAd142.				
	• Administration of RAd501 alone gave a low CTL response, but no humoral response, suggesting a lower level of antigen may be required to stimulate CTL.				
gp160 (311–320)	gp120 (MN)	IGPGRAFYTT	Vaccine	mouse (H-2D^d)	Lapham1996
	Vaccine *Vector/Type:* B. abortus complex				
	• B. abortus-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Peptide-HLA interaction	mouse (H-2D^d)	Takeshita1995
	• XGPXRXXXXI are critical for binding, consistent with H-2D^d motif XGPX(RKH)XXX(X)(LIF)				
gp160 (311–320)	Env	RGPGRAFTVTI	Vaccine	mouse (H-2D^d)	Hanke1999a, Hanke1999b
	Vaccine *Vector/Type:* DNA *HIV component:* V3				
	• Vaccinated mice elicited a CTL response to a gene gun-delivered multiepitope vaccine to two epitopes studied that are known to elicit CTL in mice: SYIPSAEKI from Plasmodium berghei and RGPGRAFTVTI from HIV-1 Env.				
	• Different vaccination protocols were tested and it was found that a gene gun mediated delivery followed by an MVA boost was as good as i. m. immunization followed by a MVA boost – this is advantageous as gene gun delivery requires far less DNA than i.m. DNA priming.				
	• CTL activity was high (60% - 70% specific lysis at effector target) when vaccinated with a single gene gun immunization and an MVA boost, and improved with two gene gun vaccinations.				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	in vitro stimulation or selectio	mouse (H-2D^d)	Nakagawa2000
	Keywords epitope processing, immunodominance.				
	Epitope name I-10.				
	• The CTL line LINE-IIIB was generated by repetitive restimulation of BALB/c spleen cells with vSC-25, IIIB gp160-expressing vaccinia.				
	• RGPGRAFVTI represents the active minimal epitope within the previously described immunodominant epitope P18IIIB (RIQRGPGRAFVTIGK, gp160(308-322)				
	• External processing of P18IIIB results in the removal of the 2 C-terminal residues (GK) of I-10 by ACE (angiotensin-1-converting-enzyme) in sera to produce I-10, and this processing is essential for target cell presentation of RIQRGPGRAFVTIGK.				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2D^d)	Haglund2002a
	Vaccine *Vector/Type:* vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2, B clade IIIB *HIV component:* Env, Gag				
	Keywords immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name p18-I10. • Different HIV strains were used for different regions: Env IIIB, Gag HXB2 • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag, Env, or both, and compared to using rec Env and Gag in vaccinia virus (rVVs). The primary response was determined by cell lysis, cytokine production and tetramer staining. • Primary CTL responses to the immunodominant Env (RGPGRAFVTI) epitope peaked 5-7 days after intraperitoneal vaccination with Env-rVSV, 40% of the CD8+ cells were tetramer positive, and this response was 6-fold higher than the response to Env-rVV. • Vaccinating with GagEnv-rVSV carrying both Gag and Env allowed recognition of both HIV-1 proteins, but at reduced levels compared to either Gag-rVSV or Env-rVSV alone. • Intranasal immunization with Env-rVSV yielded CTL responses that were strong but reduced compared to an intraperitoneal route.				
gp160 (311–320)	Env (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2D^{d})	Haglund2002b
	Vaccine *Vector/Type:* vaccinia, vesicular stomatitis virus (VSV) *Strain:* B clade HXB2 *HIV component:* Env, Gag **Keywords** immunodominance. **Epitope name** p18-I10. • Different HIV strains were used for different regions: Env IIIB, Gag HXB2 • BALB/c mice were vaccinated with rec vesicular stomatitis virus (rVSV) expressing either HIV-1 Gag or Env, or both, and retention of memory responses and recall responses were studied by tetramer staining and IFN-gamma production. • Seven months after vaccination with Env-rVSV, 6% of the CD8+ cells were tetramer positive for the immunodominant Env epitope; these cells had a memory phenotype, CD44-Hi positive. • Env in rec vaccinia virus (Env-rVV) elicited a strong recall response, with up to 45% to the CD8+ T-cell population tetramer positive and activated (expressing CD62L-Lo), and capable of IFN-gamma production. • A prime with Env-rVSV and heterologous boost of Env-rVV gave remarkably high levels of memory cells, with approximately 1/3 of the CD8+ splenocytes being Env specific memory cells 150 days after the boost. • A Gag-rVSV or EnvGag-rVSV prime and with a heterologous Gag-rVV or EnvGag-rVV boost combination gave 40% tetramer positive CD8+ cells, but the fraction of IFN-gamma producing cells was only about 25%. Still the heterologous vector prime-boost combination showed a profound benefit. • A HIV-1 protein rVSV prime, rVV boost was a more potent combination than a vector reversal of a rVV prime and rVSV boost.				
gp160 (311–320)	gp120 (V3 loop) (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2D^{d})	Staats2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* Cholera toxin (CT), GM-CSF, IL-12, IL-18, IL-1alpha • Cholera toxin (CT) is a potent adjuvant used in animal studies that is not safe in humans, so combinations of cytokins were used in nasal immunization of BALB/c mice V3 peptides to attempt to replace CT as a potent adjuvant. • Peptide vaccine induced CTL activity was significantly increased by IL-1alpha , IL-18, and GMCSF given alone as adjuvant, but CT gave more potent CTL activity than any single cytokine. • Combinations of cytokins could be more potent that CT as an adjuvant. The highest tetramer binding of H-2Dd peptide-specific PBMC after nasal immunization was observed with IL-1alpha plus IL-18 as adjuvant. • Nasal immunization with HIV peptide in the presence of IL-1alpha, IL-12 and GM- CSF induced IFN-gamma-secreting cells in the cervical lymph node, the lung and the spleen, and was associated with upregulation of MHC class II and B7.1 on nonlymphocytes in NALT/nasal mucosal cells. • Consistent results were obtained for the IIIB and the MN peptides.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2D^{d})	Wierzbicki2002
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* beta-glucan lentinan, IL2/Ig, liposome, PLG **Keywords** immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• BALB/c mice were give an oral immunization with (PLG)-encapsulated plasmid DNA expressing gp160 and a boost of rec gp160 vaccinia vectors (rVV) with addition of murine IL-2/Ig plasmid or lentinan-associated liposomes. Lentinan increased CTL activity as measured by Cr-release assays against the immunodominant epitope RGPGRAFVTI, but didn't alter Ab responses. IL-2/Ig increased both type I and II activities, and increased Env specific CTL and Abs. Administration of liposomes and PLG microparticles with adjuvants facilitated gastrointestinal uptake.				
gp160 (311–320)	gp120 (LAI)	RGPGRAFVTI	Vaccine	mouse (H-2D^d)	Horner2001
	Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Gag, gp120 *Adjuvant:* CpG immunostimulatory sequence (ISS) **Epitope name** P18. • Immunostimulatory sequences (ISS), also known as CpG motifs, stimulate innate immunity and enhance vaccine-specific immune responses. • Intranasal immunization (i.n.) of BALB/c mice was more effective than intradermal (i.d.), and immunization with a gp120-ISS conjugate was more potent than immunizing with gp120 and separate ISS molecule – increased IgG1, IgG2a, IFN-gamma, MIP1-alpha and MIP1-beta production was observed, and only i.n. immunization gave IgA responses. • The highest mucosal CTL activity in both the Lamina Propria and the Peyer's Patch was observed following intranasal delivery with the gp120/ISS conjugate. • Cytokine, chemokine and CTL responses following gp120/ISS conjugate vaccination were CD4+ T-cell independent; gp120 specific antibodies were dependent on helper T cells.				
gp160 (311–320)	gp160 (V3) (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2D^d)	Takahashi2002
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** acute infection. **Epitope name** I10. • During acute infection, high doses of virus result in "clonal exhaustion", a depletion of antigen specific T-cells. • Recently stimulated CTL from BALB/c mice vaccinated with gp160-vaccinia showed a dose- and time-dependent induction of apoptosis when stimulated with antigenic peptide or H-2Dd/peptide tetramers. • Restimulated CTL showed an upregulation of CD3-chain phosphorylation in comparison to cells stimulated with target cells, indicative of TCR-mediated apoptosis. Furthermore, apoptosis was inhibited by cyclosporin A and U0126, a mitogen activated kinase inhibitor specific for the ERK1/ERK2 MAPK kinase pathway, and a caspase 3 inhibitor.				
gp160 (311–320)	gp160 (V3) (MN)	IGPGRAFYAT	Vaccine	mouse (H-2D^d)	Takahashi2002
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** acute infection. **Epitope name** MNT10. • During acute infection, high doses of virus result in "clonal exhaustion", a depletion of antigen specific T-cells. • Recently stimulated CTL from BALB/c mice vaccinated with gp160-vaccinia showed a dose- and time-dependent induction of apoptosis when stimulated with antigenic peptide or H-2Dd/peptide tetramers. • Restimulated CTL showed an upregulation of CD3-chain phosphorylation in comparison to cells stimulated with target cells, indicative of TCR-mediated apoptosis. Furthermore, apoptosis was inhibited by cyclosporin A and U0126, a mitogen activated kinase inhibitor specific for the ERK1/ERK2 MAPK kinase pathway, and a caspase 3 inhibitor.				
gp160 (311–320)	gp160 (V3) (HIV-IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2Dd)	Oh2003a
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* IL-15, IL-2 **Epitope name** P18-I10. **Assay type** cytokine production, Tetramer binding, Chromium-release assay. **Donor HLA** H-2d.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• IL-2 and IL-15 in vaccinia constructs were given with an HIV gp160 vaccinia vaccine to BALB/c mice. Both IL-2 and IL-15 induced strong and long-lasting antibody responses. Short-term CTL responses against HIV gp120 were enhanced by IL-2, but IL-15 enhanced both immediate CD8+ T cell responses and CD8+ T memory cells.				
gp160 (311–320)	gp160 (IIIB)	RGPGRAFVTI	Vaccine	mouse (H-2Dd)	Oh2003b
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* V3 *Adjuvant:* B7, ICAM, LFA-3 **Epitope name** P18-I10. **Assay type** proliferation, CD8 T-cell Elispot - IFNγ, Tetramer binding. **Donor HLA** H-2d. • BALB/c mice were vaccinated with T-cell depleted splenocytes pulsed with peptides given in combination with immunostimulatory molecules B7, ICAM or LFA expressed in a recombinant pox virus. Increasing antigen gave an increased frequency of CD8+ T-cells, but the co-stimulatory molecules increased the avidity of the response.				
gp160 (311–320)	(89.6)	IGPGRAFYAR	Vaccine	mouse (H-2Dd)	Sailaja2003
	Vaccine *Vector/Type:* DNA *HIV component:* gp120 *Adjuvant:* Flex, a dendric cell growth factor **Keywords** dendritic cells. **Assay type** Intracellular cytokine staining. **Donor HLA** H-2d. • BALB/c mice were given a DNA vaccine that contained gp120 DNA covalently attached to the extracellular domain of the Fms-like tyrosine kinase receptor-3 ligand (FLex), a dendritic cell growth factor. • Mice vaccinated i.m. with the FLex:gp120 chimeric gene gave a DC expansion similar to native Flex protein. • gp120-specific stable CD8+ T-cell responses lasted 114 days after a prime/boost, and were observed in the presence and absence of Flex-DNA-induced dendritic cell (DC) expansion; strong Ab responses required DC expansion.				
gp160 (311–320)	gp120 (V3 loop)	RGPGRAFVTI	Vaccine	mouse (H-2Dd)	Wang2003
	Vaccine *Vector/Type:* herpes simplex virus type-1 (HSV-1) amplicon *HIV component:* gp120 **Keywords** kinetics, memory cells. **Assay type** Tetramer binding, JAM cytotoxicity assay. **Donor HLA** H-2d. • Prime-boost combinations of gp120 combined with herpes simplex virus type-1 (HSV-1) amplicon particles, or gp120 in naked amplicon plasmid DNA, were compared in BLAB/c mice. Plasmid prime with particle boosts gave the strong primary (2 weeks) and memory responses (4 months). • CD8+ T-cells reached their peak 8-28 days after the initial amplicon delivery.				
gp160 (311–320)	gp160 (318–327 IIIB)	RGPGRAFVTI	Vaccine	mouse (L^d)	Tobery1997
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* Env, Nef • An HIV-1 Env vaccine was targeted for rapid cytoplasmic degradation. • The rapidly degraded form rapidly stimulated CTL to this peptide, faster than the normal vaccinia-env. • The rapidly degraded form also stimulated greater specific CTL lysis and higher CTLp frequencies than normal Env. • Similar results were obtained for a Nef protein designed for rapid degradation.				
gp160 (312–320)	gp120 (V3 loop) (IIIB)	GPGRAFVTI	Vaccine	mouse ($H\text{-}2^d$)	Vázquez Blomquist2002
	Vaccine *Vector/Type:* fowlpoxvirus *Strain:* B clade BRVA, B clade IIIB, B clade JY1, B clade LR150, B clade MN, B clade RF *HIV component:* V3 **Keywords** vaccine-specific epitope characteristics, immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• BALB/c mice were vaccinated with a polyepitope V3 vaccine in a fowlpoxvirus carrying concatonated 15 mer sections of the V3 loops of HIV-1 isolates LR150, JY1, RF , MN, BRVA and IIIB with 5-aa linkers between, fused to the N-term of p64K protein from Neisseria meningitidis. • Intraperitoneal immunization elicited the strongest V3-specific IFN-gamma response in splenocytes, compared to intravenous and subcutaneous immunization. Intraperitoneal immunization conferred protection in a recombinant vaccinia virus challenge model. • The immunodominant response was directed against the IIIB peptide (the IIIB immunizing peptide was SIRIQRGPGRAFVTI, the peptide used to probe the response by Elispot was GPGRAFVTI). • Low CTL responses were also detected to the LR150 (SRGIRIGPGRAILAT) and RF (RKRITMGPGRVYYTT) peptides, no responses were detected to the JY1 (RQSTPIGLGQALYTT), BRVA (RKSITKGPGRVIYAT), or MN (RKRIHIGPGRAFYTT) peptides.			
gp160 (314–322)	gp120 (314–322) • Study of peptide binding to HLA-B27.	GRAFVTIGK	Peptide-HLA interaction	human (B27)	Jardetzky1991
gp160 (337–361)	gp120 (337–368 LAI) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160 • CD4+ CTL clones were obtained from an HIV-1 vaccinia-env vaccinee.	KWNNTLKQIDSKLREQFGN-NKTIIF	Vaccine	human (CD4+ CTL)	Johnson1994a
gp160 (339–354)	gp120 (339–361 LAI) **Vaccine** *Vector/Type:* vaccinia *HIV component:* gp160 • CD4+ CTL isolated from LAI IIIB gp160 vaccinees.	NNTLKQIDSKLREQFG	Vaccine	human (CD4+ CTL)	Johnson1994b
gp160 (340–348)	gp120 (346–354 CM243 subtype CRF01) **Keywords** HIV exposed persistently seronegative (HEPS). **Epitope name** E340-348. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in HIV+ control study subject 053 who carried HLA-A11.	RVLKQVTEK	HIV-1 infection	human (A11)	Sriwanthana2001
gp160 (340–348)	gp120 (346–354 CM243 subtype CRF01) **Keywords** inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it. • This epitope was not conserved in other subtypes, and exact matches were rare.	RVLKQVTEK	HIV-1 infection	human (A11)	Bond2001
gp160 (340–349)	gp120 (W6.ID) **Vaccine** *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 **Keywords** immunodominance.	NTLKQIVIKL	Vaccine	chimpanzee (Patr-B*14)	Balla-Jhagjhoorsingh1999a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• An HIV-1 rgp120 vaccine induced strong humoral and cellular immune response in sibling chimpanzees, but only one of the two made a detectable CTL response to this Patr-B*14 restricted immunodominant epitope.				
gp160 (369–375)	gp120 (374–380 BRU)	PEIVTHS	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions.				
gp160 (375–383)	gp120 (379–387 LAI)	SFNCGGEFF	HIV-1 infection	human (B*1516)	Frahm2004
	• C. Brander notes this is a B*1516 epitope.				
gp160 (375–383)	gp120 (375–383 IIIB)	SFTCGGEFF	HIV-1 infection	human (B15)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • An additional variant that gave a positive, though reduced, CTL response: SSTCGGEFF and SFTCGGGFF. • SFTCGGGVF was an escape mutant.				
gp160 (375–383)	gp120 (375–383 SF2)	SFNCGGEFF	HIV-1 infection	human (B15)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B15+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/1 group 3.				
gp160 (375–383)	gp120 (375–383 IIIB)	SFNCGGEFF	HIV-1 infection	human (B63, B15)	Wilson1997a
	• This is the optimal peptide for two CTL clones that recognize this epitope in the context of two different HLA molecules, Cw4 and B15. • Predominant form in proviral DNA of the individual with B15 restricted CTL was SFTCGGEFF and this was recognized. • Recognition of a minor autologous variant (SFNCRGEFF) from the B15 donor was greatly reduced.				
gp160 (375–383)	gp120 (376–383 PV22)	SFNCGGEFF	HIV-1 infection	human (C*0401)	Frahm2004
	• C. Brander notes this is a C*0401 epitope.				
gp160 (375–383)	gp120	SFNCGGEFF	HIV-1 infection	human (Cw*0401, Cw*0407)	Bird2002
	Keywords HIV exposed persistently seronegative (HEPS), cross-presentation by different HLA. • 4/123 (2 HIV-1 positive, 2 HEPS) Kenyan female sex workers carried the novel allele HLA Cw*0407. • HLA Cw*0407 did not differ from Cw*0401 in the region associated with the binding pocket, and Cw*0407 was shown to cross-present a previously defined Cw*0401 epitope, SFNCGGEFF (gp120).				
gp160 (375–383)	gp120 (376–383 PV22)	SFNCGGEFF	HIV-1 infection	human (Cw4)	Johnson1993
	• Conserved epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (375–383)	gp120 (376–383 PV22)	SFNCGGEFF	HIV-1 infection	human (Cw4)	Wolinsky1996
	• Longitudinal study of epitope variation *in vivo*.				
gp160 (375–383)	gp120 (376–383)	SFNCGGEFF	HIV-1 infection, HIV-1 exposed seronegative	human (Cw4)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-Cw4 women, 1/2 HEPS and 10/11 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in 6 of the 10/11 responsive HIV-1 infected women, and not in the HEPS case.				
gp160 (376–383)	gp120	FNCGGEFF		human (Cw4)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 sequence: TNCRGEFL – no cross-reactivity [Johnson1993]				
gp160 (376–384)	gp120 (376–384 IIIB)	FNCGGEFFY	HIV-1 infection	human (A29)	Wilson1997a
	• This is the optimal peptide for two CTL clones derived from two different donors. • FNCRGEFFY and FNCRGGFFY are major and minor autologous variants in one of the donors, and showed reduced or no stimulatory activity for CTL from the host. • The IIIB form and the form FNCAGEFFY were present in the other donor, and the CTL line had reduced activity with the FNCAGEFFY form relative to the index peptide.				
gp160 (376–384)	gp120 (376–384 IIIB)	PNCGGEFFY	HIV-1 infection	human (A29)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • PNCRGEFFY was an escape variant.				
gp160 (376–384)	gp120 (376–384 LAI)	FNCGGEFFY	HIV-1 infection	human (A29)	Mollet2000
	Keywords HAART. **Epitope name** E2. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (376–384)	gp120	FNCGGEFFY	HIV-1 infection	human (A29)	Kaul2003
	Keywords immunodominance, genital and mucosal immunity. **Assay type** Intracellular cytokine staining. • Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher. • The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).			
gp160 (376–384)	gp120 (376–384)	FNCGGEFFY	HIV-1 infection	human (B8)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** FNC. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • One of the 7/8 study subjects that were HLA B8 recognized this CTL epitope. • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.			
gp160 (376–384)	gp160	FNCGGEFFY	HIV-1 infection	human (B8)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** FNC. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.			
gp160 (376–387)	gp120 (381–392 BRU)	KNCGGEFFYCNS	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions.				
gp160 (377–387)	gp120 (377–387)	NSGGEFFYSNS		human (A2)	Hickling1990
	• Peptides recognized by class I restricted CTL can bind to class II.				
gp160 (383–391)	gp120 (385–393)	FYCNTTQLF	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • FYCNTTQLF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
gp160 (410–429)	gp120 (410–429 PV22)	GSDTITLPCRIKQFINMWQE	in vitro stimulation or selectio	human (CD4+DRA)	Bouhdoud2000
	• CTL were studied through PBMC stimulation *in vitro* by gp120 pulsed autologous monocytes. • Human CD4+ CTL clone (Een217) is an MHC class II HLA-DRA restricted CTL clone that can lyse antigen presenting HLA-DRA-transfected murine L cells – natural variants of the epitope resulted in an anergic response. • Low concentrations of the HXB2-derived variant (GSDTITLPCRIKQIINMWQK) induced T cell anergy – higher concentrations could induce proliferation and cytotoxic activity.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CDC42 (TGDIITLPCRIKQII-NRWQV), Eli (TNTNITLQCRIKQIIKMVAG) and Z3 (CTGNITLPCRIKQIIMNWQE) variants did not induce proliferation, cytotoxic or anergic responses.				
gp160 (416–424)	Env (413–421 SF2)	LPCRIKQII	HIV-1 infection	human (B*5101)	Tomiyama1999
	Keywords inter-clade comparisons, rate of progression.				
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)				
	• 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%				
	• Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed.				
	• Four of the six epitopes were highly conserved among B subtype sequences, LPCRIKQII is not conserved.				
gp160 (416–424)	gp160 (416–424 LAI)	LPCRIKQII		human (B*5101)	Frahm2004
	• C. Brander notes this is a B*5101 epitope.				
gp160 (416–424)	gp120 (378–385)	LPCRIKQII	HIV-1 infection, HIV-1 exposed seronegative	human (B51)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS).				
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (416–429)	gp120 (410–429 H3DCG)	LPCRIKQFINMWQE	HIV-1 infection	human (DR4 CD4+)	Siliciano1988
	• CD4+ CTL restricted by class II HLA-DR4, targets primed by CD4 mediated uptake of gp120.				
gp160 (416–435)	gp120 (421–440 LAI)	LPCRIKQFINMWQEVGKAMY	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions.				
gp160 (419–427)	gp120 (424–432 HXB2)	RIKQIINMW		human (A*3201)	Harrer1996b
	• C. Brander notes that this is an A*3201 epitope in the 1999 database.				
gp160 (419–427)	gp120 (419–427 HXB2)	RIKQIINMW		human (A*3201)	Frahm2004
	• C. Brander notes this is an A*3201 epitope.				
gp160 (419–427)	gp120 (419–427)	RIKQIINMW?	HIV-1 infection	human (A29, A32)	Betts2000
	Keywords immunodominance.				
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant.				
	• 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.				
	• 1/11 of the A2+ individuals was A29 and responded to RIKQIINMW, and another responder was A32 and these are thought to be presenting molecules.				
	• The sequence is unclear – Betts calls both peptide 30 and peptide 32 gp120 419–427 and the peptide sequences are not provided.				
gp160 (419–427)	gp120 (424–432 LAI)	RIKQFINMW	HIV-1 infection	human (A32)	Ray1998
	• Autologous virus was used to detect CTL in two individuals, and in both cases strain-specific autologous CTL were found.				
	• The autologous epitope sequence was RIKQIINMW, MN and RF were KIKQFINMW and RIKQFVNMW respectively, and all were reactive with CTL clones.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (419–427)	gp120 (420–428)	RIKQIINMW	HIV-1 infection	human (A32)	Ferris1999
	• This epitope is processed by a TAP1/2 dependent mechanism.				
gp160 (419–427)	gp120	RIKQIINMW	HIV-1 infection	human (A32)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** A32-RW10(gp120). **Donor HLA** A32,A?,B44,B?; A30,A32,B18,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient B displayed the greatest response to epitope B44-AW11(p24) and also responded to A32-PW10(RT) in both PB and LN samples, while a third response against epitope A32-RW10(gp120) was only detected in the LN sample. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).			
gp160 (421–435)	gp120 (421–440 LAI)	KQFINMWQEVGKAMY	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV.				
gp160 (421–436)	gp120 (MN)	KQIINMWQEVGKAMYA	HIV-1 infection	chimpanzee	Lubeck1997
	• Epitope-specific CTL detected in chimpanzees immunized with adenovirus-HIV-1 MN gp160 recombinant. • CTL response may account for protection against subsequent HIV-1 SF2 challenge in a chimpanzee lacking neutralizing antibodies. • Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human (A2)	Cease1987
	• Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	mouse (H-$2^{a, b, f}$)	Shirai1992
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 • In a murine system multiple class I molecules can present to CTL.				
gp160 (432–451)	gp120 (439–458 IIIB)	KAMYAPPISGQIRCSSNITG	Vaccine	macaque	Wagner1998b
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* CD4BS, Gag, gp120, V3				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock. • CTL specific for this epitope could be found both before and after SHIV challenge.				
gp160 (434–443)	gp120 (431–440)	MYAPPIGGQI	Vaccine	mouse (H-2K^{d})	Duarte1996
	Vaccine *Vector/Type:* peptide • Tolerization of CTL response with continued administration of soluble peptide.				
gp160 (435–443)	Env (89.6)	YAPPISGQI	Vaccine	macaque	Barouch2000, Shen2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade 89.6, SIV *HIV component:* Env, Gag *Adjuvant:* IL2/Ig **Epitope name** p41A. • Different HIV strains were used for different regions: SIVmac239 Gag and HIV-1 89.6P Env • Monkeys that received the DNA vaccines augmented with IL-2/Ig were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, stable CD4+ T-cell counts, preserved virus-specific CD4+ T-cell responses, low to undetectable viral loads, and no evidence of disease or mortality by day 140 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and were half were dead by day 140. • IL2/Ig consisting of interleukin-2 (IL-2) for immune stimulation, and the Fc portion of immunoglobulin G (IgG) for stability, was delivered either as protein or as DNA – both enhance the CTL response to vaccination, DNA IL2/Ig giving the most intense response. • Responses to a dominant Mamu A*01 gag epitope SIV Gag p11C (CTPYDINQM) and a subdominant epitope HIV-1 Env p41A (YAPPISGQI) were tracked and had good durability prior to challenge, and the higher the prechallenge peak p11C CTL response, the lower the post-challenge viral load. • No NAb responses were detected in the vaccinated monkeys prior to challenge, and comparable peak NAb titers developed in vaccinated monkeys and control monkeys with preserved CD4+ T-cells. • Shen *et al.* 2000 is an accompanying commentary.				
gp160 (435–443)	Env (89.6)	YAPPISGQI	Vaccine	macaque	Barouch2001b
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade 89.6, SIV *HIV component:* Env, Gag-Pol *Adjuvant:* IL2/Ig **Keywords** immunodominance. **Epitope name** p41A. • Different HIV strains were used for different regions: SIVmac239 Gag/Pol and HIV-1 89.6P Env • Four monkeys were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL to the immunodominant SIV gag epitope in 4/4 animals, and 1/4 made a response to the HIV Env epitope YAPPISGQI, as determined by tetramer staining and chromium release assays. • The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge – monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168.				
gp160 (435–443)		YAPPISGQI	SHIV infection	macaque (Mamu A*01)	Egan1999
	• SHIV-infected rhesus macaques have high frequencies of response to the SIVmac epitope gag p11C,C-M (CTPYDINQM) but only a fraction of A*01 monkeys tested have responses to SIVmac pol epitope STPPLVRLV and HIV-1 env epitope YAPPISGQI.				
gp160 (435–443)	gp41 (89.6)	YAPPISGQI	SHIV infection, Vaccine	macaque (Mamu A*01)	Barouch2001a
	Vaccine *Vector/Type:* DNA, modified vaccinia Ankara (MVA) *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Env, Gag *Adjuvant:* IL2/Ig **Keywords** immunodominance. **Epitope name** p41A.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mamu-A*01+ rhesus monkeys infected with SHIV-89.6 and SHIV-HXBc2 make immunodominant responses to SIV Gag p11C epitope (CTPYDINQM) and a subdominant response to HIV-1 Env p41A epitope (YAPPISGQI) • The binding affinities are the same for the two Mamu A*01 epitopes, so that is not what dictates the dominance. • Monkeys vaccinated with MVA vectors carrying SIV gag/pol and HIV-1 env showed the same p11C epitope dominance and p41A epitope subdominance, but co-dominance was observed and the response to p41A increased when DNA vaccination was done using the SIV and HIV genes under CMV promotor control with IL2-IG adjuvant.				
gp160 (444–453)	Env	RCSSNITGLL		human (B56)	De Groot2001
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conservered regions of HIV that might serve as epitopes. • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 of the predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay. • RCSSNITGLL was newly defined as an epitope in this study, and was shown to stimulate an ELISPOT response, despite not detectably binding to HLA-B7.				
gp160 (489–508)	Env (496–506 BH10, LAI)	VKIEPLGVAPTKAKRRVVQR	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is VAPTKAKRRVV) has similarity with the mast/stem cell growth factor receptor precursor fragment VVPTKADKRRSV.				
gp160 (489–508)	Env (497–512 BH10, LAI)	VKIEPLGVAPTKAKRRVVQR	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is APTKAKRRVVQREKRA) has similarity with the human interferon-related IFRD2 (PC4-B) protein fragment ARTKARSRVRDKRA.				
gp160 (489–508)	gp120 (494–513 BRU)	VKIEPLGVAPTKAKRRVVQR	HIV-1 infection	human (A2)	Dadaglio1991
	• Defined through blocking CTL activity, and Env deletions.				
gp160 (519–543)	gp41 (519–543)	FLGFLGAAGSTMGAASLTL-TVQARC	HIV-1 infection	human (Cw7)	Nehete1998a
	• Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one. • HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B. • HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing.				
gp160 (529–537)	Env (529–)	TMGAASITL	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* gp160 *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Env529. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was an intermediate A2 binder that did not induce CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 5/17 HIV+ HLA-A2 subjects.				
gp160 (552–571)	Env (552–571)	QSNLLRAIEAQQHMLQLTVW	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human	Wilson1996
	Keywords responses in children, mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study. • RAIDAQQHL and RVIEAQQHL, naturally occurring variants, were found in mother and are recognized.				
gp160 (557–565)	gp41 (557–565)	RAIEAQQHL	HIV-1 infection	human	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A*0201, A32, B60, B78, and responded to RAIEAQQHL, previously noted to be B51.				
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human	Wilson1999a
	Keywords mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • This epitope was invariant in both the mother and her infant.				
gp160 (557–565)	Env (555–567 BH10, LAI)	RAIEAQQHL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LLRAIEAQQHLL) has similarity with human MHC class II regulatory factor RFX1 fragment LLRLMEDQQHMA.				
gp160 (557–565)	gp41 (557–665)	RAIEAQQWQ	HIV-1 infection	human (B*5101)	Samri2000
	Keywords HAART, escape. **Epitope name** E3. • The epitope was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition.				
gp160 (557–565)	gp41 (557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human (B51)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB. • KAIEAQQHL, a variant found in HIV-1 NY5CG, was also recognized. • RAIEAQQHM, a variant found in HIV-1 JRCSF, was also recognized. • RAIDAQQHL, a variant found in HIV-1 ETR, was also recognized. • RAIKAQQHL, a variant found in HIV-1 CDC42, was also recognized.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (557–565)	gp41 (557–565)	RAIEAQQHL	HIV-1 infection	human (B51)	Ferris1999
	• This epitope can be processed by a TAP1/2 dependent mechanism.				
gp160 (557–565)	gp41 (557–565)	RAIEAQQWQ	HIV-1 infection	human (B51)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** RAI. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B51+				
gp160 (557–565)	gp41 (47–55)	RAIEAQQHL	HIV-1 infection	human (B51)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
gp160 (557–565)	gp41 (557–565 LAI)	RAIEAQQHL	HIV-1 infection	human (B51)	Mollet2000
	Keywords HAART. **Epitope name** E3. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
gp160 (557–565)	Env (gp160) (557–565)	RAIEAQQHL	HIV-1 infection	human (Cw*0304)	Currier2002a
	Keywords inter-clade comparisons. • Cross-reactive responses were found in PBMC isolated from individuals infected with either B or CRF01_AE clade viruses, as determined by Elispot assays of target cells expressing recombinant vaccinia viruses expressing HIV-1 gag, env, nef and pol from many clades. • CTL from subject US101, infected with a clade B virus, displayed broad cross-reactivity to HIV-1 clade A, B, C, D, CRF01_AE, F G, recognized this epitope. Clade B and C had a L->M change in the C-term position that was tolerated. The H clade Env was not cross-reactive, and had the sequence RAIAARQHM.				
gp160 (557–565)	gp41 (46–54)	RAIEAQQHL		human (Cw*0304)	Frahm2004
gp160 (557–565)	gp41 (46–54)	RAIEAQQHL		human (Cw*15)	Frahm2004
gp160 (565–573)	Env (565–)	LLQLTVWGI	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Env *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Env565. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CD8+ T-cell IFN gamma responses in mice, but responses to the peptide were not detected in 17 HIV+ HLA-A2 subjects.				
gp160 (565–573)	Env (731–739)	LLQLTVWGI	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind four of the five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802).				
gp160 (570–589)	gp41 (571–590 LAI)	VWGIKQLQARILAVERYLKD	Vaccine	human (CD4+ CTL(DR-1))	Kent1997a
	Vaccine *Vector/Type:* vaccinia prime with gp160 boost *Strain:* B clade LAI *HIV component:* gp160 • VWGIKQLQARILAVERYLKD, present in HIV-1 LAI, was the immunizing strain. • VWGIKQLQARVLAVERYLKD, present in HIV-1 MN, was also recognized. • VWGIKQPQARVLAVERYLRD was the form carried by the autologous strain that infected the vaccinee. • Lysis of the target cells by CD4+ CTL was inhibited with the addition of the peptide representing the autologous strain. • The infecting virus epitope also antagonized the proliferative functions of the CD4+ CTL clone. • The behavior of the autologous strain presents a possible mechanism for vaccine failure since the infecting virus not only escapes CTL activity, but inhibits the ability of CTL to recognize other variants.				
gp160 (572–590)	gp41 (572–590 BRU)	GIKQLQARILAVERYLKDQ	Vaccine	human (DPw4.2)	Hammond1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* gp160 • CD4+ CTL.				
gp160 (575–599)	gp41 (575–599 IIIB)	QLQARILAVERYLKDQQLL-GIWGCS	HIV-1 infection	human (B14)	Jassoy1992
	• Epitope recognized by CTL clone derived from CSF.				
gp160 (583–592)	gp41 (583–592 PV22)	VERYLKDQQL	HIV-1 infection	human (B14)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human	Price1995
	• Study of cytokines released by HIV-1 specific activated CTL.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human	Borrow1994
	• Three out of five patients with HIV-1 symptomatic infection controlled their viral infection well and mounted an early, strong HIV-1 specific MHC restricted CTL response. • One of the three, study subject BORI, specifically recognized this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (584–592)	gp41 (584–592 HXB2) **Keywords** HAART. **Epitope name** E4. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.	ERYLKDQQL	HIV-1 infection	human (A32, B14)	Mollet2000
gp160 (584–592)	gp41 **Keywords** HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.	ERYLRDQQL	HIV-1 infection	human (B*14)	Kaul2002
gp160 (584–592)	gp41 (584–592 PV22) • C. Brander notes this is a B*1402 epitope.	ERYLKDQQL	HIV-1 infection	human (B*1402)	Frahm2004
gp160 (584–592)	gp41 • CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules.	ERYLKDQQL	HIV-1 infection	human (B14)	Wagner1998a
gp160 (584–592)	gp41 (584–592) **Keywords** HAART. • Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV *in vivo* activated specific CTL such that by day 260 CTL activities were undetectable. • ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant. • Sporadic breakthrough in viremia resulted in increases in CTLp. • Peptide-tetramer staining demonstrated that declining levels of *in vivo*-activated CTL were associated with a decrease in expression of CD38. • Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load.	ERYLKDQQL	HIV-1 infection	human (B14)	Kalams1999b
gp160 (584–592)	gp41 (591–599 SF2) • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A3, -A32, -B7, -B14.	ERYLKDQQL	HIV-1 infection	human (B14)	Lieberman1997a
gp160 (584–592)	gp41 (591–599 SF2) **Keywords** inter-clade comparisons. • The consensus sequence for clades B, C, and D is ERYLKDQQL. • The consensus sequence for clade A is ERYLRDQQL and it is equally reactive.	ERYLKDQQL	HIV-1 infection	human (B14)	Cao1997a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The consensus sequence for clade E is ERYLKDQKF and it is not reactive.				
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 exposed seronegative	human (B14)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A and D subtype consensus are identical to the B clade epitope, ERyLkDQQL.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Sipsas1997
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Yang1996
	• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL. • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones. • The distinction was thought to be due to lower expression of RT relative to Env and Gag. • CTL can lyse infected cells early after infection, possibly prior to viral production.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Yang1997a
	Assay type CTL suppression of replication. • CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*. • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation. • CTL suppress HIV replication more efficiently in HLA-matched cells.				
gp160 (584–592)	gp41 (584–592 PV22)	ERYLKDQQL	HIV-1 infection	human (B14)	Johnson1992
	• Two overlapping CTL epitopes were mapped with different HLA restriction (also see YLKDQQLL HLA-B8)				
gp160 (584–592)	gp41 (584–592 PV22)	ERYLKDQQL	HIV-1 infection	human (B14)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.				
gp160 (584–592)	gp41 (584–592 HXB2)	ERYLKDQQL	HIV-1 infection	human (B14)	Kalams1994, Kalams1996
	• Longitudinal study of T cell receptor usage in a single individual. • Persistence of oligoclonal response to this epitope for over 5 years.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	Peptide-HLA interaction	human (B14)	DiBrino1994a
	• Epitope studied in the context of HLA-B14 binding.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Hammond1995
	• This peptide can be processed for HLA-B14 presentation in a TAP-1/2 independent pathway.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Kalams1996
	• CTL response to this epitope was studied in 5 HLA-B14 positive persons. • CTL responses were detected in all five, and CTL clones were isolated from 4/5. • A diverse repertoire of TCRs recognized this epitope, with similar fine specificities. • 3/5 subjects showed no variation in viral sequence, 2/5 had a dominant variant that resulted in poor recognition, ERYLQDQQL. • A minor CTL response specific for the ERYLQDQQL could be detected by two individuals, but the major CTL response was to the ERYLKDQQL form even when it was the minority form.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Some single amino acid substitutions were well tolerated by most of the CTL clones tested, but others, particularly in the center three amino acid positions, abrogated peptide stimulatory activity.				
gp160 (584–592)	gp120 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Ferris1999, Hammond1995
	• This epitope is processed by both TAP1/2 dependent and independent mechanisms.				
gp160 (584–592)	gp41	ERYLKDQQL		human (B14)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective. • HIV-2 sequence: EKYLQDQAR – no cross-reactivity [Johnson1992]				
gp160 (584–592)	gp41 (SF2)	ERYLKDQQL	HIV-1 infection	human (B14)	Goulder2001a
	Keywords acute infection. **Epitope name** EL9. • Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia. • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation. • Recognized by two A*0201-positive chronically infected subjects.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Islam2001
	Keywords HAART, TCR usage. **Epitope name** 588K. • Transcript frequencies of four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL,and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL. • CTL clone M21 uses the Vβ 4, CDR3 VKDGA, Jβ 1.2 TCR beta gene, and clone E15 uses the Vβ 4, CDR3 VEDWGGAS Jβ 2.1 TCR beta gene, and D87 uses Vβ8, ALNRVD, Jβ2.1. • Responses were stable even through HAART with undetectable viral loads but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time.				
gp160 (584–592)	gp41 (589–597 SF2)	ERYLKDQQL	HIV-1 infection	human (B14)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3.				
gp160 (584–592)	gp41 (589–597)	ERYLRDQQL	HIV-1 infection, HIV-1 exposed seronegative	human (B14)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (584–592)	gp41 (JRCSF)	ERYLKDQQL	HIV-1 infection	human (B14)	Severino2000
	• Primary HLA-B14+ CD4+ CD3+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the B14-restricted CTL clone 15160/D75 specific for ERYLKDQQL, and viral inhibition was MHC-restricted. • Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL. • DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture.				
gp160 (584–592)	gp41 (SF2)	ERYLKQQL	HIV-1 infection	human (B14)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
gp160 (584–592)	Env (589–597)	ERYLKDQQL	HIV-1 infection	human (B14)	Guillon2002
	Keywords early-expressed proteins, kinetics. • An early-expressed Nef protein was modified to contain Env and Pol epitopes to enable the study the effect of expression kinetics on CTL mediated suppression of replication. The "EpiNef" construct was inserted into a recombinant vaccinia virus which was used to infect a target cell line; the target cells were lysed by CTL clones specific for the Env and Pol epitopes indicating that they were properly processed.				
gp160 (584–592)	gp41 (584–592)	ERYLKDQQL	HIV-1 infection	human (B14)	Yang2002
	Keywords class I down-regulation by Nef. • Nef down-modulates class I protein expression, and this study demonstrates directly that Nef-deleted HIV-1 NL-43 can be more effectively killed *in vitro* than NL-43 with an intact Nef. The effect was shown to be specific for class I presentation of epitopes, and unlike Nef, deleting Vpr did not alter CTL susceptibility of NL43 infected cells. The CTL clone 15160D75, specific for the class I B14 presented epitope ERYLKDQQL, was one of four used in this study.				
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 infection	human (B14)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** B14-EL9(gp41). **Donor HLA** A32,A?,B7,B14. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (584–592)	gp41	ERYLKDQQL	HIV-1 infection, Vaccine	human (B14)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].			
gp160 (584–592)	gp41 (subtype B)	ERYLKDQQL	HIV-1 exposed seronegative	human (B14, B*1402)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among B and D clade viruses. • The Clade A version of the epitope is ERYLRDQQL.				
gp160 (584–594)	gp41 (584–594)	ERYLKDQQLLG	HIV-1 infection	human	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A1, B8, B14, Cw7, Cw8. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
gp160 (585–592)	gp41 (584–591 SF2)	RYLRDQQL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 2/4 HIV-1+ people tested. • RYLRDQQL bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
gp160 (585–592)	gp41 (590–597 LAI)	RYLKDQQL	HIV-1 infection	human (B27)	Shankar1996

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (585–593)	gp41 (74–82)	RYLKDQQLL	HIV-1 infection	human (A*23)	Frahm2004
gp160 (585–593)	gp41 (585–593)	RYLKDQQLL	HIV-1 infection	human (A*2301)	Cao2003

Keywords acute infection, early-expressed proteins.
Assay type CD8 T-cell Elispot - IFNγ.
Donor HLA A*2301, B*3501, B*1503 (B72), Cw2, Cw7.

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

gp160 (585–593)	gp41 (584–591 SF2)	RYLRDQQLL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997

- Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402.
- This peptide induced CTL in 4/4 HIV-1+ people tested.
- RYLRDQQLL bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.

gp160 (585–593)	gp41 (591–598 LAI)	RYLKDQQLL		human (A*2402)	Frahm2004

- C. Brander notes this is an A*2402 epitope.

gp160 (585–593)	gp41	RYLKDQQLL	HIV-1 infection	human (A24)	Altfeld2002

Keywords HAART, supervised treatment interruptions (STI).
Epitope name A24-RL9(gp41).
Donor HLA A24,A?,B7,B27.

- Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles.
- 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN.
- 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN.
- Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses.
- Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).

gp160 (585–593)	Env	RYLKDQQLL	HIV-1 infection	human (A24)	Montefiori2003

Keywords acute infection, early treatment.
Epitope name RW8.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type CD8 T-cell Elispot - IFNγ. **Donor HLA** A2, A24, B38, B60, Cw2, Cw12. • HIV-1+ patient AC10 underwent early HAART treatment, which was discontiuned 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.				
gp160 (585–595)	gp41 (584–591 SF2)	RYLRDQQLLGI	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 4/4 HIV-1+ people tested. • RYLRDQQLLGI bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
gp160 (585–595)	Env (584–594)	RYLRDQQLLGI	Vaccine	human (A*2402)	Kawana-Tachikawa2002
	Vaccine *Vector/Type:* Sendai virus vector system (SeV) **Epitope name** Env584-11. • A Sendai virus vector system (SeV) was developd that expressed HLA-A*2402-restricted class I/peptide complexes; this system could be used to detect responses and has the potential to elicit immune responses. • MHC class I/peptide tetramers could be made using this system that bound to epitope-specific CTLs in PBMCs. • Cells transfection with SeV modified to express A*2402-HIV epitope complexes induced CTL mediated specific cell lysis.				
gp160 (586–593)	gp160	YLRDQQLL	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls, ML887.				
gp160 (586–593)	gp41 (584–591 NL43)	YLKDQQLL	HIV-1 infection	human (A*2402)	Dai1992
	• The lysine (K) is critical for eliciting a HLA-A24 CTL response. • C. Brander notes that this is an A*2402 epitope in the 1999 database, and suggested that the epitope is RYLKQQLL.				
gp160 (586–593)	gp41 (591–598)	YLRDQQLL	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS), immunodominance. • Variants (R)YL(R/K)DQQLL are specific for the A/B clade. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Among HLA-A24 women, 3/4 HEPS and 10/10 HIV-1 infected women recognized this epitope, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only. • The dominant response to this HLA allele was to this epitope in all 3/4 HEPS cases but in only 4 of the 10/10 HIV-1 infected women. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.				
gp160 (586–593)	gp41 (580–587 CM243 subtype CRF01) **Keywords** inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • The only HLA-A24 FSW tested did not recognized the E clade version of this epitope RYLKDQKLL, which differs from the previously defined B clade version by one amino acid, YLKDQQLL, with an additional amino acid added on.	YLKDQQLL	HIV-1 infection	human (A24)	Bond2001
gp160 (586–593)	gp41 (subtype A) **Vaccine** *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].	YLKDQQLL	HIV-1 infection, Vaccine	human, macaque (A24, B8)	Hanke2000, Wee2002
gp160 (586–593)	gp41 (586–593 LAI) **Keywords** HAART. **Epitope name** E1. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.	YLKDQQLL	HIV-1 infection	human (A24, B8)	Mollet2000
gp160 (586–593)	gp41 (586–593) • C. Brander notes this is a B*0801 epitope.	YLKDQQLL	HIV-1 infection	human (B*0801)	Frahm2004
gp160 (586–593)	gp41 (586–593) • Two overlapping CTL epitopes were mapped with different HLA restriction (also see ERYLKDQQL HLA-B14)	YLKDQQLL	HIV-1 infection	human (B8)	Johnson1992

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	Peptide-HLA interaction	human (B8)	Sutton1993
	• Predicted epitope based on B8-binding motifs, from larger peptide QLQARILAVERYLKDQQLLGIWGCS.				
gp160 (586–593)	gp41 (76–83)	YLKDQQLL		human (B8)	Goulder1997g
	• Included in a study of the B8 binding motif.				
gp160 (586–593)	gp41	YLKDQQLL		human (B8)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive. • HIV-2 sequence: YLQDQARL – no cross-reactivity [Johnson1992]				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	HIV-1 infection, HIV-1 exposed seronegative	human (B8)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (586–593)	gp41 (586–593)	YLKDQQLL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
gp160 (586–598)	gp41 (586–598)	YLRDQQLLGIWGC	HIV-1 infection	human (Cw7)	Nehete1998a
	• Three long-term non-progressors and one asymptomatic HIV+ individual were studied and found to have HLA class I C-restricted CD8+ Env-specific CTLs – Cw7 specific CTL were found against three peptides, including this one. • HLA-C antigens are expressed on lymphoid cells to a lesser extent, 10% of either HLA-A or HLA-B. • HLA-C confers protection against lysis by natural killer cells and by non-MHC-restricted effector T cells and Cw7 directly governs this resistance to lysis – the authors hypothesize that pathogens that inhibit antigen expression and class I expression may particularly down regulate Cw7, thus triggering non-MHC restricted killing.				
gp160 (594–608)	gp41 (SF2)	GIWGCSGKLICTTAV	HIV-1 infection	human (B17(57))	Carmichael1996
	Epitope name Peptide2. **Assay type** Chromium-release assay. • Cross-reactivity of Env-specific CTL clones from 14 seropositive HIV-1 infected patients was tested using peptides based on 3 B clade variants (MN, IIIB, and RF). The proportion of CTL clones that cross-recognized conserved variants was low. Most CTL clones recognized only one peptide variant, indicating most Env responses are not cross-reactive within the B clade. • This HLA B17(57) epitope was newly identified within gp41 of HIV-1 SF2. SF2 and IIIB have identical sequences within this peptide, but the T-cell clone that recognizes this peptide does not recognize the MN (gFwgcsgklicttTv) or RF (giwgcsgklicttTv) variants of this peptide.				
gp160 (594–608)	gp41	GIWGCSGKLICTTAV	HIV-1 infection	human (B57)	Jin1998b
	• Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction. • Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK.				
gp160 (606–614)	gp41 (605–615 LAI)	TAVPWNASW	Vaccine	human (B*3501)	Frahm2004
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C. Brander notes this is a B*3501 epitope.				
gp160 (606–614)	gp41 (606–614 HXB2)	TAVPWNASW	HIV-1 infection	human (B*3501)	Ferris1996
	Keywords epitope processing.				
	• Natural form of this peptide is not glycosylated, suggesting initial Class I processing may occur in the cytosol.				
gp160 (606–614)	gp41 (605–615 LAI)	TAVPWNASW	Vaccine	human (B35)	Johnson1994b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• Epitope for vaccine induced CD8+ clone.				
gp160 (606–614)	gp41 (606–614 LAI)	TAVPWNASW	Vaccine	human (B35)	Johnson1994a
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• HLA restricted CTL response to epitope in HIV-1 vaccinia-env vaccinees.				
gp160 (606–614)	gp41 (606–614 LAI)	TAVPWNASW	Vaccine	human (B35)	Hammond1995
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				
	• Peptide only processed by a TAP-1/2-dependent pathway.				
gp160 (606–614)	gp41 (606–614)	TAVPWNASW	HIV-1 infection	human (B35)	Ferris1999
	• This epitope is processed by a TAP1/2 dependent mechanism.				
gp160 (606–614)	gp41 (subtype B)	TAVPWNASW	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	Keywords inter-clade comparisons.				
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection.				
	• Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world.				
	• Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes.				
	• This epitope is conserved among A, B and D clade viruses.				
gp160 (606–614)	gp41 (606–614)	TAVPWNASW	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS).				
	• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
gp160 (606–614)	gp41 (606–614)	TAVPWNASW	HIV-1 infection	human (B35)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins.				
	Assay type CD8 T-cell Elispot - IFNγ.				
	Donor HLA A3, A33, B14, B35, Cw*0401, Cw0802.				
	• All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.				
	• All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
gp160 (634–648)	gp41 (641–655 SF2)	EIDNYTNTIYTLLEE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A1, A2, B51, and B57.				
gp160 (678–686)	Env (679–687 subtype B)	WLWYIKIFI	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period. • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual. • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.				
gp160 (680–688)	gp41 (679–687 SF2)	WYIKIFIMI	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • WYIKIFIFMI bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
gp160 (681–689)	Env (681–)	YIKIFIMIV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Env *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Env681. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was a good A2 binder that induced CTL and CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.				
gp160 (685–693)	Env (686–694 subtype B)	FIMIVGGLV	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual. • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses. • ALTERNATIVE EPITOPE: IMIVGGLVGL – no CTL response was shown to the peptides FIMIVGGLV or IMIVGGLVGL.				
gp160 (698–707)	Env (696–706)	VFAVLSIVNR	HIV-1 infection	human (A*3303)	Hossain2001, Takiguchi2000
	• HLA-A33 a very common allele in Asian, with HLA-A*3303 the most common among the Japanese. New A*3303 epitopes were defined to better characterize the immune response in this population. • The anchor motif for HLA*3303 (A, I, L, V, F, Y in position 2 (F and Y bind most strongly), and R (K is also tolerated) in the C-terminal position) was used to define 82 potentially reactive peptides in Env; 37/82 peptides bound to A*3303; 3/37 peptides could induce peptide-specific CTL in bulk PBMC cultures from 1/3 HLA A*3303 positive individuals tested. • CTL clones were isolated that killed target cells in a concentration dependent manner after pulsing with the VFAVLSIVNR peptide, that could also kill cells transfected with env expressed from a vaccinia vector. Bulk cultures were tested from six additional people, and only 1/6 reacted with this peptide, but the peptide is in a highly variable region.				
gp160 (698–707)	gp41 (187–196)	VFAVLSIVNR	HIV-1 infection	human (A*3303)	Frahm2004
gp160 (700–708)	Env (695–705 BH10, LAI)	AVLSVVNRV	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LRIVFAVLSVV) has similarity with the human chemokine-factor 3 fragment LRLVFALVTAV .				
gp160 (700–708)	gp41 (705–714)	AVLSVVNRV	HIV-1 infection	human (A2)	Ferris1999
	• This epitope is processed by a TAP1/2 dependent mechanism.				
gp160 (701–720)	gp41 (701–720 BH10)	VLSIVNRVRQGYSPLSFQTH	HIV-1 infection	human (A32)	Safrit1994a
	• Recognized by CTL derived from acute seroconverter.				
gp160 (702–721)	Env (702–721)	LSIVNRVRQGYSPLSFQTLT	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
gp160 (704–712)	gp160 (704–712 LAI)	IVNRNRQGY		human (A*3002)	Frahm2004, Goulder2001a
	• C. Brander notes this is an A*3002 epitope.				
gp160 (704–712)	gp41	IVNRVRQGY	HIV-1 infection	human (A*3002)	Goulder2001a
	Epitope name IY9 (gp41). • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood. • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean. • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant. • In subject 199 four additional A*3002 epitopes were identified. • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)				
gp160 (742–761)	Env (742–761) **Keywords** inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.	RDRSIRLVSGFLALAWDDLR	HIV-1 infection	human	Novitsky2002
gp160 (747–755)	gp41 (747–755) • Studied in the context of HLA-A2 peptide binding.	RLVNGSLAL	HIV-1 infection	human (A2)	Parker1992
gp160 (747–755)	gp41 (741–749 CM243 subtype CRF01) **Keywords** HIV exposed persistently seronegative (HEPS). **Epitope name** E747-755. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2.	RLVSGFLAL	HIV-1 infection	human (A2)	Sriwanthana2001
gp160 (747–755)	gp41 (741–749 CM243 subtype CRF01) **Keywords** inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 2/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids, RLVNGSLAL. • This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, C, and G.	RLVSGFLAL	HIV-1 infection	human (A2)	Bond2001
gp160 (754–768)	gp41 (SF2) **Epitope name** Peptide78. **Assay type** Chromium-release assay. • Cross-reactivity of Env-specific CTL clones from 14 seropositive HIV-1 infected patients was tested using peptides based on 3 B clade variants (MN, IIIB, and RF). The proportion of CTL clones that cross-recognized conserved variants was low. Most CTL clones recognized only one peptide variant, indicating most Env responses are not cross-reactive within the B clade. • This HLA B22(55) epitope was defined using SF2 peptides. The CTL clone that recognized it did not cross-recognize the MN, IIIB, or RF variants of this peptide.	ALIWERDLRSLCLFSY	HIV-1 infection	human (B22(55))	Carmichael1996

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (754–768)	gp41	ALIWEDLRSLCLFSY	HIV-1 infection	human (B55)	Jin1998b
• Progressive HIV-1 infection and CD4 decline was associated decreased the IL-2-expandable HIV-1 CTL response in 10 asymptomatic HIV-infected patients – this observation may be partially due to a reduction and impaired function of T helper cells, CTL exhaustion and APC dysfunction. • Continued presence of HIV-1 specific memory cells (CTLp) was observed in three patients, one to GIWGCSGKLICTTAV, one to ALIWEDLRSLCLFSY, and one to PIPIHYCAPAGFAILKCNNK.					
gp160 (760–767)	gp41 (760–767)	LRSLFLFS	HIV-1 infection	human (A*2301)	Cao2003
Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*2301, B*3501, B*1503 (B72), Cw2, Cw7. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.					
gp160 (767–775)	gp41 (766–774 SF2)	SYRRLRDLL	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 1/4 HIV-1+ people tested. • SYRRLRDLL bound to A*2402 moderately, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.					
gp160 (767–780)	gp41 (606–614 LAI)	SYHRLRDLLLIVTR	HIV-1 infection	human (A31)	Hammond1995
• Peptide only processed by a TAP-1/2-dependent pathway. • CTL from an acute seroconverter.					
gp160 (769–777)	gp41 (769–777 BH10)	HRLRDLLLI	HIV-1 infection	human	Safrit1994a
• Recognized by CTL derived from acute seroconverter.					
gp160 (770–778)	Env (679–777)	RLRDLLLIV	HIV-1 infection	human (A*0201)	Kmieciak1998a
Keywords binding affinity. • CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL – all have A2 anchor residues. • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*. • Peptides 5.3 and D2 bound to HLA A*0201 with low affinity.					
gp160 (770–780)	gp41 (775–785)	RLRDLLLIVTR	HIV-1 infection	human	Betts2000
Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope that has been previously noted to be HLA A3.1, as well as seven others.				
gp160 (770–780)	gp41 (768–778 NL43) • CD8+ T cell clone.	RLRDLLLIVTR	HIV-1 infection	human (A*0301)	Takahashi1991
gp160 (770–780)	gp41 (775–785 LAI) • C. Brander notes this is an A*0301 epitope.	RLRDLLLIVTR	HIV-1 infection	human (A*0301)	Frahm2004
gp160 (770–780)	gp41 (770–780 BH10) • Recognized by CTL derived from acute seroconverter. • C. Brander notes that this is an A*3101 epitope in the 1999 database.	RLRDLLLIVTR	HIV-1 infection	human (A*3101)	Safrit1994a, Safrit1994b
gp160 (770–780)	gp160 (770–780 LAI) • C. Brander notes this is an A*3002 epitope.	RLRDLLLIVTR		human (A*3101)	Frahm2004
gp160 (770–780)	gp41 (768–778 NL43) **Keywords** inter-clade comparisons. • The consensus peptide of clade B is RLRDLLLIVTR. • The consensus peptide of clades A, C and E is RLRDFILIVTR and it is less reactive. • The consensus peptide of clade D is SLRDLLLIVTR and it is less reactive.	RLRDLLLIVTR	HIV-1 infection	human (A3)	Cao1997a
gp160 (770–780)	gp41 (775–785) **Keywords** HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.	RLRDLLLIVTR	HIV-1 infection, HIV-1 exposed seronegative	human (A3)	Kaul2001a
gp160 (770–780)	gp41 (770–780) **Keywords** rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant.	RLRDLLLIVTR	HIV-1 infection	human (A3)	Day2001
gp160 (770–780)	Nef (73–82) **Keywords** rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant. • In two of the subjects, RLRDLLLIVTR was the dominant epitope.	RLRDLLLIVTR	HIV-1 infection	human (A3)	Day2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (770–780)	gp41 (769–780)	RLRDLLLIVTR	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-RR11. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.			
gp160 (770–780)	gp41 (770–780)	RLRDLLLIVTR	HIV-1 infection	human (A31)	Ferris1999, Hammond1995
	• This epitope is processed by a TAP1/2 dependent mechanism.				
gp160 (770–780)	gp41 (770–780)	RLRDLLLIVTR	HIV-1 infection	human (A31)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A31, B44, B60, Cw3, Cw16. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.			
gp160 (777–785)	gp41 (782–790 LAI)	IVTRIVELL		human (A*6802)	Frahm2004
	• C. Brander notes this is an A*6802 epitope.				
gp160 (781–802)	gp120 (788–809)	IVELLGRRGWEALKYWWNL-LQY	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (781–802)	gp41 (788–809 HXB2)	IVELLGRRGWEALKYWWNL-LQY	HIV-1 infection	human (B27)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping.				
gp160 (786–794)	gp41 (791–799 LAI)	GRRGWEALK	HIV-1 infection	human (B27)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes. • Also: J. Liebermann 1992 and pers. comm. J. Liebermann.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (786–795)	gp41 (791–800 LAI)	GRRGWEALKY	HIV-1 infection	human (B*2705)	Frahm2004
	• C. Brander notes this is a B*2705 epitope.				
gp160 (786–795)	gp41 (791–800 LAI)	GRRGWEALKY	HIV-1 infection	human (B27)	Lieberman1998
	• Optimal peptide mapped by titration J. Lieberman, pers. comm.				
gp160 (786–795)	gp41 (786–795)	GRRGWEALKY	HIV-1 infection	human (B27)	Day2001
gp160 (787–795)	gp160 (787–795)	RRGWEVLKY	HIV-1 infection	human (A*0101)	Frahm2004
gp160 (787–795)	gp41 (787–795)	RRGWEVLKY	HIV-1 infection	human (A1)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A1, B8, B14, Cw7, Cw8. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
gp160 (794–802)	gp160 (794–802 LAI)	KYCWNLLQY		human (A*3002)	Frahm2004, Goulder2001a
	• C. Brander notes this is an A*3002 epitope.				
gp160 (794–802)	gp41	KYCWNLLQY	HIV-1 infection	human (A*3002)	Goulder2001a
	Epitope name KY9 (gp41). • HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule. • A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood. • Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean. • In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant. • In subject 199 four additional A*3002 epitopes were identified. • Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)				
gp160 (794–802)	gp41 (283–291)	KYCWNLLQY	HIV-1 infection	human (A*3002)	Frahm2004
gp160 (794–814)	gp41 (SF2)	KYCWNLLQYWSQELKNSAV-SL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
gp160 (795–816)	gp41 (802–823 HXB2)	YWWNLLQYWSQELKNSAVN-LLN	HIV-1 infection	human	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping.				
gp160 (799–807)	Env (800–808 subtype B)	LLQYWSQEL	Vaccine	human (A2.1)	Kundu1998a
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period. • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual. • CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.				
gp160 (805–814)	Env (799–813 BH10, LAI)	QELKNSAVSL	HIV-1 infection	human	Maksiutov2002
	• This study employs an antigenic similarity matrix to compare HIV-1 antigenic determinants with human proteins. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is LLQYWSQELKNSAVS) has similarity with the complement component C6 fragment LTQFSSEELKNSGLT. • This CTL epitope (the HIV-1 LAI fragment with high similarity to a human protein overlapping this epitope is NSAVSLLNATAIAVA) also has similarity with the human INT-2 proto-oncogene protein precursor (fibroblast growth factor-3) fragment NSAYSILEITAVEVG.				
gp160 (805–814)	gp41 (810–819 LAI)	QELKNSAVSL		human (B*4001)	Frahm2004
	• C. Brander notes this is a B*4001,B60 epitope.				
gp160 (805–814)	gp41 (SF2)	QELKNSAVSL	HIV-1 infection	human (B60(B*4001))	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes. • B60 is present in 10-20% of the Caucasoid and very common in Asian populations.				
gp160 (805–814)	gp41 (805–814)	QELKNSAVSL	HIV-1 infection	human (B60/B61)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to five B61-restricted epitopes tested. • All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.				
gp160 (813–822)	gp41 (814–823 LAI)	SLLNATDIAV	Vaccine	human (A*0201)	Dupuis1995
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 • Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823. • Noted to be A*0201 in Brander *et al.*, 1999 database.				
gp160 (813–822)	gp41 (818–827 LAI)	SLLNATDIAV	Vaccine	human (A*0201)	Frahm2004
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C. Brander notes this is an A*0201 epitope.				
gp160 (813–822)	gp41 (814–823) **Keywords** dendritic cells. • Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients. • 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated. • SLLNATDIAV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, and 3 of these had a detectable CTL response – the other two had either the sequence SLFNAIDIAV or SLLNTTDIVV and no detectable CTL response. • CTL demonstrated against peptide-coated target, epitope is naturally processed and enhancible with vaccine.	SLLNATDIAV	HIV-1 infection	human (A2)	Kundu1998b
gp160 (813–822)	gp41 (818–827) **Keywords** immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes, including this epitope.	SLLNATDIAV	HIV-1 infection	human (A2)	Betts2000
gp160 (813–822)	gp41 (SF2) **Keywords** acute infection. **Epitope name** SV10. • Dominant CTL epitope in acute infection of patient AC13– response to this epitope corresponded to reduction of initial viremia. • Several other subdominant CTL epitopes were identified in the acute phase, but a response to SL9, SLYNTVATL, was not evident until 18 months post-presentation.	SLLNATAIAV	HIV-1 infection	human (A2)	Goulder2001a
gp160 (813–822)	gp41 (77–85 SF2) **Keywords** HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 1/4 group 3.	SLLNATDIAV	HIV-1 infection	human (A2)	Altfeld2001b
gp160 (813–822)	gp41 (814–823 CM243 subtype CRF01) **Keywords** HIV exposed persistently seronegative (HEPS). **Epitope name** E813-82. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2.	SLLNATAIAV	HIV-1 infection	human (A2)	Sriwanthana2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (813–822)	gp41 (814–823 CM243)	SLLNATAIAV	HIV-1 infection	human (A2)	Bond2001

Keywords inter-clade comparisons.

- More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by one amino acid, SLLNATDIAV.
- This epitope was somewhat conserved 4/8 subtypes: CRF01 (E), B, D, and F.

gp160 (813–822)	gp41 (813–822)	SLLNATDIAV	HIV-1 infection	human (A2)	Day2001

Keywords rate of progression, acute infection.

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.

gp160 (813–822)	gp41 (813–822 IIIB)	SLLNATAIAV	Vaccine	mouse (A2)	Kiszka2002

Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade IIIB *HIV component:* gp160, gp160ΔV3 *Adjuvant:* IL-12

Keywords vaccine-specific epitope characteristics.

Epitope name D2.

- Transgenic mice expressing a HLA-A2/Kb chimeric protein were vaccinated with a full length gp160 or with gp160deltaV3, with the V3 loop deleted. Mice given gp160deltaV3 had a broader immune response than those given gp160, with increased responses to conserved HLA-A2 epitopes in the C1 region of gp120, KLTPLCVTL, and the C-term region of gp41, SLLNATAIAV.
- Greater resistance was conferred by the gp160deltaV3 than the gp160 vaccine to a challenge of vaccinia expressing heterologous gp160 from primary isolates (VI-06 and 89.6), and the resistance was conferred by CD8+ T-cells.

gp160 (813–822)	Env (813–)	SLLNATDIAV	HIV-1 infection	human (A2)	Corbet2003

Keywords binding affinity, inter-clade comparisons, computational epitope prediction.

Epitope name Env813.

Assay type CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay.

- HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.
- This epitope was one of the previously identified HLA-A2 epitopes studied.
- None of the 17 HIV-infected HLA-A2+ people in this study recognized this epitope.

gp160 (813–822)	Env (814–823 subtype B)	SLLNATDIAV	Vaccine	human (A2.1)	Kundu1998a

Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160

Keywords binding affinity.

- Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period.
- Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity.
- Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual.
- CTL responses after reimmunization may include recall responses – only individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL to overlapping peptides in this region gave a positive response in the greatest number of patients. • ALTERNATIVE EPITOPES: LLNATDIAV and LLNATDIAVA – CTL were induced by vaccine in those that had the sequence SLLNATAIAVA in their own infection, but not in those with: NLLNTIAIAVA or NLFNTTAIAVA or SLLNATAITVA.				
gp160 (813–822)	gp41 (814–823 LAI)	SLLNATDIAV	Vaccine	mouse (A2.1)	Peter2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 720), P30, PLG **Keywords** binding affinity, vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR27. • The stability of peptide binding to HLA-A2.1 was determined for six HLA-A2.1 peptides included in this vaccine study – ILKEPVHGV (RT), SLYNTVATL (p17), SLLNATDIAV (gp41) and LLWKGEGAV (RT) all bound with high affinity comparable to a influenza epitope reference (GILGFVFTL), while RGPGRAFVTI and VIYQYMDDL bound with a lower affinity (relative binding activity = 0.01). • The four high-affinity peptides formed stable complexes with half-lives ranging between 8 and 32 hours, while the low affinity peptides had half lives of less than an hour. • HLA-A2.1 transgenic mice were immunized with the six HIV-1 peptides and P30, as a universal T-helper epitope, with IFA or Montanide or microspheres as adjuvants. • All peptides except VIYQYMDDL induced a stong CTL response in Cr-release assays - stronger responses were observed when peptides were delivered alone, indicating immunodominance when the combination was used.				
gp160 (813–822)	gp41 (814–823 LAI)	SLLNATDIAV	Vaccine	mouse (A2.1)	Peter2002
	Vaccine *Vector/Type:* peptide *Strain:* B clade LAI *Adjuvant:* Incomplete Freund's Adjuvant (IFA), IL-12, P30 **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** LR27. • When HIV-1 peptides were used to vaccinate HLA-A2.1 transgenic A2-Kb mice, strong responses to five peptides were observed when the peptides were given individually, but immunodominance limited the response to some of the peptides when they were given in combination [Peter2001]. IL-12 can counteract immunodominance in BALB/c mice, so it was given with the multiple epitope vaccination, and was instead found to specifically eliminate the HLA-A2.1-epitope CTL responses, but not Kb CTL responses. This was possibly a consequence of transient depletion of T-cells, B cells and macropahges in the spleen.				
gp160 (813–822)	gp41	SLLNATDIAV	HIV-1 infection	human (A68)	Altfeld2001c
	Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** gp41 SV10. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • This epitope binds to three HLA-A2 supertype alleles: A*6802 (highest affinity), A*0202 and A*0203 (but not A*0201 and not A*0206) • This epitope did not elicit an ELISPOT response in 22 chronic HIV HLA-A2 infections, but elicited a strong response in 1/12 acute HLA-A2 infections – this individual, AC13, was HLA A*0201/68 B44/14 and also had a strong response to HLA-A2 vpr epitope AIIRILQQL.				
gp160 (813–828)	gp41 (MN)	SLLNATAIAVAEGTDR	HIV-1 infection	human	Chitnis2003
	Keywords assay standardization, HAART. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 17 perinatally HIV-1 infected children (0.08-16 years) were evaluated for HLA-A2-restricted IFN-gamma CD8+ CTL responses against 4 immunodominant peptides that carry HLA-A2 epitopes. Two peptides were from gp120 (one at position 112, one from the V3 loop), and one each was from gp41 and Gag. 15/17 patients responded to the Gag peptide, 13/17 to the gp41 and the non-V3 gp120 peptides, and 11/17 responded to the V3 loop. 4 children recognized all 4 peptides.				
gp160 (814–822)	Env (815–823)	LLNATAIAV	HIV-1 infection	human (A*0201)	Kmieciak1998a
	Keywords binding affinity. • CTL responses in six patients to four Env epitopes were studied: D2: LLNATAIAV, 5.3: RLRDLLLIV, D1: KLTPLCVTL, and 4.3: QMHEDIISL—all have A2 anchor residues. • The C terminal epitopes (D2 and 5.3) were highly variable and the variability was considered responsible for limited CTL response, while D1 and 4.3, N-terminal epitopes, were much more conserved and gave evidence of high levels of CTL response *in vitro*. • Peptides 5.3 and D2 bound to HLA A*0201 with low affinity and were variable, particularly D2. • Substitutions in peptide D2: llnTIaiav did not abrogate the response, but diminished it. • In a longitudinal study, the CTL response to the variable D2 epitope diminished over time, while the response to the conserved epitope D1 stayed higher.				
gp160 (814–822)	gp41 (815–823 LAI)	LLNATDIAV	Vaccine	human (A2)	Dupuis1995
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 • Of two CTL clones, one reacted only with 815-823, the other with 814-823 and 815-823.				
gp160 (814–822)	Env (815–823)	LLNATAIAV	HIV-1 infection	human (A2)	Kmieciak1998b
	• Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length env gene product.				
gp160 (822–832)	gp41 (SF2)	VAEGTDRVIEI	HIV-1 infection	human	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of individuals that had a CTL response to this epitope (HLA presenting molecule uncertain) broken down by group: 0 group 1, 1 group 2, and 0 group 3.				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	HIV-1 exposed seronegative	human	Pinto1995
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV.				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	HIV-1 infection	human (A2)	Clerici1991a
	• Helper and cytotoxic T cells can be stimulated by this peptide (Th4)				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	mouse (H-$2^{d, p, u, q}$)	Shirai1992
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 • In a murine system multiple class I molecules can present to CTL.				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	mouse (H-$2^{d, p, u, q}$)	Shirai1996b
	Vaccine *Vector/Type:* vaccinia *HIV component:* gp160				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple murine MHC can cross-present this epitope (HP53), and P18 RIQRGPGRAFVTIGK, to specific CTL.				
gp160 (828–836)	gp41 (829–837 LAI) **Vaccine** *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 • CTL from HLA-A2 positive subject react with this peptide.	RVIEVLQRA	Vaccine	human (A2)	Dupuis1995
gp160 (828–836)	gp41 (829–837 CM243 subtype CRF01) **Keywords** inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by three amino acids, RvievLqRa. • This epitope was only conserved in CRF01 (subtype E), and identities were rare.	KVIEVAQGA	HIV-1 infection	human (A2)	Bond2001
gp160 (828–836)	Env (829–837 subtype B) **Vaccine** *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 **Keywords** binding affinity. • Ten HIV-1+ HLA A2 asymptomatic individuals were given two courses of HIV-1 MN rgp160 vaccine over a 2 year period. • Two hundred and fifty three HIV-1 peptides of 9 or 10 aa possessing the HLA-A2.1 binding motif (Leu at position 2, Val at the C terminus) were identified in gp160, of which 25 had a high or intermediate binding affinity. • Eleven peptides were studied that had high HLA-A2 binding affinity – a CTL response was detected to 9/11 peptides in at least 1 individual. • CTL responses after reimmunization may include recall responses – individuals with vaccine cross-reactive sequences prior to vaccination showed detectable CTL responses.	RVIEVLQRA	Vaccine	human (A2.1)	Kundu1998a
gp160 (830–854)	gp41 (831–853) • Study of cytokines released by HIV-1 specific activated CTL.	IEVVQGAYRAIIRHIPRRI-RQGLERI	HIV-1 infection	human	Price1995
gp160 (831–838)	Env (830–837) • HLA-A33 a very common allele in Asia, with HLA-A*3303 the most common among the Japanese. New A*3303 epitopes were defined to better characterize the immune response in this population. • The anchor motif for HLA*3303 (A, I, L, V, F, Y in position 2 (F and Y bind most strongly), and R (K is also tolerated) in the C-terminal position) was used to define 82 potentially reactive peptides in Env; 37/82 peptides bound to A*3303; 3/37 peptides could induce peptide-specific CTL in bulk PBMC cultures from 1/3 HLA A*3303 positive individuals tested. • 2/3 peptides that reacted with the bulk culture, EVAQRAYR and VIEVAQRAYR, were overlapping, with one encompassing the other, but EVAQRAYR was shown to be the one that was reactive with a CTL clone. • CTL clones were isolated that killed target cells in a concentration dependent manner after pulsing with the EVAQRAYR peptide, that could also kill cells transfected with env expressed from a vaccinia vector. Bulk cultures were tested from six additional people, and only 2/6 reacted with this peptide, but the peptide is in a highly variable region.	EVAQRAYR	HIV-1 infection	human (A*3303)	Hossain2001, Takiguchi2000
gp160 (831–838)	gp41 (320–327)	EVAQRAYR	HIV-1 infection	human (A*3303)	Frahm2004
gp160 (835–843)	Env (834–842 SF2) **Keywords** rate of progression.	RAYRAILHI	HIV-1 infection	human (B*5101)	Tomiyama1999

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed. • This peptide could stimulate CTL from one person, however this CTL clone did not recognize B*5101 positive target cells infected with HIV-1 recombinant vaccinia expressing Env, so it was not confirmed that this peptide was a properly processed epitope.				
gp160 (837–856)	gp120 (844–863)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
gp160 (837–856)	gp120 (844–863 SF2)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI gp160. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A2, A26, B7, and B38.				
gp160 (837–856)	gp120 (844–863 LAI)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human (B35)	Shankar1996
gp160 (837–856)	gp41 (844–863 HXB2)	YRAIRHIPRRIRQGLERILL	HIV-1 infection	human (B8)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping.				
gp160 (842–856)	gp41 (SF2)	HIPRRIRQGLERALL	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • The only Env peptide recognized was gp41 HIPRRIRQGLERALL.				
gp160 (843–851)	gp41 (848–856 LAI)	IPRRIRQGL		human (B*0702)	Frahm2004
	• C. Brander notes this is a B*0702 epitope.				
gp160 (843–851)	gp41 (848–856 LAI)	IPRRIRQGL		human (B7)	Brander1995b
	Keywords mother-to-infant transmission. • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.				
gp160 (843–851)		IPRRIRQGL	HIV-1 infection	human (B7)	Soudeyns1999
	Keywords immunodominance, escape. • Following primary infection, progressive diversification and accumulation of mutations of HIV-env nucleotide sequences was observed, focused in V2 in one individual and in V8 in another. • The patient with the V2 diversification showed only transient CTL against Env and Nef. • The patient with the V8 diversification had an immunodominant CTL response to V8 epitope IPRRIRQGL, and multiple escape variants emerged within a year: ipTrirqgl and ipTrirqgF, which abrogated the CT response *in vitro*, and also iprrLqgl and iprrirqDl which gave diminished responses.				
gp160 (843–851)	gp41 (848–856 LAI)	IPRRIRQGL	HIV-1 infection	human (B7)	Cao1997a
	Keywords inter-clade comparisons. • The consensus peptide of clades A, B, D, and F is IPRRIRQGL. • The consensus peptide of clade C is iprrirqgF, and it is equally reactive.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (843–851)	gp41 (848–856 subtype B)	IPRRIRQGL	HIV-1 infection	human (B7)	Wilson1998b
	Keywords inter-clade comparisons, acute infection. • The extent of CTL interclade cross-reactivity from CTL isolated from individuals newly infected with B clade virus was studied, and extensive cross-reactivity was observed. • Two HLA B7 individuals had CTL response to B_LAI, A_92UG037 and C_92BR025 gp160, but were B clade strain MN non-responders – the authors note that the B7 epitope IPRRIRQGL is conserved between the LAI and clade A and C strains, but that MN has a non-conservative Arg to Thr substitution at position three that may be contributing to the specificity of the response in the HLA B7 individuals.				
gp160 (843–851)	gp41 (843–851 HXB2)	IPRRIRQGL	HIV-1 infection	human (B7)	Hay1999b
	Keywords rate of progression, immunodominance. • CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201. • The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted. • Despite the initial narrow response to two epitopes, no other CTL responses developed. • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak. • Variants were observed *in vivo*, the most common form of the viral epitope at presentation at 3 months was the only form that did not elicit a CTL response: iprrTrqgl; the other forms detected were iprrirqgF, iprriLqgF, VprrirqgF and they could elicit a CTL response although the response to iprriLqgF was reduced. • A second rapid progressor had a detectable CTL response exclusively to this epitope.				
gp160 (843–851)	gp41 (subtype A)	IPRRIRQGF	HIV-1 infection	human (B7)	Cao2000
	Keywords inter-clade comparisons. • HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D. • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype. • This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection, is cross-reactive with subtypes A and B, but not in subtype D.				
gp160 (843–851)	gp41	IPRRIRQGL	HIV-1 infection	human (B7)	Islam2001
	Keywords rate of progression, acute infection. • Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS. • This individual had a dominant response to IPRRIRQGL with strong *in vivo* activated responses and *in vitro* stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred with in both epitopes. • At 3 months post-presentation, seven IPRRIRQGL CTL clones were obtained, five used the T-cell receptor Vβ 6S1 and Jβ 2.7 and had the CDR3 WAASS, two used Vβ16S1, ERSPPGD, Jβ 2.7 and one CTL clone isolated at 39 months was Vβ 14S1, CR3 PTAAG, and Jβ 2.1 – all of these clones persisted over the course of the infection, even to time of death, despite the loss of CTL functional responses over time.				
gp160 (843–851)	gp41 (843–851 SF2)	IPRRIRQGL	HIV-1 infection	human (B7)	Altfeld2001b
	Keywords HAART, acute infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 2/4 group 1, 1/3 group 2, and 1/1 group 3.				
gp160 (843–851)	gp41 (848–856)	IPRRIRQGL	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • IPRRIRQGL cross-reacts with clades A, B and D. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B7 women, 2/5 HEPS and 5/6 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in 2 of the 5/6 HIV-1 infected women that responded to the epitope, but in neither of the 2/5 HEPS cases. • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.				
gp160 (843–851)	gp41 (843–851)	IPRRIRQGL	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.				
gp160 (843–851)	gp41 (SF2)	IPRRIRQGL	HIV-1 infection	human (B7)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
gp160 (843–851)	gp41 (842–852)	IPRRIRQGL	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** B7-IL9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • Only two epitopes were detected during acute infection in patient AC-06, B7 restricted gp41 epitope IPRRIRQGL and Gag GPGHKARVL. GPGHKARVL was the first targeted peptide, and remained immunodominant through the 34 month study period. • 6/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.				
gp160 (843–851)	gp41	IPRRIRQGL	HIV-1 infection	human (B7)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** B7-IL9(gp41). **Donor HLA** A24,A?,B7,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).				
gp160 (843–851)	Env	IPRRIRQGL	HIV-1 infection	human (B7)	Bobbitt2003
	Keywords class I down-regulation by Nef. **Epitope name** EW10. **Assay type** Chromium-release assay, Flow cytometric CTL assay. • Nef, through Nef-mediated MHC-1 down-regulation, is not the only viral protein to influence levels of HIV-specific CTL recognition. The Rev L60F mutation, a common natural variant, can decrease CTL recognition of late gene products. The Rev mutation impacts the early to late gene switch, reducing late gene product production (Gag, Pol, Env, Vpu, Vpr and Vif), while increasing Nef production, both of which reduce the impact CTL recognition of late gene products. As expected, Rev L60F rendered HIV infected cells more resistant to CTL that recognized epitopes from the late proteins Env and Gag. Gag expression is more profoundly reduced than Env, and Gag-specific CTL were more profoundly affected. Conversely CTL against an epitope in an early gene product, Tat, were more effeciently recognized when infected with viruses carrying the Rev L60F mutation. • Patients in the asymptomic phase with active immune responses had more CTL resistant viruses, with lower Rev activity, lower Gag expression and greater resistance to Gag-specific CTL killing, while viruses isolated from people with AIDS were more sensitive to CTL killing.				
gp160 (843–851)	gp41 (843–851)	IPRRIRQGL	HIV-1 infection	human (B7)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A3, B7, B14, cw*0702, Cw*0802.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
gp160 (845–856)	gp41 (852–863 HXB2)	RRIRQGLERILL	HIV-1 infection	human (A30, B8)	Lieberman1992
	• CTL epitope defined by T cell line and peptide mapping.				
gp160 (845–856)	gp41 (852–863 LAI)	RRIRQGLERILL	HIV-1 infection	human (B7)	Shankar1996
gp160 (846–854)		RIRQGLERA	HIV-1 infection	human (A*0205)	Sabbaj2002b
	Keywords HAART. **Epitope name** Env-RA9. **Donor HLA** A*0205 A*3002 B*1402 B*5301 Cw*0401 Cw*0802. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Patient 00RCH28 was African American, not on HAART, had a viral load of 5900 and CD4 count of 889, and she also recognized IN(219-227), KIQNFRVYY, A*3002. • Among HIV+ individuals who carried HLA A02, 6/21 (29%) recognized this epitope.				
gp160 (846–854)	gp41 (335–343)	RIRQGLERA	HIV-1 infection	human (A*0205)	Frahm2004
gp160 (849–856)	gp41 (849–856)	QGLERALL	HIV-1 infection	human (B8)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A1, B8, B14, Cw7, Cw8. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				

II-B-20 Env CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	gp160 (LAI, MN)		Vaccine	human	Belshe1998
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Protease • The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers.				
Env	gp160 (LAV)		HIV-1 infection	human	Zheng1999
	Keywords epitope processing, dendritic cells. • Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone. • Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway.				
Env	Env (IIIB)		HIV-1 infection	human	Wasik2000
	Keywords rate of progression, Th1. • HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of IL-2, as well as beta-chemokines, relative to other HIV+ infants. • No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors. • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.				
Env	gp120		HIV-1 infection	human	Soudeyns2000
	Keywords HAART. • Analysis of T cell receptor beta chain variable region repertoire indicates that antiretroviral therapy (ART) and highly active antiretroviral therapy (HAART) decrease global CD8 T cell oligoclonality during primary HIV infection. • A sharp decline in HIV-1 gp120-specific CTL clones was observed in HAART-treated subjects.				
Env	Env (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp41, Protease, V3 • The vaccine used was a rec canarypox with HIV-1 gp120 MN, tm/gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36)) • Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36. • Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160.				
Env	Env		HIV-1 infection	human	Gamberg1999
	Keywords TCR usage. • 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens. • Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env (LAI, MN)		Vaccine	human	Gorse1999b
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade SF2 *HIV component:* Env, Gag, Nef, Protease • The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120. • In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients. • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity.				
Env	Env (LAI)		HIV-1 infection	human	Buseyne1998b
	Keywords inter-clade comparisons. • In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.				
Env	gp120 (IIIB)		Vaccine	macaque	Shiver1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp120, gp160 • DNA vaccinations of Rhesus monkeys with a gp120 or gp160 DNA vaccine elicited a strong CD8 cytotoxic T cell response.				
Env	gp160		HIV-1 infection	macaque	Kent1997b
	• Macaques can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response. • A strong CTL response against env, pol and gag antigens can be detected. • The CTL response peaked by 4 weeks and declined dramatically by 8 weeks. • The response in the lymph nodes and peripheral blood was comparable.				
Env	gp160		Vaccine	mouse	Kim1997c
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12 • A gag/pol, vif or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice. • When IL-12 was present, CTL response could be detected even without *in vitro* stimulation.				
Env	gp160		Vaccine	mouse	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12 • A gag/pol or env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice. • When CD86 was present, CTL response could be detected even without *in vitro* stimulation.				
Env	gp120 (HXBc2)		Vaccine	macaque	Letvin1997
	Vaccine *Vector/Type:* DNA prime with gp160 boost *Strain:* B clade HXBc2 *HIV component:* gp160 • Vaccination of Macaques mulatta (Rhesus monkeys) with an HXBc2 env DNA prime and a protein boost elicited a T cell proliferative response, a CTL response, and type-specific neutralizing antibodies. • Vaccinated animals challenged with SHIV-HXB2 were protected from infection.				
Env	gp120 (MN)		Vaccine	human	MacGregor1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* Env, Rev • An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 ug, was safe. • The CTL response to gp120 was enhanced in 0/4 patients in the 30 μg group, 2/3 patients in the 100 μg group, and 0/3 in the 300 μg group – but the non-responding patients in the 300 μg group had a strong CTL response prior to vaccination, and the CTL results are inconclusive.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	gp120 (IIIB)		HIV-1 infection	human	Trickett1998
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection. • Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Env was seen in one patient.				
Env	gp120 (LAI)		HIV-1 infection	human	Legrand1997
	• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat. • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef. • Early responses to Pol, Rev, Vif and Tat were rare.				
Env	gp120 (LAI)		Vaccine	human	Corey1998
	Vaccine *Vector/Type:* vaccinia prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* gp160 • Vaccinia-naive subjects were vaccinated with vaccinia-gp160 LAI and boosted with gp120 SF2, LAI, MN, or 160 MN. • 26/51 had an anti-Env CTL response, and those that were boosted with gp120 tended to produce Abs that neutralized autologous laboratory strains with some cross-reactivity.				
Env	Env (IIIB)		HIV-1 infection	human	Betts1997
	Keywords inter-clade comparisons. • 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins. • A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients.				
Env	Env		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function. • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.				
Env	Env (IIIB)		HIV-1 infection	human	Betts1999
	Keywords rate of progression. • This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection.				
Env	Env (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.				
Env	Env		HIV-1 exposed seronegative	human	Goh1999
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype. • In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins.				
Env	Env (LAI, MN)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT • A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env (LAI)		Vaccine	macaque	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag **Keywords** Th1, Th2. • Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone. • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.			
Env	Env (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease • A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers.				
Env	Env (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86 • The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.				
Env	gp120 (IIIB)		Vaccine	macaque	Notka1999
	Vaccine *Vector/Type:* Semliki-Forest Virus with virus-like particle boost *Strain:* B clade IIIB *HIV component:* Gag, gp120 • Immunization of SIV Pr56Gag-derived VLPs with HIV-1 gp120 anchored on their surface induced Abs, CTL and Th responses to HIV gp120; priming with the HIV antigens in Semliki-Forest Viruses enhanced the immunological outcome. • Immunized monkeys challenged with SHIV showed a more rapid reduction of plasma viremia.				
Env	Env		HIV-1 exposed seronegative	human	Akridge1999
	• This study suggests that HIV-1-resistance in exposed and uninfected individuals is not only associated with the 32-bp deletion in the HIV-1 co-receptor CCR5, but can be related to HIV-1 specific CTL immunity.				
Env	gp120 (BRU)		HIV-1 infection	human	Aladdin1999
	Keywords rate of progression. • In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.				
Env	gp120		HIV-1 infection	human	Aladdin2000
	Keywords HAART. • The administration of IL-2 caused an initial enhancement of CD4 cell counts that was accompanied by a decrease in CTL activity – IL-2 therapy did not reduce initial HIV viral load and viral replication was ultimately enhanced.				
Env	Env		HIV-1 infection	human	Jin1998a
	• CTL precursor frequencies were determined in HIV-1 infected pregnant women, and higher CTLp frequencies to Pol and SF2 Nef, but not IIIB Nef, were found in non-transmitting mothers than in transmitting mothers – Nef CTL responses have been found in uninfected infants born to HIV+ women (Lazuriaga95); • Very different CTLp frequencies were observed in env depending on whether IIIB, MN, RF, BK, or SF2 was used as antigen – no association between env specific CTL and transmission was observed.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env		Vaccine		Zavala2001
	Vaccine *Vector/Type:* vaccinia *HIV component:* Env **Keywords** review. • This paper is a review of vaccinia in the context of vaccines strategies that use different vectors to prime and boost, and emphasizes a unique capacity of vaccinia to very efficiently boost memory T-cell responses. • HIV is discussed in the context of Gonazalo *et al.* 1999, where a V3 CTL epitope expressed in reFlu was boosted most effectively by vaccinia expressing the full Env.				
Env	Env		Vaccine	macaque	Akahata2000
	Vaccine *Vector/Type:* DNA *Strain:* ZF1 *HIV component:* complete genome • Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging. • Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153) • 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected. • PBMC from all vaccinated monkeys produced IFN-gamma, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response. • 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit. • 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit.				
Env	gp120		HIV-1 infection	human	Young2001
	• Addition of recombinant rec human IL12 (rhIL12) to cultures increased HIV-specific lysis of HIV-Gag, Pol and gp120 vaccinia expressed antigens (11/15 tested increased lysis by > 5%) if the culture was derived from HIV+ individuals who had CD4 cells/ul > 500. • 2/10 individuals with <200 CD4 cells/ul, and 3/10 individuals with 200-500 CD4cells/ul, had an increase of >5% upon treatment of the culture with rhIL12, so a few individuals in late stage disease had CD8 cells that maintained responsiveness to rhIL12.				
Env	Env (subtype A, B, D)		HIV-1 infection	human	Cao2000
	Keywords inter-clade comparisons. • HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D. • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.				
Env	Env		Vaccine	human	AVEG022PT2001
	Vaccine *Vector/Type:* canarypox, protein *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Env, Gag, Protease *Adjuvant:* MF59 • Different HIV strains were used for different regions: MN (gp120), LAI (gp120, protease and gag), and SF2 gp120 • 26/42 subjects who received CP vac-env-pro vaccine had a CTL response measured by Cr-release, while only 3/17 who were vaccinated with rec gp120 had a CTL response. • A combination of a CP vac-env-pro vaccine with rec gp120 gave CD8+ T-cells in 62% of subjects, and NAbs in 91% of subjects.				
Env	Env		HIV-1 infection	human	White2001
	• HIV-specific CTL activity was detected in the female reproductive tract of only 1/3 HIV-infected women who underwent a hysterectomy, although CTL could be identified in the PBMC of all three women.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env (IIIB)		HIV-1 infection	human	Jin2000a
	Keywords rate of progression.				
	• The CTL precursor level (CTLp) was measured in long term non-progressors (LTNP) with low viral load using limiting dilution analysis and measuring CTL against Env Gag and Pol expressed in vaccinia in autologous targets.				
	• LTNPs have high memory CTL numbers and low viral load.				
Env	Env (IIIB)		HIV-1 infection	human	Jin2000a
	Keywords HAART, rate of progression.				
	• The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay.				
	• LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load.				
Env	Env		HIV-1 exposed seronegative	human	Rowland-Jones2001
	Keywords review, HIV exposed persistently seronegative (HEPS).				
	• This is a review that summarizes observations about HIV-specific CTL found in the HIV-1 exposed persistently seronegative (HEPS) population.				
	• The CTL responses assayed by ELISPOT and by CTL precursor frequencies by limiting dilution analysis indicate that CTL in HEPS individuals tend to be of a lower magnitude than in chronic HIV-1 infections – the responses in HEPS cases are below the level of detection by tetramer assays.				
	• CD8+ CTL responses tend to be detectable in HEPS subjects only if they are recently exposed, and the response diminishes if exposure is reduced – it is not clear if there is a stable memory population in HEPS cases.				
	• CD8+ CTL responses in the HEPS population are associated with HIV-1 specific CD4+ T cell responses, assayed by proliferation assays, IL-2 secretion, and ELISPOT, and the authors consider the possibility that HIV-1-specific T-help responses improve the "quality" of the CD8+ response in HEPS individuals relative to HIV-1 infected individuals, who tend to have a poor HIV-1-specific T-help response.				
	• HIV-1 specific CD8+ CTL responses in HIV-1 infected individuals show reduced levels of perforin, and the T cells may not mature properly, and although similar studies have not been conducted in HEPS individuals this is considered as a possible difference in the CTL immune response in HEPS and HIV-1 infected people.				
Env			Vaccine	mouse	Nabel2002
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol				
	Keywords review.				
	• Env DNA constructs were designed that were codon optimized for human genes, express Env in the absence of the regulatory protein Rev, both increasing Env expression levels, deletions in the cleavage site and in the fusion domain. These constructs increased Ab responses to Env, while not diminishing CTL responses, when injected into mice.				
	• Removing N-linked glycosylation sites did not alter the humoral or cellular immune responses to this HIV protein, as has been seen in analogous SIV experiments.				
Env			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission.				
	• 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env.				
	• Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Kuhn2002, Wasik1999
	Keywords HAART, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission, rate of progression.				
	• In HIV-infected infants HIV-specific, CTL responses were not detectable in cord blood or in PBMC collected shortly after birth and were absent or remained very low in 3 infants with a rapidly progressive disease. For those who progressed more slowly, the HIV-specific CTL activity varied.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The two infants with high levels of Env peptide-stimulated IL-2 responses had the highest CTLp frequencies. • Stronger responses were detected after initiation of the antiretroviral therapy. • Two babies that were not infected though born to HIV+ mothers had detectable though low HIV-specific CTLp responses to Env (1/2), Pol (2/2), Gag (1/2) cord blood and transiently in PBMC after birth. • Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Aldhous1994, Kuhn2002
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • Six of nine HIV vertically infected infants had HIV-1 specific CTL responses to vaccinia expressed Tat (4/6), Pol (6/6), Env (1/6), or Gag (1/6), but not all responses were detected at all time points. • Two of eleven babies that were not infected though born to HIV+ mothers had detectable responses Tat (1/2), Pol (2/2), Gag (1/2). • Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Kuhn2002, McFarland1994
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • Only 9% of HIV+ infants had HIV-specific CTL against Env or Gag in unstimulated PBMC. After CD3 stimulation of PBMC, Gag and Env specific CTL were found in PBMC from 91% and 78% of HIV-infected children, respectively, with high precursor frequencies. • 2/9 babies that were not infected though born to HIV+ mothers had detectable responses to Env. • Reviewed in [Kuhn2002].				
Env			HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.				
Env			HIV-1 infection	human	Trabattoni2002
	Keywords HAART. • CD8+ T-cells that were stimulated by HIV-1 Env expressing targets from 25 HIV+ patients receiving ART and 17 ART-naive patients were compared. CTL from the individuals receiving ART showed increased TNFalpha production and a reduction of perforin and granzyme expressing CTL, suggesting a functional defect in ART-treated individuals, and a potential benefit of immunomodulants during therapy.				
Env	(HXB2)		HIV-1 infection	human	Edwards2002
	Keywords rate of progression. • 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag. • Nef and/or Pol CTL responses were detected in 86% of the subjects. • The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load. • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count. • Nef and Env responses did not correlate with either CD4 counts or viral load.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env		Vaccine	mouse	Ishii2001
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* cationic liposome, GM-CSF, IL-2 **Keywords** Th2. • Vaccination route of HIV-1 DNA immunization with gp160 and Rev genes was compared including intranasal (i.n.), intramuscular (i.m.), and topical application of DNA directly on the skin after elimination of keratinocyte layers using a strong adhesive. Topical exposure resulted in high level CTL responses, IFN-gamma and IL-4 production, and delayed type hypersensitivity (DTH). Topical application favored Th2 responses. • DNA delivered topically with adjuvant-like cationic liposomes gave a stronger response than DNA alone, and co-administration of the DNA vaccine with IL-12 and GM-CSF expression vectors enhanced cytotoxic activity and DTH.			
Env			HIV-1 infection	human	Larsson2002b
	Keywords HAART, dendritic cells. • Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.				
Env	(IIIB)		HIV-1 infection	human	Trickett2002
	Keywords immunotherapy. • Conditions were optimized for ex-vivo expansion of CD8+ and CD4+ T-cells with the goal of functional T-cell production for autologous immunotherapy. 10,000-fold expansions were obtained in 14 days with optimized concentrations of IL-2, anti-CD3 and anti-CD28 coated microspheres, and decreasing amounts of serum over the first 8 days.				
Env	(IIIB)		HIV-1 and HCV co-infection	human	Lauer2002
	Keywords rate of progression. • HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins. • All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load. • Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted. • HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.				
Env			HIV-1 infection	human	Luzuriaga1995
	Keywords responses in children. • 2/3 infants infected in utero had detectable HIV-1 Gag and Env specific CTL responses, one by 4 months, one by 11 months of age. Levels of the responses varied at different time point. Pol responses were not detected. • 2/4 infants infected intrapartum had detectable responses, one note until 11 months, one not until 42 months. • HIV-specific CTL were not detected in ten HIV- infants that were born to HIV+ mothers.				
Env			Vaccine	human	Gupta2002
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *HIV component:* Env, Gag • A safety and immunogeniticity study of a vaccine dosing schedule was studied in a trial conducted in high and low risk study subjects. There was a 76% cumulative probability of detecting a Gag or Env CTL response by day 728.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env			HIV-1 infection	human	Scott2001

Keywords HAART, responses in children.

- CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age.
- Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses.
- One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol.
- Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.

Env	(IIIB)		HIV-1 infection	human	Ortiz2001

Keywords HAART, supervised treatment interruptions (STI).

- Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.
- One of seven subjects with a detectable NAb response had an augmented neutralization titer in response to STI.

Env	(SF2)		HIV-1 infection	human	Tomiyama2002

Keywords class I down-regulation by Nef.
Donor HLA B*3501, A*2402, B*5101, B*3303.

- Nef down-regulates class I molecules, and the killing activity of HLA B*3501, A*2402, B*5101 and B*3303-restricted HIV-1-epitope specific CTL clones was inhibited by an HIV-1 strain carrying Nef, relative to a Nef-deleted virus; while Nef-induced HLA class I down-regulation inhibited lysis, it did not abolish cytokine production by HIV-1-specific CD8+ T-cells.

Env	Env (gp160) (IIIB)		Vaccine	macaque	Akahata2003

Vaccine *Vector/Type:* DNA *Strain:* B clade NL43 *HIV component:* Env

- Four monkeys were injected i.m. with a SHIV plasmid (SHIV-NM-3rn ZF1*) which encodes all viral proteins driven by the SIV LTR promoter. Infectivity is prevented by the introduction of mutations within the zinc-finger motifs of the nucleocapsid (NC) that prevents RNA packaging. An original NC ZF1 mutant plasmid was constructed using NL43 (Akahata 275:116-124 (2000) – the SHIV construct was made as an alternative to get improved expression in macaques using an SIV promotor. CTL were detected by lysis of HIV-1 Env IIIB or SIV Gag mac239 expressing expressing target cells, and a T cell proliferative response to Env was observed. Env-directed antibodies were detected by ELISA. All vaccinated macaques had a low peak viral loads that fell below the level of detection within 6 weeks post-challenge with autologous SHIV SHIV-NM-3rn.

Env	Env (MN)		SIV infection, SHIV infection	macaque	Calarota2003

Keywords assay standardization.
Assay type CD8 T-cell Elispot - IFNγ.

- The senstitivity of gamma INF Elispot assays can be enhanced for the detection of low frequency responses, like after ART, by adding IL-15 to the assay.
- CD8+ T-cells from SHIV and SIV infected macaques with peptide pools from Gag and Env were used to test this system.

Env	Env			human	Currier2003

Keywords inter-clade comparisons.
Assay type Flow cytometric CTL assay.

- CD8-cellular immune responses from 21 HIV-1 infected patients from Kenya infected with subtype A, C, D, and unique recombinants were studied for cross-recognition of Gag, Env, and Nef vaccinia-expressed proteins representing subtypes A-H, including CRF01.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Both subtype-specific and cross-reactive CTL were observed, with a skewing of responses towards the infecting subtype in the nine subjects with full length sequence available. The magnitude of the responses to Gag were the highest, less to Nef, and still less to Env. • For Gag, 8/21 subjects responded to at least 7/8 different subtype proteins, 7 had a mixed response, recognizing some subtypes but not others, and 6 responded to only one or none of the different subtype proteins. For Env, 4/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 7 responded to one or none. For Nef, 5/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 6 responded to one or none.				
Env	Env (HIV-1 IIIB)		HIV-1 exposed seronegative	human	Fowke2000
	Keywords HIV exposed persistently seronegative (HEPS). **Assay type** cytokine production. • A cohort of Nairobi sex-workers were defined as resistant to HIV-infection by virtue of remaining seronegative despite repeated high risk exposures. 24 were tested for HIV specific T-helper responses detemined by IL-2 production *in vitro* in response to gp120 peptides or soluble gp120 protein. • 7/17 resistant women showed IL-2 stimulation which was greater than or equal to 2.0, and specific CTL responses were detected in 15/22 resistant women as compared to 0/12 of the control low-risk subjects.				
Env			computer prediction	(A*0201, B*3501)	Schönbach2002
	Keywords inter-clade comparisons, computational epitope prediction. • Computational methods (artificial neural networks, hidden Markov models, binding matrices based on HLA association rates) were used to identify HLA-A*0201 and HLA-B*3501 HIV T-cell epitope candidates from 533 Gag, Env and Pol sequences of which 374 were derived from HIV-1, 97 were derived from HIV-2 and 62 from SIV. Comparisons to known epitopes and between clades were made.				
Env			Vaccine	human (A1, A2, A24, B62, A25, A26, A30, A31, B8, B17, B39, B51, B57, B60, B62, B70)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 • HLA-B62 responses dominated the responses against an Env vaccine in an individual (022JAV) who was HLA A2, A26, B35, B62. The strongest response was against the MN peptide 381-400; a response diminished by half was observed against vaccinia expressed clade A and clade C relative to clade B. • Class I presentation of Env CTL responses in vaccinee 022A12K: A25 > B39, A1 and B8 were undetectable. • Class I presentation of Env CTL responses in vaccinee 022A12N: B57 » A2 > A26 and B60. • Class I presentation of Env CTL responses in vaccinee 034GP3: A31 > A24 > B62 > B51. • Class I presentation of Env CTL responses in vaccinee 0348PP: B17 > B70, A1 and A30 were undetectable.				
Env	gp120 (303–327)		HIV-1 infection	human (A2, A3, A11, B27)	Ferrari2000
	Keywords inter-clade comparisons. • One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles. • For this cluster of epitopes spanning the tip of the V3 loop, they suggest including a sequence from each clade.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env			Vaccine	human (A2, B8)	Ferrari2001
	Vaccine *Vector/Type:* canarypox prime with gp120 boost, canarypox prime with gp160 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Nef, Pol **Keywords** vaccine-induced epitopes. • Different HIV strains were used for different regions: gp41 LAI, Gag LAI, gp120 MN, gp120 SF2 • No HLA-A*0201 or B8 responses were made against the Env vaccine in individuals carrying these alleles, despite these being common presenting molecules for CTL responses to natural infections.				
Env	Env		HIV-1 infection	human (B*35)	Jin2002
	Keywords rate of progression. • Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501. • Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env. • The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Env	gp41 (842–850 IIIB, BH8)		HIV-1 infection	human (B7)	Pantaleo1997, Soudeyns1997
	• Clonotype-specific PCR and analysis of *in vivo* HIV-specific CTL showed that in early infection HIV-specific CTL clones preferentially accumulate in blood rather than lymph nodes and that they accumulate prior to down-regulation of virus.				
Env	gp160 (MN)		Vaccine	mouse (H-2^{d})	Vinner1999
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* gp120, gp160 • Mammalian codon optimization renders gp160 expression Rev independent, increases gp160 expression levels, and DNA vaccination of BALB/c mice yields a higher antibody response with an earlier onset than wild type. • Secreted gp120 gave higher antibody titers than membrane bound gp160. • In contrast to antibodies, synthetic codon-optimized DNA did not alter the CTL response, wild type genes generated equally strong CTL responses.				
Env	(IIIB)		Vaccine	mouse (H-2^{d})	Kato2000
	Vaccine *Vector/Type:* peptide *HIV component:* V3 *Adjuvant:* Cholera toxin (CT), GM-CSF, IL-4 • A multicomponent peptide vaccine VC1 with cholera toxin adjuvant was given to mice. • Immunization of BALB/c mice with VC1 and CT induced a strong CTL response which was enhanced by IL-12 expressing plasmids. • Immunization with VC1 and CT resulted in HIV-1 specific IgA antibody responses, which were increased by the combination of IL-4 or GM-CSF expressing plasmids.				
Env	gp160 (IIIB)		Vaccine	mouse (H-2^{d})	Kaneko2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* PLG • A PLG-microparticle encapsulated DNA encoding gp160 was given to mice. • Oral DNA vaccination of BALB/c mice induced mucosal and systemic gp160 glycoprotein-specific cellular and humoral immune responses, and mice vaccinated orally had higher resistance to HIV-env expressing vaccinia intrarectal challenge than mice vaccinated i.m.				
Env	Env		Vaccine	mouse (H-2^{d})	Ishii1997
	Vaccine *Vector/Type:* DNA with CMV promotor with cationic liposome *HIV component:* gp160, Rev				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor)				
Env	Env		Vaccine	mouse (H-2^d)	Xin2001
	Vaccine *Vector/Type:* adeno-associated virus (AAV) *HIV component:* Env, Rev, Tat *Adjuvant:* IL-2 • An AAV vector expressing HIV-1 env, tat, and rev genes (AAV-HIV vector) was used to vaccinate BALB/c mice. • A single injection stimulated and long lasting serum IgG, fecal IgA, and HIV-specific CTL. • Boosting enhanced the humoral response, and IL2 enhanced T-cell immunity.				
Env	Env		Vaccine	mouse (H-2^d)	Gonzalo1999
	Vaccine *Vector/Type:* vaccinia, influenza *Strain:* B clade IIIB *HIV component:* Env, V3 • The use of two different live vectors for priming and boosting has a synergistic effect on the immune response against HIV-1 – a 5-6 fold enhanced CTL response in Balb/c mice occurred when they were immunized with rec influenza virus (Flu-Env) expressing the V3 loop epitope from HIV-1 strain IIIB, and boosted with a vaccinia virus recombinant (VV-Env) expressing the complete HIV-1-IIIB env protein, comared to either immunogen alone.				
Env	Env (subtype B)		Vaccine	mouse (H-2^d)	McGettigan2001
	Vaccine *Vector/Type:* rabies virus *Strain:* B clade 89.6, B clade NL43 *HIV component:* gp160 • BALB/c were immunized with a replication competent recombinant rabies virus (RV) vaccine expressing HIV-1 gp160. • A single vaccination induced induced strong and long-lasting (4.5 months) gp160-specific CTL cytotoxic responses. • Although the greatest specific lysis was achieved when the vaccine strain was also used as the *in vitro* the target strain to assess the response, there was extensive CTL cross-reactivity against other B clade HIV-1 envelope proteins, implying CTL recognition of multiple epitopes within the HIV-1 envelope protein.				
Env	gp120		Vaccine	mouse (H-2Dd)	Bagley2003
	Vaccine *Vector/Type:* DNA *HIV component:* gp120 *Adjuvant:* Cholera toxin (CT) **Assay type** T-cell Elispot, Chromium-release assay. • BALBc mice were immunized intramuscularly with single plasmids encoding gp120, or cholera toxin catalytic domain (CTA1) and gp120, or with a dicistronic DNA vaccine expressing both CTA1 and gp120. Vaccination including CTA elicited stronger and longer lasting Ab responses and T-cell responses to gp120.				
Env	Env (SIV)		SIV infection	macaque (Mamu-A*11, -B*03, -B*04, and -B*17)	Dzuris2000
	• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here.				

II-B-21 Nef CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (1–16)	Nef (1–16)	MGGKWSKSSIVGWPAV	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (13–20)	Nef (13–20 LAI)	WPTVRERM	HIV-1 infection	human (B*0801)	Frahm2004, Goulder1997g
	• C. Brander notes this is a B*0801 epitope.				
Nef (13–20)	Nef (HXB2)	WPTVRERM	HIV-1 infection	(B*0801)	Peng2001
	Keywords class I down-regulation by Nef. • Deletion of the 19 N-terminal amino acids from Nef including the myristolation signal eliminates Nef-induced down-regulation of MHC class I and CD4 molecules. Such a construct has the potential to serve as a more potent immunogen. The known T-cell epitopes that that would be disputed by this deletion are minimal, including the HLA-B8 CTL epitope WPTVRERM.				
Nef (13–20)	Nef (13–20 LAI)	WPTVRERM	HIV-1 infection	human (B8)	Goulder1997g
	• Unusual epitope for HLA-B8, but compatible with crystal structure predictions.				
Nef (13–20)	Nef (13–20)	WPTVRERM	HIV-1 infection	human (B8)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others.				
Nef (13–20)	Nef (13–20 SF2)	WPTVRERM	HIV-1 infection	human (B8)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/3 group 2, and 1/2 group 3.				
Nef (13–20)	Nef (13–20)	WPTVRERM	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual.				
Nef (19–27)	Nef (19–27)	RMRRAEPAA	HIV-1 infection	human (B*1501)	Frahm2004
Nef (19–27)	Nef (19–27)	RMRRAEPAA	HIV-1 infection	human (B62)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA A*0201, A29, B58, B62, Cw*0301, Cw*1601. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
Nef (37–45)	Nef (37–45)	LEKHGAITS	HIV-1 infection	human (B*4001)	Frahm2004
Nef (37–45)	Nef (37–45)	LEKHGAITS		human (B*50)	Frahm2004
Nef (42–50)	Nef (44–52 HXB3)	ALTSSNTAA	Vaccine	mouse (HLA-A201 transgenic)	Sandberg2000
	Vaccine *Vector/Type:* DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** binding affinity, computational epitope prediction. • Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly. • A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun. • ALTSSNTAA was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant. • ALTSSNTAA bound weakly to HLA-A2, but it had the strongest CTL response among the three elicited by the DNA vaccine and a strong response to the peptide vaccination.				
Nef (48–56)	Nef (58–66 JRFL)	TAATNADCA	Vaccine	mouse (H-2^b)	Liang2002
	Vaccine *Vector/Type:* DNA *Strain:* B clade JRFL • BALB/c, C3H/HeN and C57BL/6 mice were given intramuscular immunization with Nef DNA constructs – C57BL/6 responded to this epitope. • The Nef mutant that lacked the myristylation site (G–>A) at position 2, and the dileucine motif (L –> A at positions 174 and 175) was impaired in terms of its ability to elicit induction of Nef-specific CD4+ and CD8+ T-cell responses. The myristylation site is critical for Nef membrane localization and function, and the di-leucine motif for the down-regulation of surface CD4 molecules, and the mutation of these regions could yield a safer vaccine. • N-terminal addition of human tissue plasminogen activator (TPA) to Nef, enhanced CD8+ T-cell responses and could compensate for the G2A, L174A, L175A mutations – this enhanced immunogenicity correlated with enhanced levels of protein expression in transfected cells.				
Nef (50–58)	Nef (50–)	ATNADCAWL	HIV-1 infection, Vaccine	human (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Nef *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Nef50. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was a low A2-binder that did not induce CTL or CD8+ T-cell IFN gamma responses in mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.				
Nef (62–81)	Nef (61–80)	EEEEVGFPVTPQVPLRPMTY	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
Nef (62–81)	Nef (61–80 SF2)	EEEEVGFPVTPQVPLRPMTY	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Twelve subjects had CTL that could recognize vaccinia-expressed LAI Nef. • Two of these 12 had CTL response to this peptide. • The responding subjects were HLA-A11, A24, B8, B35, and HLA not determined.				
Nef (62–81)	Nef (61–80 SF2)	EEEEVGFVTPQVPLRPMTY	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
Nef (62–81)	Nef (SF2)	EEEEVGFPVTPQVPLRPMTY	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY.				
Nef (66–80)	Nef (66–80 BRU)	VGFPVTPQVPLRMT	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.				
Nef (66–80)	Nef (64–78)	VGFPVTPQVPLRMT	HIV-1 infection	human (A1, B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (66–97)	Nef (66–97 LAI)	VGFPVTPQVPLRPMTYKAA-VDLSHFLKEKGGL	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide. • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual. • 5/12 tested had an IgG response to this peptide.				
Nef (67–81)	Nef (67–81)	GFPVRPQVPLRPMTY	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (68–76)	Nef (68–76)	FPVTPQVPL	HIV-1 infection	human (B*0702)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (68–76)	Nef (72–80 SF2)	FPVRPQVPL	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained. • 3/7 B35-positive individuals had a CTL response to this epitope. • An R to T substitution at position 4 abrogates specific lysis, but not binding to B*3501.				
Nef (68–76)	Nef (72–80)	FPVRPQVPL	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A. • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals. • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm. • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
Nef (68–76)	Nef (72–80 SF2)	FPVRPQVPL	HIV-1 infection	human (B35)	Shiga1996
	• Binds HLA-B*3501.				
Nef (68–76)	(SF2)	FPVRPQVPL	HIV-1 infection	human (B35)	Kawana1999
	Keywords rate of progression. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation.				
Nef (68–76)	Nef (66–74)	FPVRPQVPL	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (68–76)	Nef (68–76 BRU)	FPVTPQVPL	HIV-1 infection	human (B35)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FPVTPQVPL was recognized in 1/13 (8%) of individuals with HLA B7, and 1/12 (8%) of individuals with HLA B35. It was a high affinity HLA binder.				
Nef (68–76)	Nef (68–76)	FPVTPQVPL	in vitro stimulation or selectio	human (B7)	Wilson1999b
	Keywords binding affinity, dendritic cells, Th1. • Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors. • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within. • B7 and A2 Nef epitopes were studied – FPVTPQVPL has a high affinity for B7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (68–76)	Nef (68–76)	FPVTPQVPL	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection.				
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)				
	• 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
	• Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes.				
	• An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes.				
	• The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested.				
	• The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.				
Nef (68–76)	Nef (68–76 BRU)	FPVTPQVPL	HIV-1 infection	human (B7)	Choppin2001
	Keywords binding affinity, epitope processing.				
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.				
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.				
	• FPVTPQVPL was recognized in 1/13 (8%) of individuals with HLA B7, and 1/12 of individuals with HLA B35. It was a high affinity HLA binder.				
Nef (68–76)	Nef (68–76)	FPVTPQVPL	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection.				
	Donor HLA A3, B7, Cw7.				
	• CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.				
	• One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.				
	• 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. Also, none of 4 individuals had detectable responses to this epitope after STI.				
Nef (68–77)	Nef (68–77 LAI)	FPVTPQVPLR	HIV-1 infection	human (B*0702)	Frahm2004
	• C. Brander notes this is a B*0702 epitope.				
Nef (68–77)	Nef (68–77 LAI)	FPVTPQVPLR	HIV-1 infection	human (B7)	Haas1996
	• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection.				
Nef (68–77)	Nef (subtype B)	FPVTPQVPLR	HIV-1 infection	human (B7)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS), escape.				
	• This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative.				
	• FPVTPQVPLR was recognized in 1 of the 6 women (ML1203), and the response was present in the last available sample prior to seroconversion, 7 months.				
	• 20/20 sequences of the infecting strain had no substitutions in this epitope, all were FPVTPQVPLR, so there was no evidence for escape.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized in 1/22 HEPS sex worker controls, ML851.				
Nef (68–77)	Nef (66–75)	FPVRPQVPLR	HIV-1 infection	human (B7)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (68–77)	Nef (68–77 SF2)	FPVTPQVPLR	HIV-1 infection	human (B7)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.				
Nef (68–77)	Nef (68–77)	FPVTPQVPLR	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.				
Nef (68–77)	Nef (68–77)	FPVTPQVPLR	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.				
Nef (68–77)	Nef (68–76)	FPVTPQVPLR	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Donor HLA** A3, B7, Cw7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. Also, none of 4 individuals had detectable responses to this epitope after STI.			
Nef (68–81)	Nef (82–95 HXB2)	FPVTPQVPLRMTY	HIV-1 infection	human	Guimaráes2002
	Keywords inter-clade comparisons. • Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region—the HXB2 sequence is FPVTPQVPLRMTY, but fpvRpqvplrmty was observed in most Brazilian sequences regardless of the subtype (A, C, D and F).				
Nef (68–84)	Nef	FPVRPQVPLRPMTYKGA		human	Jubier-Maurin1999
	Keywords inter-clade comparisons. • 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants. • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes.				
Nef (70–84)	Nef (70–84 HXB2)	VTPQVPLRPMTYKAA	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 34% of the study subjects, and it was the second most frequently recognized peptide.				
Nef (71–79)	Nef (71–79 LAI)	TPQVPLRPM	HIV-1 infection	human (B*0702)	Frahm2004
	• C. Brander notes this is a B*0702 epitope.				
Nef (71–79)	Nef (71–79 BRU)	TPQVPLRPM	HIV-1 infection	human (B35)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPQVPLRPM was recognized in 1/10 (10%) of individuals with HLA B7, and 1/10 (10%) of individuals with HLA B35. It was a moderate affinity HLA binder.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (71–79)	Nef (71–79 SF2)	TPQVPLRPM	HIV-1 infection	human (B7)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.			
Nef (71–79)	Nef (71–79)	TPQVPLRPM	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.			
Nef (71–79)	Nef (71–79 BRU)	TPQVPLRPM	HIV-1 infection	human (B7)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPQVPLRPM was recognized in 1/10 (10%) of individuals with HLA B7, and 1/10 (10%) individuals with HLA B35. It was a moderate affinity HLA binder.			
Nef (71–79)	Nef (71–79)	TPQVPLRPM	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-TM9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (71–79)	Nef	TPQVPLRPM	HIV-1 infection	human (B7)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** B7-TM9(Nef). **Donor HLA** A32,A?,B7,B14; A24,A?,B7,B27. • Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient A displayed the greatest response to epitope B14-EL9(gp41), a strong response to B7-TL9(p24), and responses to B7-TM9(Nef) and A32-PW10(RT). Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).			
Nef (71–81)	Nef (75–85 SF2)	RPQVPLRPMTY	HIV-1 infection	human (B*3501)	Tomiyama1997
	• A CTL clone responsive to this epitope was obtained. • 4/7 B35-positive individuals had a strong CTL response to this epitope. • An R to T substitution at position 1 abrogates specific lysis, but not binding to B*3501. • An R to H substitution at position 7 did not alter reactivity.				
Nef (71–81)	Nef (75–85)	RPQVPLRPMTY	HIV-1 infection	human (B*3501)	Tomiyama2000a
	• CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A. • A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals. • CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm. • The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)				
Nef (71–81)	Nef (75–85 SF2)	RPQVPLRPMTY	HIV-1 infection	human (B35)	Shiga1996
	• Binds HLA-B*3501.				
Nef (71–81)	(SF2)	RPQVPLRPMTY	HIV-1 infection	human (B35)	Kawana1999
	Keywords binding affinity, rate of progression, escape. • HLA B35 is associated with rapid disease progression. • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals. • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation. • rpqvplrpmtF was found in 9/10 of the B35+ individuals, none of the B35- individuals—the Y–>F substituted peptide had a similar binding affinity with B35 and was recognized by a CTL clone equally with wildtype.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (71–81)	Nef (69–79)	RPQVPLRPMTY	HIV-1 infection	human (B35)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (71–81)	Nef (71–81 BRU)	TPQVPLRPMTY	HIV-1 infection	human (B35)	Choppin2001
	Keywords binding affinity, epitope processing.				
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.				
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.				
	• TPQVPLRPMTY was recognized in 9/12 (75%) of individuals with HLA B7, and 5/10 (50%) of individuals with HLA B35. It was a moderate affinity HLA binder, and the C-term Y readily cleaved *in vitro*.				
Nef (71–81)	Nef	RPQVPLRPMTY	HIV-1 infection, Vaccine	human, macaque (B51)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag				
	Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.				
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (71–81)	Nef (71–81 BRU)	TPQVPLRPMTY	HIV-1 infection	human (B7)	Choppin2001
	Keywords binding affinity, epitope processing.				
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.				
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.				
	• TPQVPLRPMTY was recognized in 9/12 (75%) of individuals with HLA B7, and 5/10 (50%) of individuals with HLA B35. It was a moderate affinity HLA binder, and the C-term Y readily cleaved *in vitro*.				
Nef (72–86)	Nef (72–86)	PQVPLRPMTYKGAFD	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons.				
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.				
	• Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.				
	• This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (72–91)	Nef (71–90 SF2)	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • Three of these 11 had CTL response to this peptide. • The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53.				
Nef (72–91)	Nef (71–90 SF2)	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
Nef (72–91)	Nef (SF2)	PQVPLRRMTYKAAVDLSHFL	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human	Garcia1997
	• The anti-Nef CTL line P1 specific for this epitope is able to kill target cells via two mechanisms. • First: Ca^{2+}-dependent, perforin-dependent Nef-specific lysis. • Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-specific targets. • Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice. • CTL mediated CD95-dependent apoptosis may play a role in pathogenesis.				
Nef (73–82)	Nef (73–82 NL43)	QVPLRPMTYK	HIV-1 infection	human (A*0301)	Koenig1990
	• 81 Tyr is critical for binding to A3.1. • C. Brander notes that this is an A*0301 epitope in the 1999 database.				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK		human (A*0301)	Frahm2004
	• C. Brander notes this is an A*0301 epitope.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	in vitro stimulation or selectio	human (A*0301)	Andrieu2003
	Keywords epitope processing, dendritic cells. • This study demonstrates that lipopeptides carrying epitopes can be taken up by human dendritic cells, processed using different pathways, and recognized by epitope-specific CD8+ T-cells originally derived from HIV+ individuals. The RT ILKEPVHGV peptide was embedded in a longer peptide fragment in the lipopeptide, and was internalized by endocytosis and processed in the cytosol by proteasomal cleavage by following an endosome-to-cytosol pathway for processing and presentation. Administration of epoxomycin, a proteasome inhibitor, completely abrogated epitope presentation to a CD8+ T-cell line, while monensin, an inhibitor of acid-dependent endosomal enzyme activity did not. • In contrast to the RT epitope, dendritic cell presentation of the Nef epitope QVPLRPMTYK embedded in a longer peptide in a lipopeptide was not inhibited by epoxomycin, but was inhibited by monensin, indicative of endocytolitic epitope processing.				
Nef (73–82)	Nef	QVPLRPMTYK	HIV-1 infection, Vaccine	human, macaque (A*0301, A11)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (73–82)		QVPLRPMTYK	HIV-1 infection	human (A03)	Sabbaj2002b
	Epitope name Nef-QK10. • Among HIV+ individuals who carried HLA A03, 9/20 (45%) recognized this epitope.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A11)	Le Borgne2000
	• Soluble factors in supernatant from both an HIV-specific cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism.				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A11)	Robertson1993
	• Development of a retroviral vector (pNeoNef) to generate autologous CTL targets. • [Hunziker1998] suggests that HLA-A2 does not in fact present this epitope. • The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, pers. comm., 2000)				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A11)	Couillin1994, Goulder1997a
	Keywords review, escape. • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response. • [Goulder1997a] is a review of immune escape that summarizes this study.				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A11)	Couillin1995
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized.				
Nef (73–82)	(LAI)	QVPLRPMTYK		(A11)	Buseyne1999, Frahm2004
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A11)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** QVP. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • One of the 2/8 HLA-A11 study subjects recognized this CTL epitope. • Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A11)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Nef (73–82)	Nef (71–80 93TH253 subtype CRF01)	QVPLRPMTYK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Sriwanthana2001
	Keywords HIV exposed persistently seronegative (HEPS). **Epitope name** N73-82. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was weakly reactive in HEPS study subjects 265 who was HLA A2/A11 and 128 who was HLA A11/A33, and after a second *in vitro* stimulation, in study subject 256 who was HLA A11/33, making it the most reactive epitope tested in HLA-A11 HEPS women, with 3/4 responding. • This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11.				
Nef (73–82)	Nef (71–80 93TH253 subtype CRF01)	QVPLRPMTYK	HIV-1 infection	human (A11)	Bond2001
	Keywords inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined. • 4/8 tested FSWs recognized this epitope. • An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – only one subject had an expanded tetramer staining T-cell population after *in vitro* stimulation. • This epitope was highly conserved in other subtypes, and exact matches were common.				
Nef (73–82)	Nef	QVPLRPMTYK	HIV-1 infection	human (A11)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** QVP. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
Nef (73–82)	Nef **Keywords** HAART. **Donor HLA** A2,A11,B8,B60,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized this epitope, one using HLA-A3, one using HLA-A11. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.	QVPLRPMTYK	HIV-1 infection	human (A11)	Appay2002
Nef (73–82)	Nef (73–81) • One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.	QVPLRPMTYK	HIV-1 infection	human (A2, A3, A11, B35)	Ferrari2000
Nef (73–82)	Nef (73–82 LAI) **Keywords** epitope processing, escape. • Mutations in Nef that flank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects.	QVPLRPMTYK	HIV-1 infection	human (A3)	Chassin1999
Nef (73–82)	Nef (73–82) **Keywords** inter-clade comparisons. • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia. • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested. • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag. • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef. • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env. • One of the patients was shown to react to this epitope: QVPLRPMTYK.	QVPLRPMTYK	HIV-1 infection	human (A3)	Durali1998
Nef (73–82)	Nef (73–82 LAI) **Keywords** review, escape. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. • Both had a response to this epitope. • [Goulder1997a] is a review of immune escape that summarizes this study.	QVPLRPMTYK	HIV-1 infection	human (A3)	Goulder1997e, Goulder1997a
Nef (73–82)	Nef (73–82) • Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response. • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response. • An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being specific for this epitope, isolated at two time points, 1 year apart.	QVPLRPMTYK	HIV-1 infection	human (A3)	Lubaki1997
Nef (73–82)	Nef (73–82) **Keywords** HAART, escape.	QVPLRPMTYK	HIV-1 infection	human (A3)	Samri2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name N1. • The epitope was recognized by patients 252#0 and 252#4 in a study of the effects of therapy escape mutations on CTL recognition.				
Nef (73–82)	Nef (73–82 SF2)	QVPLRRMTYK	HIV-1 infection	human (A3)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 1/4 group 2, and 1/2 group 3.				
Nef (73–82)	Nef (SF2)	QVPLRPMTYK	HIV-1 infection	human (A3)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-QK10. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 3/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 5/7 individuals had detectable responses to this epitope after STI.				
Nef (73–82)	Nef	QVPLRPMTYK	HIV-1 infection	human (A3)	Appay2002
	Keywords HAART. **Donor HLA** A3,B44,B64,Bw4,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized this epitope, one using HLA-A3, one using HLA-A11. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A3, B7, B14, cw*0702, Cw*0802.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A3 supertype)	Mollet2000
	Keywords HAART, supertype. **Epitope name** N1. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
Nef (73–82)	Nef (94–103)	QVPLRPMTYK	HIV-1 infection	human (A3 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801).				
Nef (73–82)	Nef (73–82 BRU)	QVPLRPMTYK	HIV-1 infection	human (A3, A11, B35)	Culmann1991
	• Nef CTL clones from HIV+ donors.				
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human (A3.1)	Koenig1995
	Keywords rate of progression, escape. • Alanine substitutions L76A, R77A, M79A, T80A significantly decreased immunogenicity of peptide. • Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health. • Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression.				
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (A3.1)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (73–82)	Nef (73–82)	QVPLRPMTYK	HIV-1 infection	human (B*0301)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.		
Nef (73–82)	Nef (73–82 LAI)	QVPLRPMTYK		human (B27)	Culmann1998
	• Optimal epitope mapped by peptide titration.				
Nef (73–82)	Nef (73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human (B35 or C4)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study.				
Nef (73–83)	Nef (73–82 BRU)	QVPLRPMTYKA	HIV-1 infection	human (A3)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • QVPLRPMTYKA was recognized in 9/15 (60%) of individuals with HLA A3. It was a high affinity HLA-A3 binder.				
Nef (74–81)	Nef (74–82)	VPLRPMTY		human (A3)	Carreno1992
	• Included in HLA-A3 binding peptide competition study.				
Nef (74–81)	Nef (73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human (B*3501)	Frahm2004
	• C. Brander notes this is a B*3501 epitope.				
Nef (74–81)	Nef (75–82)	VPLRPMTY	Peptide-HLA interaction	human (B*3501)	Smith1996
	• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex.				
Nef (74–81)	Nef	VPLRPMTY	HIV-1 infection	human (B*3501)	Ostrowski2000
	Keywords dendritic cells. • The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients. • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes. • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
Nef (74–81)	Nef (subtype B)	VPLRPMTY	HIV-1 exposed seronegative	human (B35)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
Nef (74–81)	Nef	VPLRPMTY	HIV-1 infection	human (B35)	Wilson2000a
	Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
Nef (74–81)	Nef (73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human (B35)	Culmann1991, McMichael1994
	Keywords review. • Review of HIV CTL epitopes – defined by B35 motif found within a larger peptide.				
Nef (74–81)	Nef (73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human (B35)	Rowland-Jones1995b
	• VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved.				
Nef (74–81)	Nef	VPLRPMTY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A and D subtype consensus are identical to the B clade epitope.				
Nef (74–81)	Nef (75–82)	VPLRPMTY	in vitro stimulation or selectio	human (B35)	Lalvani1997
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers. • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (74–81)	Nef (subtype B)	VPLRPMTY	HIV-1 exposed seronegative	human (B35)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A, B, and D clade viruses.				
Nef (74–81)	Nef	VPLRPMTY		human (B35)	Rowland-Jones1999
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5. • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones1995b]				
Nef (74–81)	Nef (74–81)	VPLRPMTY	HIV-1 infection	human (B35)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** VPL. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • One of two HLA B35+ among the eight study subjects recognized this epitope. • Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment.				
Nef (74–81)	Nef (75–82)	VPLRPMTY	HIV-1 infection, HIV-1 exposed seronegative	human (B35)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Subject ML 857 shifted from a A*6802 DTVLEDINL and B35 (H/N)PDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion.				
Nef (74–81)		VPLRPMTY	HIV-1 infection	human (B35)	Sabbaj2002b
	Epitope name Nef-VY8. • Among HIV+ individuals who carried HLA B35, 12/22 (55%) recognized this epitope. • Among HIV+ individuals who carried HLA B*5301, 0/11 (0%) recognized this epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (74–81)	Nef (74–81 BRU)	VPLRPMTY	HIV-1 infection	human (B35)	Choppin2001

Keywords binding affinity, epitope processing.

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- VPLRPMTY was recognized in 5/16 (31%) of individuals with HLA B35, and it was a moderate affinity HLA binder. Cleavage at the C-term Y was frequent *in vitro*.

Nef (74–81)		VPLRPMTY	HIV-1 infection, Vaccine	human, macaque (B35)	Hanke2000, Wee2002

Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].

Nef (74–81)	Nef (74–81)	VPLRPMTY	HIV-1 infection	human (B35)	Cao2003

Keywords acute infection, early treatment.
Assay type CD8 T-cell Elispot - IFNγ.
Donor HLA A1, A3, B8, B35.

- CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. SubjectBroadcast message from root Thu May 27 21:34:36 2004...n of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma vBattery Low Notification from APM BIOS (8% 0:12)or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.

Nef (74–82)	Nef (73–82)	VPLRPMTYK	Peptide-HLA interaction	human (A11)	Zhang1993

- Exploration of A11 binding motif.

Nef (75–82)	Nef (75–82 LAI)	PLRPMTYK	HIV-1 infection	human (A*1101)	McMichael1994

Keywords review.

- Review of HIV CTL epitopes.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C. Brander notes that this is an A*1101 epitope in the 1999 database.				
Nef (75–82)	Nef (75–82 LAI) • C. Brander notes this is an A*1101 epitope.	PLRPMTYK	HIV-1 infection	human (A*1101)	Frahm2004
Nef (77–85)	Nef (79–85) **Keywords** acute infection, early treatment. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A3, A33, B14, B35, Cw*0401, Cw*0802. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.	RPMTYKAAV	HIV-1 infection	human	Cao2003
Nef (77–85)	Nef (77–85 LAI) **Keywords** escape. • Structural constraints on the Nef protein may prevent escape. • Noted in Brander 1999, this database, to be B*0702.	RPMTYKAAL	HIV-1 infection	human (B*0702)	Bauer1997
Nef (77–85)	Nef (77–85 LAI) • C. Brander notes this is a B*0702 epitope.	RPMTYKAAL	HIV-1 infection	human (B*0702)	Frahm2004
Nef (77–85)	Nef (75–83 IIIB) **Keywords** binding affinity, TCR usage. • Study of tetramer staining of B7 around RPMTYKAAL gave quantitative results that were very different than functional measurements based on an ELISPOT assay. • Autologous clones were checked and 39/40 clones from two time points had the variant sequence RPMTYKGAL – tetramers based on RPMTYKGAL gave a more intense and uniform staining and bound with higher affinity to the RPMTYKGAL Vβ14 TCR.	RPMTYKAAL	HIV-1 infection	human (B7)	Oxenius2001b
Nef (77–85)	Nef (77–85 SF2) **Keywords** HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 0/3 group 2, and 1/1 group 3.	RPMTYKAAL	HIV-1 infection	human (B7)	Altfeld2001b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (77–85)	Nef (77–85)	RPMTYKAAL	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.			
Nef (77–85)	Nef (77–85)	RPMTYKAAV	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.			
Nef (77–85)	Nef (77–85 BRU)	RPMTYKAAV	HIV-1 infection	human (B7)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • RPMTYKAAV was recognized in 7/10 (70%) of individuals with HLA B7, and 0/3 (0%) of individuals with HLA B35. It was a moderate affinity HLA binder.			
Nef (77–85)	Nef (77–85)	RPMTYKAAL	HIV-1 infection	human (B7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** B7-RL9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 3/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (77–85)	Nef (77–85)	RPMTYKAAV	HIV-1 infection	human (B7)	Yu2002a

Keywords dynamics, supervised treatment interruptions (STI), acute infection.
Epitope name B7-RV9.
Donor HLA A3, B7, Cw7.

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 2/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 3/4 individuals had detectable responses to this epitope after STI.

Nef (77–91)	Nef (77–91)	RPMTYKGAFDLSFFL	HIV-1 infection	human	Novitsky2002

Keywords inter-clade comparisons.

- HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.
- Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.
- This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.

Nef (79–87)	Nef (81–89 HXB3)	MTYKAALDL	Vaccine	mouse (HLA-A201 transgenic)	Sandberg2000

Vaccine *Vector/Type:* DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Keywords binding affinity, computational epitope prediction.

- Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly.
- A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor coated on, gold particles delivered to abdominal skin by gene gun.
- MTYKAALDL bound weakly to HLA-A2, but the DNA nef vaccine elicited a good CTL response.

Nef (80–94)	Nef (80–94 HXB2)	TYKAAVDLSHFLKEK	HIV-1 infection	human	Addo2003

Keywords supervised treatment interruptions (STI), immunodominance, early treatment.
Assay type T-cell Elispot.

- Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI.
- 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized.
- A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed.
- The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.
- Responses to this peptide were detected in 47% of the study subjects, and it was the most frequently recognized peptide.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (82–91)	Nef (82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human (C*0802)	Nixon1999
	Keywords HAART. • A patient who made a mono-specific CTL response to this Nef specific epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous. • Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped. • The patient went from having an activated effector population (detected by CTLp and clone specific RNA) to a non-activated quiescent population (detected by the CTL-clone specific DNA)				
Nef (82–91)	Nef (82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human (C*0802(Cw8))	Frahm2004
	• C. Brander notes this is a C*0802(Cw8) epitope.				
Nef (82–91)	Nef (82–91 SF2)	KAAVDLSHFL	HIV-1 infection	human (Cw8)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-Cw8+ individuals that had a CTL response to this epitope broken down by group: 1/3 group 1, 0/0 group 2, and 0/1 group 3.				
Nef (82–91)	Nef (SF2)	KAAVDLSHFL	HIV-1 infection	human (Cw8)	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual.				
Nef (82–96)	Nef (82–96)	KGAFDLSFFLKEKGG	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (82–101)	Nef (81–100 SF2)	KAAVDLSHFLKEKGGLEGLI	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • Three of these 11 had CTL response to this peptide. • The responding subjects were HLA-A1, A2, B8, B14; HLA-A11, A24, B8, B53.				
Nef (82–101)	Nef (SF2)	KAAVDLSHFLKEKGGLEGLI	HIV-1 infection	human	Altfeld2001a
	• HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study. • Nef peptides PQVPLRRMTYKAAVDLSHFL, KAAVDLSHFLKEKGGLEGLI and EEEEVGFPVTPQVPLRPMTY were recognized and the first two share KAAVDLSHFL (a Cw8 epitope), the first and last share PQVPLRPMTY.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (83–91)	Nef (83–91 BRU)	AAVDLSHFL	HIV-1 infection	human (A2)	Choppin2001

Keywords binding affinity, epitope processing.

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- AAVDLSHFL was recognized in 3/18 (17%) of individuals with HLA A2. It was a low affinity HLA binder.

Nef (83–91)	Nef (83–91)	AAVDLSHFL	HIV-1 infection	human (B60, B62, Cw*0802, Cw8)	Cao2003

Keywords acute infection, early treatment.
Assay type CD8 T-cell Elispot - IFNγ.
Donor HLA A*0201, A23, B44, B62, Cw3, Cw4; A1, A3, B7, B14, Cw*0702, Cw*0802; A*0201, A31, B44, B60, Cw3, Cw16; A1, A1, B8, B14, Cw7, Cw8.

- All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env.
- Four different individuals recognized this epitope during a primary infection, and it was shown to be presented by HLA B60, B62, C2*0802, and Cw8.
- All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.
- More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.

Nef (83–91)	Nef (83–91)	AALDLSHFL		human (Cw*03)	Frahm2004
Nef (83–91)	Nef (85–93 HXB3)	AALDLSHFL	Vaccine	mouse (HLA-A201 transgenic)	Sandberg2000

Vaccine *Vector/Type:* DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
Keywords binding affinity, computational epitope prediction.

- Ten Nef 9-mer peptides were predicted to have strong binding affinity for HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly.
- A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun.
- AALDLSHFL was predicted to have a strong binding capacity for HLA-A2, and did, but it was the only one of the peptides recognized that was a strong binder, the other two recognized peptides were weak binders.
- AALDLSHFL was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant and gave a strong response to the peptide.

Nef (83–92)	Nef (81–90 93TH253 subtype CRF01)	GAFDLSFFLK	HIV-1 infection	human (A11)	Sriwanthana2001

Keywords HIV exposed persistently seronegative (HEPS).

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name N83-92. • This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand. • HLA-A11 is very common in this population, and was enriched among the HEPS sexworkers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed. • This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11.				
Nef (83–92)	Nef (81–90 93TH253 subtype CRF01) **Keywords** inter-clade comparisons. • HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive. • 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 finding and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified. • This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined. • 4/8 tested FSWs recognized this epitope. • This epitope was only conserved in CRF01 and subtype C, and exact matches were uncommon.	GAFDLSFFLK	HIV-1 infection	human (A11)	Bond2001
Nef (83–92)	Nef (83–92) **Keywords** acute infection, early treatment. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*0201, A11, B51, B61, Cw2, Cw14. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag.	AAVDLSHFLK	HIV-1 infection	human (A11)	Cao2003
Nef (83–94)	Nef (83–94 BRU) • Epitope defined by boundaries of overlapping peptides that stimulate Nef CTL clones.	AAVDLSHFLKEK	HIV-1 infection	human (A11)	Culmann1991
Nef (84–91)	Nef (84–91 LAI)	AVDLSHFL	HIV-1 infection	human (Bw62)	Culmann-Penciolelli1994
Nef (84–91)	Nef (84–91) **Keywords** immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.	AVDLSHFL	HIV-1 infection	human (Bw62)	Betts2000
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection	human (A*03)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A*1101)	Frahm2004
	• C. Brander notes this is an A*1101 epitope.				
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection	human (A*1101)	Fukada2002
	Keywords inter-clade comparisons. • Counterparts for eight known clade B HLA A*1101 epitopes were generated for clade E (CRF01). Three epitopes, identical among clade A-E, were cross-reactive and recognized by clade E infected individuals. The clade E and B analogs to three more HLA A*1101 epitopes was recognized in a clade specific manner. Two other HLA A*1101 clade B defined epitopes were found not to have stimulated a response in clade E infected individuals. • AVDLSHFLK was found to elicit clade-specific responses in clade B (AVDLSHFLK is most common, aLdlshflk is a common variant also found in clade A) and clade E (aFdlsFflk is most common and is also common in clade C). AVDLSHFLK was strongly recognized by CTL from 2/5 B clade infected Japanese subjects, as was aLdlshflk, and aFdlsFflk by CTL from 5/7 E clade infected Thai subjects. • The binding of aFdlsFflk to HLA A*1101 was 10-50 times lower than the other variants, and bulk CTL generated from individuals did not cross-react with the cross-clade peptides.				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A11)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes. • C. Brander notes that this is an A*1101 epitope in the 1999 database.				
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection	human (A11)	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope.				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A11)	Couillin1994, Goulder1997a
	Keywords review, escape. • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response. • [Goulder1997a] is a review of immune escape that summarizes this study.				
Nef (84–92)	Nef (84–92 LAI)	AVDLSHFLK	HIV-1 infection	human (A11)	Couillin1995
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized.				
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection	human (A11)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, acute infection. **Epitope name** AVD. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope. • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up.				
Nef (84–92)	Nef (82–90)	AVDLSHFLK	HIV-1 infection	human (A11)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (84–92)	Nef (84–92 SF2)	AVDLSHFLK	HIV-1 infection	human (A11)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3.				
Nef (84–92)	Nef (84–92)	AVDLSHFLK	HIV-1 infection, HIV-1 exposed seronegative	human (A11)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Nef (84–92)	Nef	AVDLSHFLK	HIV-1 infection	human (A11)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** AVD. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
Nef (84–92)	Nef	AVDLSHFLK	HIV-1 infection, Vaccine	human, macaque (A11)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (84–92)	Nef (84–92 BRU)	AVDLSHFLK	HIV-1 infection	human (A3)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • AVDLSHFLK was recognized in 4/12 (33%) of individuals with HLA A3. It was a high affinity HLA-A3 binder.			
Nef (84–92)	Nef (84–94)	AVDLSHFLK	HIV-1 infection	human (A3)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** A3-ALK9. **Donor HLA** A3, B7, Cw7. • CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied. • One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7. • 0/14 HLA-A3 positive individuals had detectable A3-restricted responses to this epitope during acute infection, but only 5/15 of HLA-A3 epitopes tested were targeted during acute infection. 1/7 individuals began to have detectable responses to this epitope after STI.			
Nef (86–94)	Nef	DLSHFLKEK	HIV-1 infection, Vaccine	human, macaque (A*0301)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].			
Nef (86–94)	Nef (86–94)	DLSHFLKEK	HIV-1 infection, HIV-1 exposed seronegative	human (A3)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Nef (86–94)	Nef (84–92 LAI)	DLSHFLKEK	HIV-1 infection	human (A3.1)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (86–100)	Nef (86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human (A2)	Robertson1993
	• Development of a retroviral vector (pNeoNef) to generate autologous targets.				
Nef (86–100)	Nef (86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human (B35)	Buseyne1993b
Nef (86–100)	Nef (86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human (B35 or C4)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study.				
Nef (87–102)	Nef	FSHFLKEKGGLEGLIY		human	Jubier-Maurin1999
	Keywords inter-clade comparisons. • 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants. • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes.				
Nef (88–100)	Nef (103–116)	SHFLKEKGGLEGL	HIV-1 infection	human	Guimaráes2002
	Keywords inter-clade comparisons. • Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region—most B subtype sequences are SHFLKEKGGLEGL, but sFflkekgglegl is found in most subtype C samples.				
Nef (90–97)	Nef (89–97)	FLKEKGGL	HIV-1 infection	human	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals that responded to SLYNTVATL reacted with seven other epitopes including this epitope previously described as presented by B8.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (A3)	Ostrowski2000
	Keywords dendritic cells. • The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo* • Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T cell help in 9 of 10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T cell help to a variable degree in most of patients. • Those CTL that didn't respond to CD40LT could expand with IL2 present, and IL15 produced by dendritic cells also contributes. • The T-helper epitope used for CD4+ T cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)				
Nef (90–97)		FLKEKGGL	HIV-1 infection	human (B*08)	Sabbaj2002b
	Epitope name Nef-FL8. • Among HIV+ individuals who carried HLA B*08, 1/3 (33%) recognized this epitope.				
Nef (90–97)	Nef (89–97 LAI)	FLKEKGGL	HIV-1 infection	human (B*0801)	Frahm2004
	• C. Brander notes this is a B*0801 epitope.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (90–97)	Nef (89–97 LAI)	FLKEKGGL	HIV-1 infection	human (B8)	Price1997
	Keywords review, escape. • CTL escape variants appeared over time in HLA-B8 HIV-1+ individual, providing evidence of immune escape. • Most variants appear at position 5, an anchor residue. • FLKE(E,N or Q)GGL showed reduced binding efficiency and recognition. • Double mutants (FIKENGGL, FLEENGGL, and FLKGNGGL) completely escaped recognition. • [Goulder1997a] is a review of immune escape that summarizes this study in the context of CTL escape to fixation.				
Nef (90–97)	Nef (90–97 IIIB)	FLKEKGGL	HIV-1 infection	human (B8)	Spiegel1999
	Keywords HAART, responses in children. • Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children. • CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef. • B7-FLKEKGGL tetramer complex was used for one of the children that was HLA-B7, and this infant showed a vigorous response (> 4% of CD8+ T cells) at 9 months of age. • HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses.				
Nef (90–97)	Nef	FLKEKGGL	Vaccine	human (B8)	Hanke1998a, Hanke1998b
	Vaccine *Vector/Type:* vaccinia • This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans.				
Nef (90–97)	Nef (88–95)	FLKEKGGL	HIV-1 infection	human (B8)	Goulder1997g
	• Natural variants for this epitope have been observed in several donors. • Substitutions Q5, N5, E5 that alter anchor position 5 are not well recognized. • Substitution I2 binds well to B8 and is recognized.				
Nef (90–97)	Nef (90–97)	FLKEKGGL	HIV-1 infection	human (B8)	Dyer1999
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective. • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load.				
Nef (90–97)	Nef (SF2)	FLKEKGGL	HIV-1 infection	human (B8)	Goulder2001a
	Epitope name FL8. • This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004. • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond. • FL8 was recognized in an additional patient, AC29, in chronic infection.				
Nef (90–97)	Nef (92–99)	FLKEKGGL	HIV-1 infection	human (B8)	Oxenius2001a
	Keywords HAART. **Epitope name** FLK. • Characterization of specific CTL phenotype patterns in response to variation of the virus load in response to antiviral therapy in 3 patients with chronic HIV-1 infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL activation in response to increasing viral load sequential, and co-segregated with apoptosis only during later stages of the response, suggesting antigen-specific cell-death is restricted to distinct CTL sub-populations.				
Nef (90–97)	Nef (92–99)	FLKEKGGL	HIV-1 infection	human (B8)	Oxenius2000
	Keywords HAART, supervised treatment interruptions (STI), immunodominance, escape, acute infection. **Epitope name** FLK. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • Six of the 7/8 study subjects that were HLA B8 recognized this early dominant CTL epitope. • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responsiveness against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII peptides – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones. • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIY-HTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent. • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197. • Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088. • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy. • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640 had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Kostense2001
	• HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load. • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional. • In 15 of the patients, the proportion of IFN gamma producing tetramer cells correlated with AIDS-free survival. • Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113) • There were more functional IFN-gamma producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells. • No correlation between elevated numbers of Nef-specific CTL cells and plasma viral load was observed.				
Nef (90–97)	Nef (88–95)	FLKEKGGL	HIV-1 infection	human (B8)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (90–97)	Nef (88–95 SF2)	FLKEKGGL	HIV-1 infection	human (B8)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/3 group 2, and 1/2 group 3.				
Nef (90–97)	Nef (89–97)	FLKEKGGL	HIV-1 infection	human (B8)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α				
Nef (90–97)	Nef (90–97)	FLKEKGGL	HIV-1 infection	human (B8)	Day2001
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual. • The response to FLKEKGGL was the second highest response in magnitude compared to all the HLA class I A- and B-restricted epitopes tested in this individual.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Goulder2000b
	• Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection.				
Nef (90–97)	Nef (90–97 BRU)	FLKEKGGL	HIV-1 infection	human (B8)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FLKEKGGL was recognized in 12/14 (86%) of individuals with HLA B8, and it was a high affinity HLA binder.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Oxenius2002b
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** FLK. • Using previously defined epitopes [Oxenius2000, Oxenius2001a] in an IFNgamma Elispot assay, 13 chronically HIV-1 infected patients were studied over a period including therapy with standard treatment interruptions (STI). • STIs induced increased recognition of CTL epitopes, but there was no correlation between CTL responses with viral rebound rates, plateau viral loads, or clearance rates.				
Nef (90–97)	Nef	FLKEKGGL	HIV-1 infection	human (B8)	Appay2002
	Keywords HAART. **Donor HLA** A2,A11,B8,B60,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized FLKEKGGL. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.				
Nef (90–97)	Nef **Keywords** HAART. **Donor HLA** A1,A3,B8,B65,Bw6. • Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART. • Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects – two patients recognized FLKEKGGL. • The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.	FLKEKGGL	HIV-1 infection	human (B8)	Appay2002
Nef (90–97)	Nef **Vaccine** *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000]. • Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].	FLKEKGGL	HIV-1 infection, Vaccine	human, macaque (B8)	Hanke2000, Wee2002
Nef (90–97)	Nef (90–97) **Keywords** binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A3, B8, B62, Cw3, Cw7. • CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.	FLKEKGGL	HIV-1 infection	human (B8)	Cao2003
Nef (90–100)	Nef (90–100 BRU) **Keywords** binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.	FLKEKGGLEGL	HIV-1 infection	human (A2)	Choppin2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • FLKEKGGLEGL was recognized in 8/12 (67%) of individuals with HLA A2. It was a low affinity HLA A2 binder.				
Nef (90–104)	Nef (90–105 HXB2)	FLKEKGGLEGLIHSQ	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • Responses to this peptide were detected in 16% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
Nef (92–100)	(LAI)	KEKGGLEGL		human (B*4001)	Frahm2004
	• C. Brander notes this is a B*4001,B60 epitope.				
Nef (92–100)		KEKGGLEGL	HIV-1 infection	human (B*4002)	Sabbaj2002b
	Keywords HAART. **Epitope name** Nef-KL9. **Donor HLA** A*0201 A*3201 B*4002 B*5301 Cw*0202 Cw*0401. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Patient 01RCH59 was Hispanic, not on HAART, and had a viral load of 5100 and CD4 count of 349 – she also recognized TERQANFL, p2p7p1p6(64-70), HLA-B*4002 and AEWDRVHPV, p24(78-86), HLA-B*4002. • Among HIV+ individuals who carried HLA B40, 3/5 (60%) recognized this epitope.				
Nef (92–100)	Nef (92–100)	KEKGGLEGL		human (B*4002)	Frahm2004
Nef (92–100)	Nef (90–98 SF2)	KEKGGLEGL	HIV-1 infection	human (B60)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 2/2 group 1, 1/1 group 2, and 0/0 group 3.				
Nef (92–100)	Nef	KEKGGLEGL	HIV-1 infection	human (B60)	Cao2002
	Keywords epitope processing.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• KM is a B60 restricted CTL clone that recognizes KEKGGLEGL. • CTL could be activated by a fusion protein of an HIV protein and anthrax lethal factor (LFn-HIV) that promotes antigen presenting cell uptake of exogenous protein and allows processing through the MHC class I pathway. This strategy for CTL detection could allow antigen presentation without generation of cells by the standard methods of using live viral vectors carrying a protein, or by loading the cells with peptides and by-passing processing.				
Nef (92–100)	Nef (92–100 NL-43)	KEKGGLEGL	HIV-1 infection	human (B60)	Ali2003
	Keywords class I down-regulation by Nef, escape. • NL43 was passaged in the presencNL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days. • NL43 was also passaged in the presence of a Nef TQGYFPDWQNY-specific CTL clone. 7/15 clones had a frameshifting or stop codon introduced by one week; F121T was also observed. The most common escape mutation for both Nef epitopes was an early stop codon at position 91. • Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51. • Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNVATL in p17 Gag.				
Nef (92–100)	Nef	KEKGGLEGL	HIV-1 infection	human (B60)	Montefiori2003
	Keywords supervised treatment interruptions (STI), early treatment. **Epitope name** KL9. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A2, A24, B38, B60, Cw2, Cw12. • HIV-1+ patient AC10 underwent early HAART treatment, which was discontiuned 1.5 years later. At this timepoint potent NAb responses against autologous virus were detected. Treatment interruption initially induced weak CD8+ responses directed against 5 epitopes. By days 873d and 923d the CTL response had broadened to target 22 epitopes; of these six were fully characterized. Eventually the virus escaped the NAb response, but escape was not accompanied by a rise in viral load, and the authors suggest the virus was contained by the CTL response.				
Nef (92–100)	Nef (92–100 NL43)	KEKGGLEGL	HIV-1 infection	human (B60)	Yang2003
	Keywords escape. **Epitope name** KL9. **Assay type** Chromium-release assay, CTL suppression of replication. • Virus was cultured in the presence of CTL lines specific for 5 different epitopes (SLYNTVATL, ILKEPVHGV, IEIKDTKEAL, SEGATPQDL, and KEKGGLEGL) to study the emergence of escape mutations. Escape varied between clones for the same epitope, and between different epitopes. Gag and RT epitope escape, if it occurred at all, tended to be monoclonal and within the epitope, indicating strong fitness constraints, while the Nef epitope escape was rapid, polyconal, and sometimes the result of upstream frameshifts. • Two cloned CTL lines recongized KEKGGEGL, STD11 and KM3. Highly resistant clones emerged after a single round of passage with both CTL clones, and multiple substitutions accrued including frameshits and stop codons, reflecting the dispensability of Nef in viral culture. • The following epitope variants were observed after passaging with clone STD11 for one week: kekggegI, kKkggegl, and 12/20 frameshifts and 1 early stop. By two weeks, a more complex polyclonal mixture was observed including: kekggegI, kKkggegl kekggegP, kekggeEl, kekggeRl, kekRgeRl, keNggeRl, and 11/22 framshifts.				
Nef (92–100)	Nef (SF2)	KEKGGLEGL	HIV-1 infection	human (B60(B*4001)	Altfeld2000b
	• This epitope was the dominant B60 (encoded by B*4001) response in 6/8 HLA-B60 individuals, and recognized in all eight.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope was also recognized two expressing HLA-B61 individuals (B61 is usually encoded by B*4002, but this study did not distinguish between B*4002, B*4003, B*4004, B*4006, and B*4008) • ELISPOT was a rapid an effective method that was used to define five novel B60 epitopes. • HLA-B60 is present in 10-20% of the Caucasoid population and B60/B61 are very common in Asian populations.				
Nef (92–100)	Nef (92–100)	KEKGGLEGL	HIV-1 infection	human (B60/B61)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to five B61-restricted epitopes tested. • All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response.				
Nef (92–112)	Nef (SF2)	KEKGGLEGLIHSQRRQDIL-DL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual. • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
Nef (92–112)	Nef (SF2)	KEKGGLEGLIHSQRRQDIL-DL	HIV-1 infection	human	Altfeld2000b
	• This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by another HLA molecule in an HLA-B60 individual. • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined.				
Nef (93–106)	Nef (93–106 BRU)	EKGGLEGLIHSQRR	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.				
Nef (97–111)	Nef (97–111)	LEGLIYSKKRQEILD	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons. • HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (102–115)	Nef (102–115 LAI)	HSQRRQDILDLWIY	HIV-1 infection	human (B7)	Goulder1997e, Goulder1997a
	Keywords review, escape. • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. • One had a strong response to this peptide, the other did not. • [Goulder1997a] is a review of immune escape that summarizes this study.				
Nef (102–121)	Nef (101–120 SF2)	HSQRRQDILDLQIYHTQGYF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • Two of these 11 had CTL response to this peptide. • The responding subjects were HLA-A2, A3, B8, B62 and HLA-A2, B21.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (103–127)	Nef (103–127 PV22)	SQRRQDILDLWIYHTQGYF-PDWQNY	HIV-1 infection	human (B13)	Jassoy1993
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF.				
Nef (103–127)	Nef (103–127)	SQRRQDILDLWIYHTQGYF-PDWQNY	HIV-1 infection	human (B13)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** SQR. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • The only study subject out of eight that was HLA B13+ recognized this epitope. • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIY-HTQGYFPDWQNY, and GEIYKRWII peptides and all responses declined during therapy initiated at day 390 but were restored when therapy become intermittent.				
Nef (105–114)	Nef (105–114 LAI)	RRQDILDLWI	HIV-1 infection	human (B*2705)	Goulder1997c
	Keywords rate of progression. • Defined as optimal epitope from within reactive peptide HSQRRQDILDLWIYHTQGYF [Nef(102-121 LAI)] • HLA-B*2705 is associated with slow HIV disease progression. • The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position.				
Nef (105–114)	Nef (105–114 LAI)	RRQDILDLWI	HIV-1 infection	human (B*2705)	Frahm2004
	• C. Brander notes this is a B*2705 epitope.				
Nef (105–114)	Nef (105–114 SF2)	RRQDILDLWI	HIV-1 infection	human (B27)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3.				
Nef (105–114)	Nef (105–114)	RRQDILDLWI	HIV-1 infection	human (B27)	Day2001
	• B27-restricted CTL response was strongest to this epitope in one individual.				
Nef (105–114)		RRQDILDLWI	HIV-1 infection	human (B27)	Sabbaj2002b
	Epitope name Nef-RI10. • Among HIV+ individuals who carried HLA B27, 1/2 (50%) recognized this epitope.				
Nef (105–115)	Nef (105–115)	KRQEILDLWVY		human (Cw*07)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (105–115)	Nef (105–115)	RRQDILDLWIY		human (Cw*07)	Frahm2004
Nef (105–115)	Nef (105–115)	RRQDILDLWIY	HIV-1 infection	human (Cw7)	Yu2002a
	Keywords dynamics, supervised treatment interruptions (STI), acute infection. **Epitope name** Cw7-RY11. **Donor HLA** A3, B7, Cw7. • AC-06 was homozygous at all three class I alleles (A3, B7, Cw7), and was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 response to RRQDILDLWIY restricted by HLA-Cw7.			
Nef (105–119)	Nef (105–119 HXB2)	RRQDILDLWIYHTQG	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 19% of the study subjects, and it was one of the 25 most frequently recognized peptides.			
Nef (106–115)	(LAI)	RQDILDLWIY		(B7)	Frahm2004, Goulder1999a
Nef (108–115)		DILDLWIY	HIV-1 infection	human (Cw*0701)	Sabbaj2002b
	Keywords HAART. **Epitope name** Nef-DY8. **Donor HLA** A*3303 A*2601 B*5801 B*8201 Cw*0302 Cw*0701. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 03RCH40 was African American, had a viral load of 2500, CD4 count of 372, was not on HAART, and also recognized the epitope ETKLGKAGY, RT(449-457), A*2601. • Among HIV+ individuals who carried HLA Cw07, 2/18 (11%) recognized this epitope.			
Nef (108–115)	Nef (108–115)	DILDLWIY	HIV-1 infection	human (Cw7)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A1, A1, B8, B14, Cw7, Cw8.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• CTL epitope responses were mapped in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized tended not to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently recognized than A1, A2, A30, and A44.				
Nef (112–126)	Nef (112–126) **Keywords** inter-clade comparisons.	LWVYHTQGYFPDWQN	HIV-1 infection	human	Novitsky2002
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein. • Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses. • This peptide was among the 28 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (112–133)	Nef (111–132)	LWIYHTQGYFPDWQNYTPG-PGV	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
Nef (112–133)	Nef (111–132 SF2)	LWIYHTQGYFPDWQNYTPG-PGV	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • Four of these 11 had CTL response to this peptide. • The responding subjects were HLA-A2, B21; HLA-A1, A3, B7, B15; HLA-A2, A26, B7, B38.				
Nef (112–133)	Nef (111–132 SF2)	LWIYHTQGYFPDWQNYTPG-PGV	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
Nef (113–125)	Nef (113–125 BRU)	WIYHTQGYFPDWQ	HIV-1 infection	human (B17)	Culmann1989
	• Nef CTL clones from HIV+ donors.				
Nef (113–127)	Nef (128–142) **Keywords** inter-clade comparisons.	WIYHTQGYFDPWQNY	HIV-1 infection	human	Guimaráes2002
	• Nef sequences were obtained from Brazilians to study epitope diversity in this geographic region – WIYHTQGYFDPWQNY displayed an (H) to (N) substitution in Brazilian Nef-gene subtype C samples, and this substitution is often found in other subtypes tested.				
Nef (113–128)	Nef (113–128 BRU)	WIYHTQGYFPDWQNYT	HIV-1 infection	human (A1)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.				
Nef (113–128)	Nef (113–128 LAI) **Keywords** HAART. **Epitope name** N2.	WIYHTQGYFPDWQNYT	HIV-1 infection	human (A1)	Mollet2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
Nef (114–127)	Nef	VYHTQGYFPDWQNY	HIV-1 infection	human	Jubier-Maurin1999
Nef (115–125)	Nef (115–125 BRU) • Nef CTL clones from HIV+ donors.	YHTQGYFPDWQ	HIV-1 infection	human (B17)	Culmann1991
Nef (115–129)	Nef (115–129 HXB2) **Keywords** supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2. • Responses to this peptide were detected in 22% of the study subjects, and it was one of the 25 most frequently recognized peptides.	YHTQGYFPDWQNYTP	HIV-1 infection	human	Addo2003
Nef (116–124)	Nef (116–124)	HTQGYFPDW		human (B*57)	Frahm2004
Nef (116–124)	Nef (116–124)	HTQGYFPDW		human (B*57)	Frahm2004
Nef (116–125)	Nef (116–125 BRU) **Keywords** inter-clade comparisons. • C. Brander notes this is a B*5701 epitope. • Subtype of B57 not determined.	HTQGYFPDWQ	HIV-1 infection	human (B*5701)	Frahm2004
Nef (116–125)	Nef (116–125) **Keywords** immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • One of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others.	HTQGYFPDWQ	HIV-1 infection	human (B57)	Betts2000
Nef (116–125)	Nef (116–125 BRU) • Nef CTL clones from HIV+ donors, optimal peptide mapped.	HTQGYFPDWQ	HIV-1 infection	human (B57)	Culmann1991
Nef (116–125)	Nef (116–125) **Keywords** HAART, acute infection.	HTQGYFPDWQ	HIV-1 infection	human (B57)	Oxenius2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name HTQ. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B57+				
Nef (116–125)		HTQGYFPDWQ	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Nef-HQ10. • Among HIV+ individuals who carried HLA B57, 0/5 (0%) recognized this epitope.				
Nef (117–127)	Nef (117–127)	TQGYFPDWQNY	HIV-1 infection	human	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA Bw62 epitope TQGYFPDWQNY, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one.				
Nef (117–127)	Nef (117–127 LAI)	TQGYFPDWQNY	HIV-1 infection	human (B*1501)	Frahm2004
	• C. Brander notes this is a B*1501 epitope.				
Nef (117–127)	Nef (117–127 NL-43)	TQGYFPDWQNY	HIV-1 infection	human (B*1501)	Ali2003
	Keywords class I down-regulation by Nef, escape. • NL43 was passaged in the presencNL43 was passaged in the presence of Nef KEKGGLEGL-specific CTL clones STD11 and KM3, rapid selection of escape mutations, including E93G, E93K, K94N+G99R, G95R+G99R, E98K, E98D, G99R, G99E, L100P, and L100I; insertions, deletions, frameshifts and an early stop codon. 34/36 (94%) of sequences carried mutations in the epitope by seven days, 36/36 (100%) by 14 days. • NL43 was also passaged in the presence of a Nef TQGYFPDWQNY-specific CTL clone. 7/15 clones had a frameshifting or stop codon introduced by one week; F121T was also observed. The most common escape mutation for both Nef epitopes was an early stop codon at position 91. • Several mutations selected by KEKGGLEGL-specific CTL were shown to impair the down regulation of class I MHC by Nef, in particular E93G, E93K, and a truncation mutation at position 51. • Nef deletion mutants increased 100-fold NL-43 susceptibility to inhibition by CTL specific for epitopes in other proteins, the A2 epitopes ILKEPVHGV in RT and SLYNVATL in p17 Gag.				
Nef (117–127)	Nef (117–127)	TQGYFPDWQNY	HIV-1 infection	human (B62)	Day2001
	Keywords immunodominance. • No immunodominant responses were detected to four B62-restricted epitopes tested.				
Nef (117–127)	Nef (117–127 LAI)	TQGYFPDWQNY	HIV-1 infection	human (Bw62)	Culmann1998
	• Optimal peptide defined by titration.				
Nef (117–128)	Nef (117–128 BRU)	TQGYFPDWQNYT	HIV-1 infection	human (B17, B37)	Culmann1991
	• Nef CTL clones from HIV+ donors.				
Nef (117–147)	Nef (117–147 LAI)	TQGYFPDWQNYTPGPGVRY-PLTFGWCYKLVP	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide. • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual. • 10/12 tested had an IgG response to this peptide.				
Nef (118–127)	Nef (118–127 LAI)	QGYFPDWQNY		human (Bw62)	McMichael1994
	Keywords review. • Review of HIV CTL epitopes.				
Nef (120–128)	Nef (120–128)	YFPDWQNYT	HIV-1 infection	human	Betts2000
	Keywords immunodominance. • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant. • 95 optimally-defined peptides from this database were used to screen for INFγ responses to other epitopes. • 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA B37 epitope IYKRWIILGL, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one.				
Nef (120–128)	Nef (120–128)	YFPDWQNYT	HIV-1 infection	human (A*29)	Frahm2004
Nef (120–128)	Nef (118–126 SF2)	YFPDWQNYT	HIV-1 infection	human (A1)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A1+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/2 group 2, and 1/2 group 3.				
Nef (120–128)	Nef (120–128 LAI)	YFPDWQNYT	HIV-1 infection	human (B*3701)	Frahm2004
	• C. Brander notes this is a B*3701 and B*5701 epitope.				
Nef (120–128)	Nef (120–128 LAI)	YFPDWQNYT	HIV-1 infection	human (B*5701)	Frahm2004
	• C. Brander notes this is a B*5701 epitope. • Subtype of B57 not determined.				
Nef (120–128)	Nef (120–128 IIIB)	FFPDWKNYT	HIV-1 infection	human (B15)	Wilson1999a
	Keywords responses in children, mother-to-infant transmission, escape. • This study describes maternal CTL responses in the context of mother-to-infant transmission. • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants. • LFPDWKNYT is an escape mutant.				
Nef (120–128)	Nef (120–128 LAI)	YFPDWQNYT	HIV-1 infection	human (B37, B57)	Culmann1998
	• Nef CTL clones from HIV+ donors – optimum peptide mapped by titration.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (120–128)		YFPDWQNYT	HIV-1 infection	human (B57)	Sabbaj2002b
	Epitope name Nef-YT9.				
	• Among HIV+ individuals who carried HLA B57, 1/5 (20%) recognized this epitope.				
Nef (120–144)	Nef (120–144 SF2)	YFPDWQNYTPGPGIRYPLT-FGWCYK	HIV-1 infection	human (A24)	Jassoy1992
	• Epitope recognized by CTL clone derived from CSF.				
Nef (122–136)	Nef (122–136)	PDWQNYTPGPGVRYP	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons.				
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.				
	• Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.				
	• This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				
Nef (122–141)	Nef (121–140 SF2)	PDWQNYTPGPGVRYPLTFGW	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein.				
	• Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef.				
	• Three of these 11 had CTL response to this peptide.				
	• The responding subjects were HLA-A2, B21; HLA-A3, A24, B7, B38.				
Nef (123–137)	Nef (123–137 IIIB)	QWQNYTPGPGVRYPL	HIV-1 infection	human	Wilson1996
	Keywords responses in children, mother-to-infant transmission, escape.				
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study.				
	• FFPDYTPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in mother and are not recognized.				
	• LFPDYKPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in infant and are not recognized.				
Nef (126–135)	Nef (126–135 BRU)	NYTPGPGVRY	HIV-1 infection	human (A24)	Choppin2001
	Keywords binding affinity, epitope processing.				
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.				
	• 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.				
	• NYTPGPGVRY was recognized in 3/10 (30%) of individuals with HLA A24. It was a moderate affinity HLA-A24 binder.				
Nef (126–138)	Nef (126–138 BRU)	NYTPGPGVRYPLT	HIV-1 infection	human (B7)	Culmann1991
	• Nef CTL clones from HIV+ donors.				
Nef (127–141)	Nef (127–141)	YTPGPGVRYPLTFGW	HIV-1 infection	human	Novitsky2002
	Keywords inter-clade comparisons.				
	• HLA, viral sequence, and Elispot data was obtained from 105 HIV-1 positive Botswanans; Elispot data was obtained from between 55 and 64 subjects for each HIV protein.				
	• Nef and p24 had the highest percentage of reactive peptides, and p24 had the highest magnitude of HIV-1 responses.				
	• This peptide was among the 8 most reactive C clade peptides from among over 350 tested spanning all HIV proteins.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (128–135)	Nef (128–135 LAI)	TPGPGVRY	in vitro stimulation or selectio	human (B*0702)	Lucchiari-Hartz2000
	Keywords epitope processing. • Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152. • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments. • Both TPGPGVRYPL and TPGPGVRY are naturally processed ligands that can be eluted from HLA-B7 molecules, both are recognized by the same CTL, and both peptides seem to be the direct product of a proteasomal digest. • The peptide TPGPGVRY is present in a high copy number, TPGPGVRYPL at a more moderate level, possibly due to a major cleavage site between the Y and P.				
Nef (128–136)		TPGPGVRYP	HIV-1 infection	human (B07)	Sabbaj2002b
	Epitope name Nef-TP9. • Among HIV+ individuals who carried HLA B07, 4/9 (44%) recognized this epitope.				
Nef (128–137)	Nef	TPGPGIRYPL	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was recognized by 1/22 HEPS control sex workers, ML851.				
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL	HIV-1 infection	human (B*0702)	Frahm2004
	• C. Brander notes this is a B*0702 epitope.				
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL	in vitro stimulation or selectio	human (B*0702)	Lucchiari-Hartz2000
	Keywords epitope processing. • Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152. • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments. • Both TPGPGVRYPL and TPGPGVRY are naturally processed ligands that can be eluted from HLA-B7 molecules, both are recognized by the same CTL, and both peptides seem to be the direct product of a proteasomal digest. • The peptide TPGPGVRY is present in a high copy number, TPGPGVRYPL at a more moderate level, possibly due to a major cleavage site between the Y and P.				
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL		human (B*4201)	Frahm2004
	• C. Brander notes this is a B*4201 epitope.				
Nef (128–137)	Nef (128–137 BRU)	TPGPGVRYPL	HIV-1 infection	human (B35)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • TPGPGVRYPL was recognized in 8/16 (50%) of individuals with HLA B7, and 1/9 (11%) of individuals with HLA B35. It was a high affinity HLA binder.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (128–137)		TPGPGVRYPL	HIV-1 infection	human (B7)	Wilson2000a
Keywords acute infection. • Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found. • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39. • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK. • The subject with A*0201 had a moderately strong response to SLYNTVATL. • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705. • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL.			
Nef (128–137)	Nef (128–137 LAI)	TPGPGVRYPL	HIV-1 infection	human (B7)	Haas1996, Haas1997
• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection. • The epitope position was taken from [Haas1997]					
Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7)	Rowland-Jones1998a
Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The D subtype consensus is identical to the B clade epitope. • The A subtype consensus is TPGPGIRYPL.					
Nef (128–137)	Nef (subtype B)	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7)	Rowland-Jones1998b
Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among B and D clade viruses. • The Clade A version of the epitope: TPGPGIRYPL.					
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	in vitro stimulation or selectio	human (B7)	Wilson1999b
Keywords immunodominance, dendritic cells, Th1. • Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors. • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within. • CTL from a B7 donor displayed no reactivity to this epitope, although it had been immunodominant in another study [Haas1996]					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (128–137)	Nef (128–137 SF2)	TPGPGVRYPL	HIV-1 infection	human (B7)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3.			
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	HIV-1 infection, HIV-1 exposed seronegative	human (B7)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B7 women, 4/5 HEPS and 5/6 HIV-1 infected women recognized this epitope. • The dominant response to this HLA allele was to this epitope in 3 of the 4/5 HEPS cases and in 2 of the 5/6 HIV-1 infected women. • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPG(V/I)RYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV.			
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	HIV-1 infection	human (B7)	Appay2000
	• Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T cells specific for HIV and CMV. • HIV-specific CD8+ T cells expressed lower levels of perforin than CMV-specific CD8+ T cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation. • In most donors, between 50% and 95% of the activated virus-specific CD8+ T cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α			
Nef (128–137)	Nef (128–137)	TPGPGVRYPL	HIV-1 infection	human (B7)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person. • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes. • An acute seroconvertor homozygous for the B7 allele recognized five B7-restricted epitopes. • The other acute seroconvertor failed to recognize any of the 11 B7-restricted epitopes tested. • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (128–137)	Nef (128–137 BRU)	TPGPGVRYPL	HIV-1 infection	human (B7)	Choppin2001

Keywords binding affinity, epitope processing.

- Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein.
- 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing.
- TPGPGVRYPL was recognized in 8/16 (50%) of individuals with HLA B7, and 1/9 (11%) of individuals with HLA B35. It was a high affinity HLA binder.

Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 infection	human (B7)	Yu2002a

Keywords dynamics, supervised treatment interruptions (STI), acute infection.
Epitope name B7-TL10.
Donor HLA A3, B7, Cw7.

- CTL responses in 18 acutely HIV-infected HLA-A3 (n=7) or -B7 (n=4) or both -A3 and B7 (n=7) positive individuals were studied.
- One individual, AC-06, was homozygous at all three class I alleles (A3, B7, Cw7), was treated during acute infection and had supervised treatment interruptions (STI). He had only two detectable CTL responses during acute infection, but after STI this broadened to 27 distinct epitopes including 15 restricted by HLA-A3, 11 by HLA-B7, and 1 by HLA-Cw7.
- 0/11 HLA-B7 individuals had detectable B7-restricted responses to this epitope during acute infection – 10/15 of HLA-B7 epitopes tested were targeted by at least one person during acute infection. 2/4 individuals had detectable responses to this epitope after STI.

Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 infection	human (B7)	Appay2002

Keywords HAART.
Donor HLA A2,A3,B7,Bw6.

- Four HIV patients with prolonged clinically successful anti-viral therapy but with ongoing evidence of replication and Nef mRNA transcription, showed specific T-cell responses by Elispot and Tetramer staining, maintained for 2-4 years after initiation of HAART.
- Nef epitope recognition was detected in all 4 subjects, gp120, Pol and Gag-specific in 1 or 2 subjects.
- The HIV-specific CD8+ T-cells had an intermediate maturation phenotype characterized by low levels of perforin and high levels of CD27 expression.

Nef (128–137)	Nef	TPGPGVRYPL	HIV-1 infection, Vaccine	human, macaque (B7)	Hanke2000, Wee2002

Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag
Keywords inter-clade comparisons, epitope processing, vaccine-specific epitope characteristics, immunodominance.

- The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].
- Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].

Nef (128–137)	Nef (subtype B)	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7(*8101))	Rowland-Jones1998b

Keywords inter-clade comparisons.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • Clade A version of the epitope: TPGPGIRYPL, clade D version: TPGPGIRYPL.				
Nef (128–137)	Nef (128–137 subtype B)	TPGPGVRYPL	HIV-1 exposed seronegative	human (B7, B*8101)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
Nef (130–139)	Nef (130–139 BRU)	GPGVRYPLTF	HIV-1 infection	human (B35)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • GPGVRYPLTF was recognized in 0/10 (0%) of individuals with HLA B7, and 1/11 (9%) of individuals with HLA B35, although it was a high affinity HLA binder.				
Nef (130–143)	Nef (130–143 LAI)	GPGVRYPLTFGWCY	HIV-1 infection	human (B*57)	Goulder1996b
	• CTL response to this epitope observed in 4 long-term survivors. • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations.				
Nef (130–143)	Nef (121–141)	GPGVRYPLTFGWCY	HIV-1 infection	human (B57)	Ferrari2000
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles.				
Nef (130–144)	Nef (130–144 HXB2)	GPGVRYPLTFGWCYK	HIV-1 infection	human	Addo2003
	Keywords supervised treatment interruptions (STI), immunodominance, early treatment. **Assay type** T-cell Elispot. • Comprehensive Elispot screening of 504 overlapping peptides that spanned all HIV-1 proteins in 57 HIV-1 infected individuals. Four groups of patients were compared: 23 were untreated; 12 patients were chronically infected and treated; 22 started treatment during acute infection, 11 continuously treated and 11 with STI. • 63% of the peptides were recognized - the most frequent responses were directed against Nef (95%) and p24-Gag (88%). p17 was the most frequently recognized protein after correction for protein length. A median of 18 peptides (range 2-42) were recognized per person. The most frequently (>20%) recognized peptides were located in conserved regions within clade B sequences. Vpu was rarely recognized. • A decrease in the total magnitude and in the breadth of CTL responses was detected in patients with treated acute infection in comparison to chronically infected treated or untreated individuals. No correlation between plasma viral load and HIV-1 specific T-cell responses was observed. • The authors did not note the reference strain, but based on the peptide sequences provided it appears to be HXB2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responses to this peptide were detected in 24% of the study subjects, and it was one of the 25 most frequently recognized peptides.				
Nef (132–144)	Nef	GIRYPLTFGWCFK		human	Jubier-Maurin1999
	Keywords inter-clade comparisons. • 41 new HIV-1 strains describing envelope subtypes of HIV-1 A-H were genetically characterized in the nef region – 34 subtypes were classified in the same subtype in nef and env and 7 of the 41 strains were recombinants. • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes.				
Nef (132–147)	Nef (132–147 BRU)	GVRYPLTFGWCYKLVP	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs.				
Nef (132–147)	Nef (132–147 BRU)	GVRYPLTFGWCYKLVP	HIV-1 infection	human (B18)	Culmann1991
	• Nef CTL clones from HIV+ donors.				
Nef (132–147)	Nef (132–147)	GVRYPLTFGWCYKLVP	Vaccine	mouse (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18 **Keywords** Th1. • DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization. • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost. • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-gamma) • Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.				
Nef (133–141)	Nef (133–141)	TRYPLTFGW	HIV-1 infection	human (A*3303)	Frahm2004
Nef (133–148)	Nef (133–148 LAI)	VRYPLTFGWCYKLVPV		human (B57)	Brander1996b
	• P. Goulder, pers. comm.				
Nef (134–141)	Nef (138–147 LAI)	RYPLTFGW	HIV-1 infection	human (A*2402)	Frahm2004
	• C. Brander notes this is an A*2402 epitope.				
Nef (134–141)	Nef (138–147 SF2)	RYPLTFGW	HIV-1 infection	human (A24)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3.				
Nef (134–141)	Nef	RYPLTFGW	HIV-1 infection	human (A24)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** A24-RW8(Nef). **Donor HLA** A24,A?,B7,B27.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient C displayed the greatest response to B27-KK10(p24), and in decreasing order also responded to A24-RW8(Nef), B7-IL9(gp41), A24-RL9(gp41), A24-YL8(gp41), and B7-TM9(Nef).			
Nef (134–141)	Nef (134–141)	RYPLTFGW	HIV-1 infection	human (A33)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A3, A33, B14, B35, Cw*0401, Cw*0802. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.			
Nef (134–141)	Nef (134–141 LAI)	RYPLTFGW		human (B27)	Culmann1998
	• Optimal peptide defined by titration.				
Nef (134–143)	Nef (138–147 SF2)	RYPLTFGWCF	HIV-1 infection	human (A*2402)	Ikeda-Moore1997
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402. • This peptide induced CTL in 3/4 HIV-1+ people tested. • RYPLTFGWCF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained.				
Nef (134–143)	Nef (138–147)	RYPLTFGWCF	Vaccine	human (A*2402)	Kawana-Tachikawa2002
	Vaccine *Vector/Type:* Sendai virus vector system (SeV) **Epitope name** Nef138-10. • A Sendai virus vector system (SeV) was developed that expressed HLA-A*2402-restricted class I/peptide complexes; this system could be used to detect responses and has the potential to elicit immune responses. • MHC class I/peptide tetramers could be made using this system that bound to epitope-specific CTLs in PBMCs. • Cells transfection with SeV modified to express A*2402-HIV epitope complexes induced CTL mediated specific cell lysis.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (134–143)	Nef (134–143 BRU)	RYPLTFGWCY	HIV-1 infection	human (A24)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • RYPLTFGWCY was recognized in 5/12 (42%) of individuals with HLA A24. It was a moderate affinity HLA-A24 binder.			
Nef (134–144)	Nef (134–144 LAI)	RYPLTFGWCYK	HIV-1 infection	human (B18)	Couillin1994, Goulder1997a
	Keywords review, escape. • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response. • [Goulder1997a] is a review of immune escape that summarizes this study.				
Nef (134–144)	Nef (134–144)	RYPLTFGWCYK	HIV-1 infection	human (B18)	Oxenius2000
	Keywords HAART, acute infection. **Epitope name** RYP. • Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • None of the 8 study subjects recognized this epitope but none were HLA B18+				
Nef (135–143)	Gag (p17)	YPLTFGWCF	HIV-1 infection	human (A2)	Kaul2003
	Keywords immunodominance, genital and mucosal immunity. **Assay type** Intracellular cytokine staining. • Predefined immunodominant peptide responses were used to compare CD8+ T cells responses in the blood and cervix of 16 HIV+ Kenyan sex workers. Cervical responses were detected in 8/10 women from whom adequate samples could be obtained. The frequency of the CD8+ T cell response in the genital tract was comparable to the blood, with a trend toward being slightly higher. • The immunodominant response was to this epitope in the PBMC of 1/16 patients (Kaul *et al.* 2001, AIDS, 107:1303).				
Nef (135–143)	Nef (135–143 LAI)	YPLTFGWCY	in vitro stimulation or selectio	human (B*0702)	Lucchiari-Hartz2000
	Keywords epitope processing. • Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152. • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments. • YPLTFGWCY is the naturally processed ligand for B7, and this epitope is the only one of the five that may require trimming at the N-termini. • YPLTFGWCY is present in low copy number in the cell, possibly due to a predominant proteasomal cleavage site between Y and P.				
Nef (135–143)	Nef (135–143 LAI)	YPLTFGWCY	HIV-1 exposed seronegative	human (B*1801)	Frahm2004
	• C. Brander notes this is a B*1801 epitope.				
Nef (135–143)	Nef (135–143)	YPLTFGWCF		human (B*53)	Frahm2004
Nef (135–143)	Nef (135–143)	YPLTFGWCY		human (B*5301)	Frahm2004

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (135–143)		YPLTFGWCY	HIV-1 infection	human (B*5301, B35)	Sabbaj2002b
	Keywords HAART. **Epitope name** Nef-YY9. **Donor HLA** A*3002 A*3201 B*4501 B*5301 Cw*0401 Cw*1202. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • Subject 00RCH33 was on HAART had a viral load of 2900 and CD4 count of 727 and also recognized the epitopes HIGPGRAFY, gp160(310-318), HLA A*3002; AETFYVDGA, RT(437-445), HLA B*4501; and RSLYNTVATLY, p17(76-86), HLA A*3002. • Among HIV+ individuals who carried HLA B53, 8/15 (53%) recognized this epitope – one subject also carried B7, previously shown to restrict this epitope. • Among HIV+ individuals who carried HLA B35, 13/19 (68%) recognized this epitope.			
Nef (135–143)	Nef (subtype D)	YPLTFGWCF	HIV-1 exposed seronegative	human (B18)	Kaul2000
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses. • Low risk individuals did not have such CD8+ cells. • CD8+ T cell epitopes: DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women.				
Nef (135–143)	Nef (135–143 LAI)	YPLTFGWCY	HIV-1 exposed seronegative	human (B18)	Culmann1991, Culmann-Penciolelli1994
	• Nef CTL clones from HIV+ donors.				
Nef (135–143)	Nef (135–143 SF2)	YPLTFGWCY	HIV-1 infection	human (B18)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B18+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 1/2 group 2, and 0/0 group 3.				
Nef (135–143)	Nef	YPLTFGWCF	HIV-1 infection	human (B18)	Kaul2002
	Keywords HIV exposed persistently seronegative (HEPS). • Neisseria gonorrhea cervititis in 9 HIV+ Kenyan sex workers caused a functional deficiency in IFN-gamma production in HIV-1 epitope-specific CD8+ T-cells, detected by intracellular cytokine production and tetramer assays, while not affecting the total number of epitope-specific CTLs. • Ghonorrhea caused the weaker HIV-1 specific CTL responses in 4 HIV-1 exposed persistently seronegative (HEPS) women to become undetectable by Elispot and tetramer assays, and CMV-specific CTL in 2 HEPS subjects were shown to have impaired function with regard to IFN-gamma production.				
Nef (135–143)	Nef	YPLTFGWCY	HIV-1 infection	human (B18)	Altfeld2002
	Keywords HAART, supervised treatment interruptions (STI). **Epitope name** B18-YY9(Nef). **Donor HLA** A30,A32,B18,B27.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peripheral blood (PB) and lymph node (LN) CD8+ T-cell responses were compared in 15 asymptomatic HIV-1 infected patients using all known optimal CTL epitopes (http://hiv-web.lanl.gov/content/hiv-db/REVIEWS/brander2001.html) for each person's class I HLA alleles. • 60 epitope responses were detected in both PB and LN samples of the 15 patients, and an additional 8 responses were detected only in LN. The total magnitude of the response was similar in LN and PB, but the percentage of CD8+ T cells in the LN is lower so the number of HIV-specific cells per million CD8+ T-cells is higher in the LN. • 1 year post-HAART treatment in five patients studied, the magnitude of the CD8 T-cell response was decreased in both LN and PB, but more dramatically in PB, and 13/25 epitope responses in the PB became undetectable, in contrast to 5/26 in the LN. • Treatment interruption following HAART induced resulted in increased viremia accompanied by the restoration of the detection of 13 epitopes that had become undetectable in the PB, and the addition of 9 novel epitope responses. • Breakdowns of epitope responses were shown for 4 individuals. Patient D displayed the greatest response to B27-KK10 (p24), and also responded to A30-RY11(p17), A32-PW10(RT), A30-KY11(RT), A32-RW10(gp120), and B18-YY9(Nef).				
Nef (135–143)	Nef (135–143)	YPLTFGWCY	HIV-1 infection, HIV-1 exposed seronegative	human (B18, B49)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS), immunodominance. • Variants YPLTFGWC(Y/F) are specific for the B/D clades. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers. • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1 infected women. • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure. • Among HLA-B18 women, 1/4 HEPS and 8/9 HIV-1 infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYVDRF(Y/F)K, while infected women tended to respond to YPLTFGWC(Y/F) • The dominant response to this HLA allele was to this epitope for the one reactive HEPS case and in all 8/9 HIV-1 infected women. • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort.				
Nef (135–143)	Nef (139–147 SF2)	YPLTFGWCF	HIV-1 infection	human (B35)	Shiga1996
	• Binds HLA-B*3501.				
Nef (135–143)	Nef (135–143 BRU)	YPLTFGWCY	HIV-1 infection	human (B35)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • YPLTFGWCY was recognized in 2/13 (15%) of individuals with HLA B7, and 11/14 (79%) of individuals with HLA B35, and it was a moderate affinity HLA binder.				
Nef (135–143)	Nef	YPLTFGWCY	HIV-1 infection	human (B35)	Sabbaj2002a
	Keywords mother-to-infant transmission. **Donor HLA** A3, A11, B35, B51.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• IFNgamma T-cell responses in breast milk of 5 HIV-1 infected women from the US and 6 from Zambia were tested with using Elispot. 11/11 women responded to Gag, 8/11 responded to Pol, 7/11 women to Nef, and 2/5 women to Env peptide pools. These responses were shown to be primarily due to CD8+ T-cells in one woman, and another woman had cytolytic responses measured by Cr-release. • T-cells in breast milk from a volunteer who was HLA A3, A11, B35, B51 induced IFNgamma after stimulation with a peptide that carries known B35 epitope YPLTFGWCY. • The frequencies of responses in the two compartments differed, and 2/4 women that responded to epitopes in Nef 101-205 and Pol 601-710 showed responses in breast milk but no detectable responses in peripheral blood cells.				
Nef (135–143)	Nef	YPLTFGWCY	HIV-1 exposed seronegative	human (B49)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is identical to the B clade epitope. • The D subtype consensus is ypltfgwcF.				
Nef (135–143)	Nef (subtype B)	YLPTFGWCY	HIV-1 exposed seronegative	human (B49)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • This epitope is conserved among A and B clade viruses. • The Clade D version of the epitope, YPLTFGWCF, was preferentially recognized by CTL.				
Nef (135–143)		YPLTFGWCY	HIV-1 infection	human (B49)	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope, YPLTFGWC(Y/F), was recognized in 1/22 HEPS sex worker controls (ML1668)				
Nef (135–143)	Nef (135–143 BRU)	YPLTFGWCY	HIV-1 infection	human (B7)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • YPLTFGWCY was recognized in 2/13 (15%) of individuals with HLA B7, and 11/14 (79%) of individuals with HLA B35, and it was a moderate affinity HLA binder.				
Nef (136–144)	Nef (136–144 BRU)	PLTFGWCYK	HIV-1 infection	human (A3)	Choppin2001
	Keywords binding affinity, epitope processing.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • PLTFGWCYK was recognized in 3/12 (25%) of individuals with HLA A3. It was a low affinity HLA-A3 binder.				
Nef (136–145)	Nef (136–145)	PLTFGWCYKL	in vitro stimulation or selectio	human (A*0201)	Wilson1999b
	Keywords binding affinity, dendritic cells, Th1. • Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors. • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within. • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL. • Noted in Brander *et al.*, 1999 this database, to be A*0201.				
Nef (136–145)	Nef (136–145 LAI)	PLTFGWCYKL		human (A*0201)	Frahm2004
	• C. Brander notes this is an A*0201 epitope.				
Nef (136–145)	Nef (136–145 LAI)	PLTFGWCYKL	in vitro stimulation or selectio	human (A*0201)	Lucchiari-Hartz2000
	Keywords epitope processing. • Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152. • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments. • The CTL that recognized PLTFGWCYKL also recognized PLTFGWCYKLV, and both forms of the epitope are naturally processed and both seem to be the direct product of a proteasomal digest, although in low copy number.				
Nef (136–145)		PLTFGWCYKL	HIV-1 infection	human (A02)	Sabbaj2002b
	Epitope name Nef-PL10. • Among HIV+ individuals who carried HLA A02, 3/29 (10%) recognized this epitope.				
Nef (136–145)	Nef (136–145)	PLTFGWCFKL	HIV-1 infection	human (A2)	Durali1998
	Keywords inter-clade comparisons. • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia. • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested. • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag. • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef. • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env. • Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL.				
Nef (136–145)	Nef (157–166)	PLTFGWCFKL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* DNA prime with vaccinia boost • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice. • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost. • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested. • PLTFGWCFKL was recognized by 1 of the HLA-A2 patients.				
Nef (136–145)	Nef (135–144 93TH253 subtype CRF01)	PLTFGWCYKL	HIV-1 infection	human (A2)	Bond2001
	Keywords inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested. • 0/4 tested FSWs recognized the E clade version of this epitope PLCFGWCFKL, which differs from the previously defined B clade version by two amino acids, PLTFGWCYKL. • This epitope was only conserved in CRF01 (subtype E) and subtype B.				
Nef (136–145)	Nef (136–145)	PLTFGWCYKL	HIV-1 infection	human (A2)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
Nef (136–145)	Nef (136–145 BRU)	PLTFGWCYKL	HIV-1 infection	human (A2)	Choppin2001
	Keywords binding affinity, epitope processing. • Seventy-three 8-11 mer peptides were generated based on putative anchor motifs in the Nef BRU sequence for HLA A2, A3, A24, B7, B8, and B35; these 73 peptides had 81 motifs. 54% bound to the predicted HLA molecule, particularly A2, B7/35, and B8. The strength of HLA-peptide binding was not directly related to the number of individuals that recognized a protein. • 20s proteasome cleavage of the Nef protein positions 66-100 showed a large fraction of peptides were cleaved ending at: 87L, 83A, 81Y, 71P, 68F and 67G. The frequency of recognition may be in part dictated by the cleavage step in processing. • PLTFGWCYKL was recognized in 9/28 (32%) of individuals with HLA A2. It was a low affinity HLA-A2 binder.				
Nef (136–146)	Nef (136–146 LAI)	PLTFGWCYKLV	in vitro stimulation or selectio	human (A*0201)	Lucchiari-Hartz2000
	Keywords epitope processing. • Five naturally processed MHC class I ligands were identified in Nef in the conserved immunogenic region Nef between 123-152. • All five could be transported by TAP, and 4/5 had N-termini that were major cleavage points for the proteasome, only one had extended precursor fragments. • The CTL that recognized PLTFGWCYKL also recognized PLTFGWCYKLV, and both forms of the epitope are naturally processed and both seem to be the direct product of a proteasomal digest, although in low copy number.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (137–145)	Nef (137–)	LTFGWCFKL	HIV-1 infection	human (A2)	Corbet2003
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Nef137. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • 3/17 HIV-infected HLA-A2+ people recognized this epitope.			
Nef (137–145)	Nef (158–166)	LTFGWCFKL	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)			
Nef (137–145)	Nef (139–147 HXB3)	LTFGWCFKL	Vaccine	mouse (HLA-A201 transgenic)	Sandberg2000
	Vaccine *Vector/Type:* DNA, peptide *Strain:* B clade HXB3 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** binding affinity, computational epitope prediction. • Ten Nef 9-mer peptides were predicted to have a strong binding affinity with HLA-A*0201 – of these, four did bind strongly by a T2 class I stabilization assay, several others bound weakly. • A CTL immune response to only 3/10 peptides was detected by a 51Cr-release assay after immunization of HLA-A201 transgenic mice with either nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by gene gun – LTFGWCFKL did not elicit a CTL response. • LTFGWCFKL was also tested by subcutaneous injection of Nef peptides in Freund's adjuvant, because it bound strongly to HLA-A*0201, and the peptide vaccination did elicit a response. • The lack of response to the nef DNA vaccine and the response to the peptide suggests LTFGWCFKL may not be processed.			
Nef (137–146)	Nef (221A)	LTFGWCFKLV	HIV-1 infection	human (A2)	Altfeld2001c
	Keywords binding affinity, inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** Nef-221a. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • 1/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT. • 2/12 acutely infected individuals recognized this epitope. • LTFGWCFKLV binds to five HLA-A2 supertype alleles:A*0203, A*0201 (highest affinity), A*0206, A*6802 and A*0202.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (137–146)	Nef (158–167)	LTFGWCFKLV	HIV-1 infection	human (A2 supertype)	Propato2001
	Keywords supertype, rate of progression. • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested, (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes. • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs. • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus. • This epitope can bind all five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802) • Tetramer staining with A2, beta2microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific sells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population.			
Nef (141–148)	Nef (141–)	WCFKLVPV	HIV-1 infection, Vaccine	human, transgenic mouse (A2)	Corbet2003
	Vaccine *Vector/Type:* peptide *HIV component:* Nef *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Nef141. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This peptide was an intermediate A2 binder that induced a CD8+ T-cell IFN gamma response in 1/6 mice. Responses were detected in 2/17 HIV+ HLA-A2 subjects.				
Nef (162–181)	Nef (161–180)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1995
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide.				
Nef (162–181)	Nef (161–180 SF2)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • One of these 11 had CTL response to this peptide.				
Nef (162–181)	Nef (101–120 SF2)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1997b
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients.				
Nef (162–181)	Nef (161–180 SF2)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • One of these 11 had CTL response to this peptide.				
Nef (166–177)	Nef (160–179 SF2)	HPVSLHGMDDPE	HIV-1 infection	human (B35)	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3.				
Nef (172–191)	Nef (171–190 SF2)	GMDDPEREVLEWRFDSRLAF	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A2, B21.				
Nef (175–184)	Nef (175–184)	DPEKEVLQWK	HIV-1 infection	human (B7)	Jin2000b
	• This a B7 epitope, a subdominant CTL response, was defined by an un-conventional approach used to predict epitopes in an HLA B7+ long-term non-progressor. • Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject, followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes.				
Nef (180–189)	Nef (180–189 LAI)	VLEWRFDSRL	HIV-1 infection	human (A*0201)	Haas1996, Haas1997
	• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection. • Noted in Brander *et al.*, 1999 this database, to be A*0201.				
Nef (180–189)	Nef (180–189 LAI)	VLEWRFDSRL		human (A*0201)	Frahm2004
	• C. Brander notes this is an A*0201 epitope.				
Nef (180–189)	Nef (180–189 LAI)	VLMWQFDSRL	Vaccine	transgenic mouse (A*0201)	Boissonnas2002
	Vaccine *Vector/Type:* peptide *Strain:* natural variants *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** binding affinity, vaccine-specific epitope characteristics. • Ten naturally occurring variants of this epitope were tested for their affinity to HLA-A*0201 and for their ability to induce gamma-IFN and cytotoxic functions through vaccination of HLA-A*0201 transgenic mice. • Only two variants could induce vaccine responses: VLMWQFDSRL, a high affinity binder, and VLQWRFDSRL a medium affinity binder to A*0201. • In vivo priming with Nef peptide VLMWQFDSRL induced cross-reactive CTL to 6/7 peptides tested (AlmwKfdsKl, vlmwKfdsrl, vlmwKfdsKl, vlQwRfdsKl, vlVwrfdTrl, and vlAwKLdsrl but not the LAI peptide vlEwrfdsrl) • In vivo priming with Nef peptide VLQWRFDTRL induced cross-reactive CTL to 3/6 variant Nef peptides (vlMwQfdsrl, vlqwrfdSrl and vlEwrfdsrl).				
Nef (180–189)	Nef (190–198)	VLEWRFDSRL	Vaccine	mouse (A*0201)	Singh2002, Sykes1999
	Vaccine *Vector/Type:* DNA *HIV component:* HIV-1 **Keywords** epitope processing, vaccine-specific epitope characteristics, immunodominance. • C3H (H-2k) transgenic mice carrying a fused HLA-A*0201 alpha1 and alpha2 and H-2Dk alpha3 hybrid class I molecule were immunized using an epidermal gene gun with an ubiquitin expression library of 32 plasmids that spanned the HIV-1 genome. Ubiquitin targets the expressed HIV-1 peptides to the proteasome. • A single immunization with the UB-HIV-1 library vaccine induced potent, stable and multivalent CTL responses against all library members.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Immunodominant epitopes SLYNTVATL (Gag), ILKEPVHGV(Pol), RIQRGPGRAFVTIGK(P18) and AFHHVAREK (Nef) elicited strong CD8+/IFN- responses and stimulated CTL that were functional in a Cr-release assay and against wild type antigen. • The presence of multiple plasmids HLA-A*0201-restricted CTL epitopes did not decrease CTL immunogenicity, and CTL responses to single peptide immunizations were comparable to responses based on mixtures of either 16 or 32 peptides.				
Nef (180–189)	Nef (180–189)	VLEWRFDSRL	in vitro stimulation or selectio	human (A2)	Wilson1999b
	Keywords binding affinity, dendritic cells, Th1. • Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors. • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within. • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL.				
Nef (180–189)	Nef (180–189)	VLEWRFDSRL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* DNA prime with vaccinia boost • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2. • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice. • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost. • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested. • VLEWRFDSRL was recognized by 2 of the HLA-A2 patients.				
Nef (180–189)	Nef (180–189 LAI)	VLEWRFDSRL	HIV-1 infection	human (A2)	Mollet2000
	Keywords HAART. **Epitope name** N3. • A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNgamma production to measure responses. • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished. • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change.				
Nef (180–189)	Nef (179–188 93TH253 subtype CRF01)	VLEWRFDSRL	HIV-1 infection	human (A2)	Bond2001
	Keywords inter-clade comparisons. • More than half of a cohort of HIV+ female sex workers (FSW) from Northern Thailand were HLA-A11 positive, and this study concentrated on A11 epitopes in this group, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 0/4 tested FSWs recognized the E clade version of this epitope VLIWKFDSAL, which differs from the previously defined B clade version by three amino acids, VLEWRFDSRL.				
Nef (180–189)	Nef (180–189)	VLEWRFDSRL	HIV-1 infection	human (A2)	Day2001
	Keywords rate of progression, acute infection. • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who coexpressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • 2 to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person.				
Nef (182–198)	Nef (182–198 BRU)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (A1, B8)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.				
Nef (182–198)	Nef (182–198 LAI)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (A2, A25(10))	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.				
Nef (182–198)	Nef (182–198 BRU)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (A25)	Cheynier1992
	• CTL isolated in children born to HIV-1 positive mothers.				
Nef (182–198)	Nef (182–198 LAI)	EWRFDSRLAFHHVAREL	HIV-1 infection	human (B35)	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.				
Nef (182–198)	Nef (182–198 LAI)	EWRFDSRLAFHHVAREL	Vaccine	mouse (H-2^d)	VanderRyst1998
	Vaccine *Vector/Type:* vaccinia, Mengo virus *Strain:* B clade LAI *HIV component:* Nef • Macaca mulatta did not have a detectable response to Rec Mengo virus-HIV-1 Nef 65-206 vaccine. • BALB/c mice had a weak response to this epitope in the Mengo virus construct – in contrast, HIV-1 Nef induces a strong CTL response in mice when presented in a vaccinia background.				
Nef (182–201)	Nef (191–205 SF2)	EWRFDSRLAFHHVARELHPE	HIV-1 infection	human	Lieberman1997a
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein. • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef. • One of these 11 had CTL response to this peptide. • The responding subject was HLA-A2, B21.				
Nef (182–205)	Nef (182–205 LAI)	EWRFDSRLAFHHVARELHP-EYFKN	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide. • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual. • None of the 12 tested had an IgG response to this peptide.				
Nef (183–191)		WRFDSRLAF	HIV-1 infection	human (B*1503)	Sabbaj2002b
	Keywords HAART. **Epitope name** Nef-WF9.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA A*2904 A*3002 B*1503 B*5802 Cw*0202 Cw*0602. • This study monitored epitope responses in HIV-1 infected minority women living in the United States. • 24 epitopes were described – 8 were novel, 8 used new restricting elements but were previously defined epitopes, and 8 were previously described. • Serial peptide truncations were used to define optimal epitopes for CTL cell lines isolated from 12 individuals, assayed by a Cr-release. • This epitope was newly defined in this study. • Subject 01RCH50 also recognized the epitope RMRGAHTNDV, RT(356-365), A*3002 – she was African American, was on HAART, had a viral load of 960 and CD4 count of 728. • Among HIV+ individuals who carried HLA B15, 3/17 (18%) recognized this epitope.				
Nef (183–191)	Nef (183–191)	WRFDSRLAF	HIV-1 infection	human (B*1503)	Frahm2004
Nef (183–191)	Nef (183–191)	WRFDSRLAF	HIV-1 infection	human (B*1503)	Cao2003
	Keywords binding affinity, acute infection, early-expressed proteins. **Assay type** CD8 T-cell Elispot - IFNγ. **Donor HLA** A*2301, B*3501, B*1503 (B72), Cw2, Cw7. • All proteins were scanned and optimal epitopes were mapped in a study of CD8+ gamma IFN T-cell responses in 21 men within 15-92 days post-HIV-1 infection. Subjects initially a showed narrow immune responses with a mean of 2.3 epitopes recognized per patient. The immune response broadened later in infection. No correlation between the plasma viral load and the number of recognized epitopes or the frequency of IFN-gamma secreting cells was observed, and there was no correlation between the functional avidity of a responses and the abundance of IFN-secreting cells that recognized the epitope. The first epitopes to be recognized did not tend to be the most avid, and earliest responses tended to be directed against Nef, Tat, Vpr, and Env. • All HIV-1 proteins except Vpu were recognized, and a responses to a total of 41 optimal epitopes were characterized; 24 had been identified previously. 48% of the total T-cell responses were directed against Nef and 43% were directed against Gag. • More common HLA alleles were less frequently used in primary infection than less common alleles, for example A3, B35, B57, and B62 were more frequently utilized than A1, A2, A30, and A44.				
Nef (186–193)	Nef (186–193 LAI)	DSRLAFHH	HIV-1 infection	human (B35)	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.				
Nef (186–194)	Nef (186–194)	DSRLAFHHM	HIV-1 infection, HIV-1 exposed seronegative	human (A24)	Kaul2001a
	Keywords HIV exposed persistently seronegative (HEPS). • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Nef (186–194)	Nef (186–194 BRU)	DSRLAFHHV		human (B51)	Connan1994
	• Resulted in the assembly of HLA-B51.				
Nef (188–196)	Nef (192–200 SF2)	KLAFHHMAR	HIV-1 infection, computer prediction	human (A*3303)	Hossain2003
	Keywords binding affinity, computational epitope prediction. **Assay type** Chromium-release assay. • HLA-A*3303 is a common HLA allele in east and southeast Asia. Pol, Gag and Nef SF2 proteins were scanned for potential A*3303 epitopes. 99 potential epitopes were synthesized, and 52/99 bound to A*3303. Six of these served as peptide-targets for lysis by PBMC from infected individuals, and clones derived from 4 of these 6 could lyse HIV-vaccinia infected target cells, indicating proper processing.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope is one of the 2/6 peptides that could induce CTL responses in the PBMC of infected individuals, but was not properly processed in a vaccinia-HIV infected target cell.				
Nef (188–196)	Nef (188–196 LAI)	RLAFHHVAR	HIV-1 infection	human (B52)	Hadida1995
	• The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions.				
Nef (188–201)	Nef (188–201 LAI)	RLAFHHVARELHPE	HIV-1 infection	human (B35 or C4)	Buseyne1993a
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children. • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures. • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study.				
Nef (190–198)		ALKHRAYEL	HIV-1 infection	human	Kaul2001c
	Keywords HIV exposed persistently seronegative (HEPS). • This study examines CTL responses in HIV exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative. • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire. • This epitope was in 1/22 HEPS controls, ML1749.				
Nef (190–198)	Nef	AFHHVAREL	HIV-1 infection	human (A*0201)	Altfeld2001c
	Keywords inter-clade comparisons, supertype, computational epitope prediction. **Epitope name** Nef AL9. • HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested. • Three additional previously described HLA-A2 epitopes were added to the set of 20, including Nef AL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acute infected individuals recognized at least 1 (median of 1 and maximum of 2) • RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study.				
Nef (190–198)	Nef	ALKHRAYEL	HIV-1 infection, Vaccine	human, macaque (A*0201)	Hanke2000, Wee2002
	Vaccine *Vector/Type:* DNA prime with modified vaccinia Ankara (MVA) boost *Strain:* A clade *HIV component:* p17 Gag, p24 Gag **Keywords** inter-clade comparisons, epitope processing, immunodominance. • The HIV-1 subtype A focused vaccine HIVA contains p24 and p17, in a reversed order relative to the Gag polyprotein to prevent myristylation of p17, which could direct the protein to the cell membrane and inhibit efficient peptide processing and class I presentation, as well as a polyepitope string of conserved, often immunodominant epitopes that were selected to have particularly good cross-reactive potential for the A-clade epidemic in Nairobi, Kenya. A DNA and MVA prime-boost vaccination protocol using the HIVA antigen will be used in a phase III clinical trial in Kenya. This epitope is included in the polyepitope string [Hanke2000].				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Multiple CD4+ or CD8+ T-cell vaccine-induced responses to peptide pools were detected using intracellular cytokine staining and IFNgamma Elispot assays after vaccination of 5 macaques. The response to the Mamu A*01 SIV p27 epitope p11C (CTPYDINQM), included in the polyepitope region, was not immunodominant in the Mamu A*01 vaccinated macaques, possibly because of processing limitations in context of the artificial polyepitope string [Wee2002].				
Nef (190–198)	Nef (190–198 LAI)	AFHHVAREL	HIV-1 exposed seronegative	human (A2)	Rowland-Jones1998a
	Keywords inter-clade comparisons. • CTL recognition reported in the context of HLA-B52 and A2.1, A2.2 and A2.4. • A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating. • The A subtype consensus is ALKHRAYEL. • The D subtype consensus is AfEHKAREm. • [Hunziker1998] suggests that HLA-A2 does not in fact present this epitope, and notes that it does not promote A2 assembly [Connan1994] – also see [Brander1998b] • [Hunziker1998] maintains that HLA-A2 does not present this epitope contrary to an earlier report [Hadida1995], (also see [Brander1998a])—despite the position of Hunziker *et al.*, Rowland-Jones and colleagues are confident that this epitope in its A clade form is presented by HLA-A*0201 and A*0202, and it is one of the most common responses seen in both seropositive and exposed-uninfected donors from Nairobi (Rupert Kaul, pers. comm.)				
Nef (190–198)	Nef (190–198)	AFHHVAREL	in vitro stimulation or selectio	human (A2)	Wilson1999b
	Keywords binding affinity, dendritic cells, Th1. • Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors. • Th1-biasing cytokines IL-12 or IFN alpha enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within. • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL.				
Nef (190–198)	Nef (190–198)	AFHHVAREL	Vaccine	human (A2)	Woodberry1999
	Vaccine *Vector/Type:* vaccinia • A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2. • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice. • CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost. • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested. • AFHHVAREL was recognized by 2 of the patients.				
Nef (190–198)	Nef (190–198 SF2)	AFHHVAREL	HIV-1 infection	human (A2)	Altfeld2001b
	Keywords HAART, acute infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Previously described and newly defined optimal epitopes were tested for CTL response. • Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 0/10 group 1, 1/6 group 2, and 0/4 group 3.				
Nef (190–198)	Nef (190–198)	ALKHRAYEL	HIV-1 infection, HIV-1 exposed seronegative	human (A2)	Kaul2001a
	Keywords inter-clade comparisons, HIV exposed persistently seronegative (HEPS). • Variants ALKHRAYEL and AFHHVAREL are A/B clade specific. • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers.				
Nef (190–198)	Nef (190–)	AFHHVAREL	HIV-1 infection	human (A2)	Corbet2003
	Keywords binding affinity, inter-clade comparisons, computational epitope prediction. **Epitope name** Nef190. **Assay type** CD8 T-cell Elispot - IFNγ, Chromium-release assay, Flow cytometric CTL assay. • HLA-A2-restricted HIV-1 CTL epitopes were computationally predicted. Binding affinities for HLA-A*0204, immunogenicity in HLA-A*0201 transgenic mice, and responses to the peptides in 17 HIV-1 infected patients were tested. 31 novel conserved A2 epitopes were detected. An average of 4 epitopes were recognized per patient. • This epitope was one of the previously identified HLA-A2 epitopes studied. • None of the 17 HIV-infected HLA-A2+ people in this study recognized this epitope.				
Nef (190–198)	Nef (subtype B)	AFHHVAREL	HIV-1 exposed seronegative	human (A2, A*0202, A*0201)	Rowland-Jones1998b
	Keywords inter-clade comparisons. • HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection. • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world. • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes. • Clade A version of the epitope: ALKHRAYEL, Clade D epitope: AFEHKAREM. • This epitope was recognized by two different exposed and uninfected prostitutes.				
Nef (190–198)	Nef (190–198 LAI)	AFHHVAREK	HIV-1 infection	human (A3)	Hadida1995
	• Naturally occurring L to K anchor substitution abrogates A2 binding, but permits HLA-A3 binding.				
Nef (192–206)	Nef (192–206 BRU)	HHVARELHPEYFKNC	HIV-1 infection	human (A1)	Hadida1992
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients.				
Nef	Nef (IIIB)		HIV-1 infection	human	Wasik2000
	Keywords rate of progression, Th1. • HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of beta-chemokines and IL-2 relative to other HIV+ infants.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors. • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs.				
Nef	Nef		HIV-1 infection	human	De Maria1997
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function. • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels.				
Nef	Nef		HIV-1 infection	human	Lubaki1999
	• Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20) • A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20.				
Nef	Nef (LAI)		Vaccine	human	Gorse1999b
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade SF2 *HIV component:* Env, Gag, Nef, Protease • The vaccine used was rec canarypox expressing HIV-1 env, gag, pol, nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120. • In vitro inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients. • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity.				
Nef	Nef		HIV-1 infection	human	Gamberg1999
	Keywords TCR usage. • 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens. • Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR betaV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases.				
Nef	Nef		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat **Keywords** HAART. • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated. • The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-gamma production, and IL-6 and IgG responses. • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.				
Nef	Nef (LAI)		HIV-1 infection	human	Buseyne1998a
	• This study showed a correlation between strong CTL memory and breadth of response in 7-12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load.				
Nef	Nef (LAI)		HIV-1 infection	human	Buseyne1998b
	Keywords inter-clade comparisons. • In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef	Nef (LAI)		Vaccine	human	Evans1999
	Vaccine *Vector/Type:* canarypox *HIV component:* Gag, gp120, gp41, Nef, Protease, RT • A Canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3-6 months after the last vaccination.				
Nef	Nef		HIV-1 infection	human	daSilva1998
	• CTL dense regions of Nef tend to lie in conserved domains with low non-synonymous substitution per site – authors consider that this may be due to a host adaptation to infection that focuses the CTL response to be directed against conserved functional domains [daSilva1998]				
Nef	Nef (LAI)		HIV-1 infection	human	Legrand1997
	• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat. • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef. • Early responses to Pol, Rev, Vif and Tat were rare.				
Nef	Nef (LAI)		HIV-1 infection	human	Zerhouni1997
	Keywords rate of progression. • CTL responses to Env, Gag, Nef and RT were tested at various phases of disease progression – 10 asymptomatic patients generally had CTL responses to all proteins, 10 ARC patients responded well to all proteins except Nef, and AIDS patients had few responses to any proteins.				
Nef	Nef		HIV-1 infection		Kuiken1999
	Keywords epitope processing. • A correlation between conserved regions of Nef and CTL epitope density was also noted in [Kuiken1999]. The authors suggest that this may be due to biological reasons such as the one described above [daSilva1998], or due to epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents. • Both p17 and Nef show a correlation between epitope density and conserved regions in the protein – in contrast, p24 is a more conserved protein and known epitopes are evenly distributed across p24.				
Nef	Nef (BRU)		HIV-1 infection	human	Aladdin1999
	Keywords rate of progression. • In vitro measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death.				
Nef	Nef (SF2)		HIV-1 infection	human	Jin1998a
	• CTL precursor frequencies were determined in HIV-1 infected pregnant women, and higher CTLp frequencies to Pol and SF2 Nef, but not IIIB Nef, were found in non-transmitting mothers than in transmitting mothers – Nef CTL responses have been found in uninfected infants born to HIV+ women (Lazuriaga95);				
Nef	(subtype C)			human	Novitsky2001
	Keywords inter-clade comparisons, immunodominance. • This study is provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort. • 37 of 45 subjects (82%) demonstrated Nef specific ELISPOT CTL responses of more than 100 SFC/106 PBMC. • Two Nef-immunodominant regions were identified, one spanned amino acid positions 67 to 96 using HXB2 numbering system while the second corresponded to amino acid positions 122 to 141.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• While there was some subtype B and C cross-reactivity, there was greater breadth and intensity of response if the CTL from HIV-1-infected individuals was probed with ELISPOT using peptides derived from the same subtype (a median of three Nef epitopes recognized within subtype C compared with one Nef epitope recognized from subtype B peptides, and ELISPOT results with a median of 763 SFC/106 PBMC among responses to HIV-1 C, versus a median of 318 SFC/106 PBMC among responses to HIV-1 B.				
Nef	Nef (subtype A, B, D)		HIV-1 infection	human	Cao2000
	Keywords inter-clade comparisons. • HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in HIV infected Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D. • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype.				
Nef	Nef		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS) **Keywords** review. • This review discusses the cellular immune response, and comments on the stimulatory role of CpG motifs and how HIV-1 DNA vaccines can boost the CTL and Th proliferative responses in asymptomatic HIV+ individuals.				
Nef			HIV-1 exposed seronegative	human	De Maria1994, Kuhn2002
	Keywords HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • 6/24 HIV uninfected infants (ages 15-50 months) born to HIV+ mothers had HIV-1 specific CTL responses to vaccinia-expressed Nef, Gag/Pol, Env. • Reviewed in [Kuhn2002].				
Nef			HIV-1 infection	human	Yusim2002
	Keywords epitope processing, escape. • Epitopes that have been described in the literature and included in this database tend to cluster in conserved regions and be absent or rarely found highly variable regions found in Nef, Env and p17. • While the uneven distribution of epitopes may be in part due to a limited cross-recognition of specific responses because of differences between peptides used to probe the immune response and autologous strains, regions with a paucity of defined epitopes also had higher frequencies of amino acids that tend to not be found in C-terminal positions of epitopes, and had lower cleavage prediction scores for epitope processing. This suggests that in the regions of the virus where variation is best tolerated traces of immune escape have left an imprint on the viral population. Epitopes also were concentrated in alpha-helix and turn regions in the proteins. • In the more conserved p24, and Pol proteins RT and Protease, epitopes are more evenly distributed.				
Nef	Nef (HXB)		HIV-1 infection	human	Lu2000a
	Keywords epitope processing, vaccine-specific epitope characteristics. • Bacillus anthrax lethal toxin (LFn)-HIV fusion proteins are candidate HIV vaccines that are safe in mice, and LFn-V3 region fusion proteins induce CD8 T cells in BALBc mice. LFn causes exogenous protein to be taken up and processed in a class I pathway. Expressed proteins from Gag p24 and nef fragments cloned into the LFn expression plasmid stimulate gag-specific CD4 proliferation and CTL responses in HIV-infected donor PBMCs *in vitro*.				
Nef	(BRU)		HIV-1 infection	human	Edwards2002
	Keywords rate of progression. • 96% (26/27) chronically infected HIV-1 infected patients elicited gamma-IFN CD8+ T-cell responses against Gag. • Nef and/or Pol CTL responses were detected in 86% of the subjects.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The magnitude and breadth of Gag and p24 T-cell responses correlated with absolute CD4 counts, and inversely correlated with viral load. • Pol and Int CTL responses correlated positively with absolute CD4+ T-cell count. • Nef and Env responses did not correlate with either CD4 counts or viral load.				
Nef			HIV-1 infection	human	Larsson2002b
	Keywords HAART, dendritic cells. • Autologous mature dendritic cells with rec vaccinia expressing Gag, Pol, Nef and Env could amplify CD8+ T-cell Elispot responses 4-38 fold in five HIV+ patients on successful HAART treatment, relative to autologous monocytes. Some weak responses could only be detected using mature dendritic cells as APCs, and this approach could be useful for detection of low frequency memory cells.				
Nef	(SF2)		HIV-1 and HCV co-infection	human	Lauer2002
	Keywords rate of progression. • HIV-1 and HCV immune responses were studied in 22 individuals who were co-infected with HIV-1 and hepatitis C virus (HCV). IFNgamma production was measured in an Elispot assay of CD8+ T-cells using targets expressing either Gag, RT, Env and Nef in a vaccinia construct, or one of seven HCV proteins. • All 22 patients targeted at least one protein. 20/22 patients recognized RT, 17/22 patients recognized Gag, 13/22 subjects recognized Env and 11/22 patients recognized Nef. Robust CTL activity was independent of disease progression or viral load. • Despite high HCV viral loads, very few HCV CD8+ T-cell Elispot responses were detected. In a control HCV infected person who did not have HIV-1, strong anti-HCV responses were mounted. • HIV-specific CD4 proliferative responses were detected in 9/17 coinfected patients, but no HCV responses were detected.				
Nef			HIV-1 infection	human	Scott2001
	Keywords HAART, responses in children. • CTL responses before and after initiation of ART were studied in 13 HIV-1 vertically infected infants <6 months of age, and 4 that were >6 months of age. • Before ART 2/13 infants <6 months of age showed IFNgamma Elispot CD8+ T-cell responses, one to Nef and one to Env and Nef, and these responses became undetectable after successful therapy– 3 infants were coinfected with CMV and all 3 had CMV-specific CD8+ T-cell responses. • One older infant, at 23 months, had CTL responses against all for proteins tested, Gag, Pol, Nef and Env, and had the lowest plasma viremia of the study group. 3/4 infants older than 6 months of age responded to either Nef or Pol. • Administration of ART over 48 weeks broadened the HIV-1-specific CTL response in 2/4 of the older children that were incomplete responders.				
Nef	(IIIB)		HIV-1 infection	human	Ortiz2001
	Keywords HAART, supervised treatment interruptions (STI). • Immune responses in eight chronically HIV-1 infected patients undergoing HAART therapy structured treatment interruptions (STI) were studied. STI boosted HIV-1 specific CTL responses and elevated CTL responses were maintained up to 22 weeks after the last treatment interruption, but viral load rebound to pretreatment levels and CD4 T-cell count decline was observed. CD8 responses in PBMC were measured by cytokine flow cytometry with gp160, Gag p55, RT-Pol and Nef expressed in vaccinia.				
Nef			Vaccine	mouse	Muthumani2002
	Vaccine *Vector/Type:* adenovirus *HIV component:* Gag-Pol, Nef, Vpr • Vpr can cause cells to go into G2 arrest, and it surpresses immune cell activation and inflammatory cytokine production, so co-immunization of BALB/c mice with recombinant adenovirus expressing Vpr and HIV-1 antigens Nef or Gag/Pol was tested to see if Vpr reduced the immune response to the other HIV antigens. • Vpr compromised CD8+ T-cell lytic responses and T-helper proliferative responses in mice co-immunized with Vpr and Nef or Gag/Pol. • In vitro, Vpr reduced T-cell cytokine production of IL-12 and TNFalpha, indicative of Vpr-mediated immune suppression.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef	Nef			human	Currier2003
	Keywords inter-clade comparisons. **Assay type** Flow cytometric CTL assay. • CD8-cellular immune responses from 21 HIV-1 infected patients from Kenya infected with subtype A, C, D, and unique recombinants were studied for cross-recognition of Gag, Env, and Nef vaccinia-expressed proteins representing subtypes A-H, including CRF01. • Both subtype-specific and cross-reactive CTL were observed, with a skewing of responses towards the infecting subtype in the nine subjects with full length sequence available. The magnitude of the responses to Gag were the highest, less to Nef, and still less to Env. • For Gag, 8/21 subjects responded to at least 7/8 different subtype proteins, 7 had a mixed response, recognizing some subtypes but not others, and 6 responded to only one or none of the different subtype proteins. For Env, 4/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 7 responded to one or none. For Nef, 5/19 subjects responded to at least 7/8 subtypes, 8 had a mixed response, and 6 responded to one or none.			
Nef	Nef (B.AU.AF064676)			human	
Nef	Nef		HIV-1 infection	human	Draenert2003
	Keywords assay standardization. **Assay type** CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • Six different HIV-1 Nef peptide sets ranging in length from 15-20 amino acids with overlap from 10-11 amino acids derived from either the B clade consensus sequences or the B clade sequence B.AU.AF064676 were used to study the impact of using different peptide design strategies to detect CD4 and CD8 T-cell responses. 20 individuals were tested using the six sets of peptides. 17/20 had CD8 T-cell responses to all peptides sets, and 15 of these 17 had CD4 T-cell responses. • Although there was a trend in detecting more CD8 T cell responses using the shorter 15-mer peptides, longer 20-mers were best for detecting more CD4 T-cell responses, but neither result was statistically significant. Similar results were seen in the 15 to 20 amino acid range for both IFN gamma Elispot and ICS assays. • Use of the consensus versus the natural strain identified slightly increased numbers of reactive peptides. Seven reactive peptides were observed with the B consensus peptides but not the B.AU.AF064676 peptides, but on the other hand four reactivites were observed using the B.AU.AF064676 peptides but not the consensus. • Using an overlap of 10 or 11 amino acids did not make a difference.			
Nef	(C consensus)		HIV-1 infection	human	Novitsky2003
	Keywords rate of progression. **Assay type** CD8 T-cell Elispot - IFNγ. • In this study, PBMC from 105 asymptomatic HIV-1 C clade infected patients from Botswana were screened for HIV-1 subtype C specific T-cell responses directed against Gag, Pol, Vif, Vpr, Tat, Rev, Vpu, Env and Nef. Nef-specific T-cell responses positively correlated with plasma viral load. In contrast, HIV-1 Gag and especially Gag p24 showed an inverse correlation with viral load.			
Nef	(C consensus)		HIV-1 infection	human	Novitsky2003
	Keywords rate of progression. **Assay type** CD8 T-cell Elispot - IFNγ. • In this study, PBMC from 105 asymptomatic HIV-1 C clade infected patients from Botswana were screened for HIV-1 subtype C specific T-cell responses directed against Gag, Pol, Vif, Vpr, Tat, Rev, Vpu, Env and Nef. Nef-specific T-cell responses positively correlated with plasma viral load. In contrast, HIV-1 Gag and especially Gag p24 showed an inverse correlation with viral load.			

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef	Nef		HIV-1 infection	human (A*0201 and Cw*08)	Shacklett2000
	• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples.				
Nef	Nef		HIV-1 infection	human (B*35)	Jin2002
	Keywords rate of progression. • Patients with HLA-B*35 variants B*3502, B*3503, B*3504, and B*5301 tend to proceed to AIDS more quickly than those with B*3501. • Of 32 patients with HLA-B*35 alleles CD8+ CTL responses were quantified using an intracellular cytokine staining assay – 75% had responses to Pol, 69% to Gag, 50% to Nef, and 41% to Env. • The overall magnitude of CTL responses did not differ between those bearing B*3501 and the others. A higher percentage of Gag responses was observed in those that had lower RNA levels that carried B*3501, and there was a negative association with viral load and CTL activity. The data is consistent with higher levels of CTL responses contributing to protection in B*3501 individuals, but not in B*3502, B*3503, B*3504, and B*5301 individuals.				
Nef	Nef (BRU)		Vaccine	mouse (H-2D^d)	Collings1999
	Vaccine *Vector/Type:* DNA *Strain:* B clade BRU *HIV component:* Nef • A comparison of DNA vaccination with HIV-1 Nef expression vectors pBN-CMV-NEF and pBN-RSV-NEF (self-replicating), pCGE2-NEF (non-replicating). • CTL immune responses were detected using all three expression vectors, while a humoral immune response to Nef was only observed in the self-replicating expression vectors; possibly antibody responses require higher levels of protein expression.				
Nef	Nef (SIV)		SIV infection	macaque (Mamu-A*11, -B*03, -B*04, and -B*17)	Dzuris2000
	• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here.				

II-B-22 HIV-1 CTL epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1			HIV-1 infection	human	Schito2001
	Keywords HAART.				
	• Longitudinal analysis (72 weeks) of 15 patients with acute or recent HIV-1 infection implies that HAART treatment alone can not completely conserve CD8+ cell homeostasis and preserve the original T-cell receptor repertoire.				
HIV-1			HIV-1 infection	human	Mackewicz2000
	• Non-cytotoxic anti-HIV responses of CD8+ T cells cultured with CD4 infected HIV cells are mediated be blocking expression of viral RNA, and do not influence viral replication steps through integration of provirus.				
HIV-1			Vaccine		Altes2002
	Keywords dynamics.				
	• This study employs a mathematical model to study the consequences of increasing the T-helper response through a vaccine, which would have counter-balancing effects in a new infection: a more intense response provides more help but also more target cells. The model indicates that if the infecting virus had a low replication rate, then CTLp and CD4 helper cells could control an infection. Only a vaccine that could increase CTL responsiveness could reduce viral set point with observed replication rates.				
	• A CD4+ T-cell response without maintained CTL response was deleterious in this model.				
HIV-1			HIV-1 infection	human	Currier2002b
	Keywords assay standardization.				
	• Elispot standardization was sought using a reference peptide pool of 23, 8-11 mer epitopes from Influenza, cytomegalovirus (CMV), and Epstein Bar Virus (EBV) presented by 11 common HLA class I molecules.				
	• 15/17 (88%) HIV- and 14/20 (70%) HIV+ individuals reacted with this test set and *in vitro* simulation of the PBMC from these individuals were capable of killing cells expressing the target antigen.				
HIV-1			HIV-1 infection	human, macaque	Wodarz2002
	Keywords dynamics, HAART.				
	• Mathematical modeling is used to support the idea that T-helper cell dysfunction results in a compromised ability to maintain an anti-HIV CTL memory response. Models suggest strategies to restore CTL memory through therapy and improve long-term immunological control of the virus.				
HIV-1			HIV-1 infection, Vaccine	human	Zinkernagel2002
	Keywords review.				
	• HIV immunity and vaccine strategies are compared with to other pathogens. We do not have a successful vaccine agains TB leprosy, HIV, HCV and most parasites, and the author suggests this is associated with the need for a strong T-cell response to these diseases. Vaccine strategies that achieve a physiological low does infection that is well controlled but persists may be required to alter the immunopathological consequences of infection with HIV.				
HIV-1			Vaccine	human	Gaschen2002
	Keywords review, inter-clade comparisons, epitope processing.				
	• The concept of using an artificial consensus sequence for vaccine design is discussed, comparing the concepts of a model ancestor sequence or a consensus sequence, with illustrations of the potential advantages of the strategy based on C-clade comparisons.				
	• See also a comment [Nickle2003], and reply [Gao2003]				
HIV-1			HIV-1 infection	human, macaque	Johnson2002
	Keywords review, class I down-regulation by Nef, escape.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Reviews evidence for CTL escape in HIV epitopes in natural human infections, and in SIV infections of macaque where viral clones with a known time of infection and multiple animals with the same HLA molecules can be tracked. • Vigorous CTL responses are made despite class I down-regulation by the Nef protein, but it may delay cytolysis of infected cells. Too great a loss of MHC proteins may enhance NK cell killing so the fitness advantage of this function of Nef may be in balance.				
HIV-1			HIV-1 infection, Vaccine	human	Newman2002
	Keywords review, epitope processing, supertype, computational epitope prediction, HIV exposed persistently seronegative (HEPS), supervised treatment interruptions (STI), immunodominance. • This extensive review covers many aspects of T-cell immunity and natural HIV infections, and considers how this knowledge might be applied to a polyepitope vaccine approach. Strategies concerning ways to avoid the creation of junctional epitopes and use of linkers to enhance processing of such constructs are discussed. • The C-terminal flanking residue (C1) was found to be associated with immunodominance of epitopes, such that R or K (positive charge) > N or Q (amide) > C, G, A, T, S (small) > F, W, Y (aromatic) > I, L, M, V (aliphatic) > D (negative). As this position is outside and proximal to the epitope, processing and cleavage is the likely reason for this observation. • Changing the C1 residue from F to K for an HLA-A2 presented epitope from HBV resulted in a change from the epitope being non-immunogenic to strongly immunogenic.				
HIV-1			HIV-1 infection, Vaccine	human	Johnston2001
	Keywords review, HIV exposed persistently seronegative (HEPS). • Reviews the current state of HIV vaccine approaches, and discusses the role of CTL induced immunity in protection or partial protection in animal studies, likening it to the CTL found in HEPS studies.				
HIV-1			HIV-1 infection	human	Klenerman2002
	Keywords binding affinity, review, escape. • The importance of breadth, or spread, of CTL responses is discussed, as narrowly focused responses can be more readily escaped. • Some HLA types and specific epitope recognition may be associated with a better disease outcome. Reasons for this are considered, including NK cell activity, epitope affinity, epitope conservation, and class I specific induction of more effective T-cell receptors.				
HIV-1			HIV-1 infection	human	Kuhn2002
	Keywords review, HIV exposed persistently seronegative (HEPS), responses in children, mother-to-infant transmission. • Intrauterine exposure of infants to HIV from their mothers results in HIV-1 specific T-helper cell proliferative responses in 1/3 of exposed uninfected babies, and HIV-1 specific CTL in some. Such responses are evident, but it is unknown whether they are associated with lack of infection, but there is some evidence that HIV-1 T-cell responses may reduce transmission in breastfeeding mothers. Summary tables are provided of CD4 and CD8 responses detected in earlier studies.				
HIV-1			HIV-1 infection	human	Kuhn2002, Levy1998
	Keywords HIV exposed persistently seronegative (HEPS), mother-to-infant transmission. • A non-HLA-specific, non-chemokine-mediated CD8+ T-cell non-cytotoxic anti-HIV response, measured by suppression of acute viral infection of CD4 cells, was detectable in approximately 16/31 (52%) of uninfected children born of infected mothers, was more commonly detected in those <1 year old, and could reflect a protective response. • Reviewed in [Kuhn2002].				
HIV-1			Vaccine	human	Altes2001
	Keywords dynamics.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mathematical modeling suggests if the effector CTL vaccine response exceeds the level of response seen in chronic infection, that a memory CTL population is established that can respond very quickly to protect from infection.				
HIV-1			Vaccine	human	Copeland2002
	Keywords review. • This review summarizes cytokines and chemokines produced by CD8+ T-cells that can interfere with HIV's infection and replication.				
HIV-1			Vaccine		Edgeworth2002
	Keywords review. • This review summarizes HIV vaccine strategies, adjuvants, current clinical trials and animal models.				
HIV-1			Vaccine		Graham2002
	Keywords review. • This review summarizes HIV vaccine approaches and clinical trials.				
HIV-1	Env (HXB2)		Vaccine	guinea pig, mouse	Chakrabarti2002
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB2 *HIV component:* gp140ΔCFI, gp160 deletions • Intramuscular injection of plasmid DNA was used to vaccinate BALB/c or Huntley guinea pigs with a series of codon-optimized modified HIV-1 HXB2 envelopes – modifications included elimination of glycosylation sites, deletions, and exchange of the V3 loop to change from a X4 or R5 phenotype. • The mutant envelope gp140deltaCFI gave the most promising result, enhancing antibody responses while retaining the ability to stimulate a strong CTL response. • gp140deltaCFI has deletions in the cleavage site, fusogenic domain and spacing of the heptad repeats, and was designed to mimic a fusion intermediate.				
HIV-1	Env (gp160) (384–467)		Vaccine	macaque, rabbit	Michel1993
	Vaccine *Vector/Type:* hepatitis B surface antigen lipoprotein particles (HsBAg) *Strain:* B clade LAI *HIV component:* V3 • Immunization with recombinant HIV1 V3/HBsAg hybrid particles into rabbits or macaques elicited and maintained for several months anti-V3 or HIV-1 Env proliferative, CTL and Ab responses.				
HIV-1	Gag (HXB2)		HIV-1 infection	human	Garba2002
	• CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins. • Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.				
HIV-1	Pol (HXB2)		HIV-1 infection	human	Garba2002
	• CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins. • Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.				
HIV-1	Env (MN)		HIV-1 infection	human	Garba2002
	• CD8+ Tcells from 25% of HIV positive individuals produce TGF-beta1 in response to stimulation with HIV proteins, and this can significantly reduce CD8+ T-cell IFN-gamma induction to HIV and vaccinia proteins. • Different peptides can preferentially induce TGF-beta1 or IFN-gamma from CD8+ T-clymphocytes from the same individual, and TGF-beta1 non-specifically suppresses HIV-specific immune responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1			HIV-1 infection	human	Altfeld2003

Keywords assay standardization, acute infection.
Assay type CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining.

- The frequency of HIV-1 specific T-cell responses was characterized in an Elispot IFN-gamma assay, using 507 overlapping peptides based on the B clade consensus sequence spanning all HIV-1 clade B proteins against PBMC from 57 HIV-1 infected patients at various disease and treatment stages. 63% of the peptides were recognized (range of 1-42 per subject, median=14). More variable peptides were targeted less frequently.
- Autologous virus sequences from six patients in acute infection spanning of HIV-1 p24, Tat and Vpr were used to scan for missed responses due to viral variation when using the consensus for peptides. 12/42 (29%) responses to these peptides were dectected only with autologous peptides, and often these autologous reponses were immunodominant. Responses were also generally higher using autologous peptides.
- A longitudinal analysis (5 yrs) of the T-cell responses in 5 patients showed that the autologous sequence elicited stronger T-cell recongition than the HIv-1 clade B consensus sequence.

HIV-1			HIV-1 infection	chimpanzee	Balla-Jhagjhoorsingh2003

Keywords review.

- This paper reviews HIV-1-specific cell-mediated immune responses in chimpanzees and discusses mechanisms that might control HIV-1 pathogenesis in chimpanzees. During the first decade of the HIV epidemic, more than 200 chimpanzees were experimentally infected with HIV. Among these only one case of declining CD4+ cells has been reported, all others have remained asymptomatic with no loss of immune function , some after 20 years of infection. In contrast to infected humans which have a skewed Th2 response, chimpanzees maintain balanced Th responses and are likely to support a fully mature CD8+ T-cell response.
- Specific HIV epitopes recognized by chimpanzees have been mapped and CTL detected , but overall the responses are at much lower levels than in humans, as viral loads are so low. Gag epitope responses are estimated to be 0.0095 to 0.0025% of the CD8+ T cell population in chimpanzee, and 1-2% in humans.
- The authors argue that the chimpanzee immune response may be effective at controlling virus because it focuses on conserved epitopes, and further speculate that long contact with lentiviruses may have put strong selection pressures on the chimpanzee MHC class I, narrowing the population's ability to respond to only the most conserved, and so useful, epitopes.

HIV-1			HIV-1 infection	human	Fagard2003

Keywords HAART, supervised treatment interruptions (STI).
Assay type CD8 T-cell Elispot - IFNγ.

- This study monitored the effects of repeated treatment interruptions (STI), in 2-week intervals, in 133 HIV-1 infected, HAART-treated patients. STIs were rarely able to control viremia without continued HAART, and increases in CD8+ T-cell response frequencies did not correlate with the level of control of viral replication. CD8+ T cell responses were measured by gamma IFN Elispot using between 2-32 different optimal HIV epitopes, selected to be appropriate for the patient's HLA type.

HIV-1				human	
HIV-1	HIV-1		HIV-1 infection	human	Feeney2003

Keywords responses in children.
Assay type CD8 T-cell Elispot - IFNγ.

- The magnitude and breadth of CD8+ T-cell responses in 18 pediatric (6-17 years) perinatally HIV-1 infected patients was determined using 1) overlapping peptides spanning all HIV-1 proteins and 2) peptides from all predefined appropriately class I HLA-restricted HIV-1 epitopes.
- Perinatally infected children's CD8+ T-cell responses were comparable in magnitude and breadth to adult responses. Many reactive peptides did not overlap with a previously characterized optimal epitope.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• On average 20% of all known pre-defined optimal epitopes presented by appropriate HLAs were recognized in these children. In two patients, autologous sequences spanning unrecognized potential epitopes usually corresponded to the reactive form of the epitope, so epitope variation alone did not account for unrecognized epitopes. • Children with detectable viremia showed a broader and greater CTL responses than HAART responsive children with undetectable viremia.				
HIV-1	HIV-1				
HIV-1			Vaccine		Hanke2003
	Keywords review. • Review of HIV vaccine development discussing diversity, the merits and difficulties of stimulating different arms of the immune response, and different strategies, including DNA vaccines, viral vectors, CTL epitope based, and protein- or peptide-based vaccines)				
HIV-1	HIV-1 (HXB2)		HIV-1 exposed seronegative	human	Hladik2003
	Keywords HIV exposed persistently seronegative (HEPS). **Assay type** CD8 T-cell Elispot - IFNγ. • Longitudinal study analyzed IFN-γ CD8+ T cell responses in highly exposed, seronegative homosexual men. Overlapping peptides spanning the Gag, Env, Nef and Pol subtype B HXB2 sequence were used to stimulate PBMC from 26 individuals, whose frequency of HIV-1 specific IFN-γ T cell responses were very low. • CD8+ T cells from 3/15 individuals (EES15, ES29, and ES63) recognized > 3 peptide pools.				
HIV-1			HIV-1 infection	human	Kousignian2003
	Keywords dynamics. **Assay type** Chromium-release assay. • The diversity of HIV protein (Gag, Pol, Env, Nef, Rev, Tat, Vif) recognition by CTLs was studied longitudinally in a cohort of 152 HIV-infected untreated individuals, and was analyzed by Markov modelling. CTL responses from 152 HIV-1 infected patients in four stages of disease progression were collected for a period of 5 years. Results show that memory CTL responses against HIV-1 proteins are acquired during early HIV-1 infection and subsequently lost. As viral load increased there was an accelerating loss of multiple protein recognition.				
HIV-1			HIV-1 infection, Vaccine	human	Lederman2003, Robbins2003
	Vaccine *Vector/Type:* gp120 depleted whole killed virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA) • Lederman and Douek is an editorial comment referring to the study presented by Robbins *et al.*, in which the authors discuss why an HIV-1 gp120-depleted inactivated HIV vaccine elicits HIV-1 specific T helper responses in 5/5 HIV+ people, but not CD8+ CTL responses. In chronically infected people it appears that stimulating Th responses in and of itself is not enough to restore strong CTL responses.				
HIV-1			Vaccine	human	Lehner2003
	Vaccine *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), CpG immunostimulatory sequence (ISS), HSP70 **Keywords** review, Th1, Th2, genital and mucosal immunity. • This review discusses the importance of mucosal and innate immunity for future vaccination strategies in HIV infection in humans. Different mucosal adjuvants are compared, and the advantages of a Th1 polarized response.				
HIV-1			HIV-1 infection	human	Onyemelukwe2002
	• Longitudinal study (1991-1997) of the clinicial presentation of 80 HIV-1 or HIV-II seropositive people in Zaria, Nigeria, who contracted HIV-1 primarily via heterosexual transmission. Main complicating diseases were tuberculosis and bacterial infections including Salmonella, Streptococcus peneumoniae and Stahhylococcus. HIV-1 progression was associated with a decline of not only CD4+ T cells, but CD8+ T cells as well – patients had CD4+ counts < 200 cells/ul, and CD8 counts were 190 cells/ul versus 440 cells/ul for controls.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1			HIV-1 infection	human	Onyemelukwe2002

- Longitudinal study (1991-1997) of the clinicial presentation of 80 HIV-1 or HIV-II seropositive people in Zaria, Nigeria, who contracted HIV-1 primarily via heterosexual transmission. Main complicating diseases were tuberculosis and bacterial infections including Salmonella, Streptococcus peneumoniae and Stahhylococcus. HIV-1 progression was associated with a decline of not only CD4+ T cells, but CD8+ T cells as well – patients had CD4+ counts < 200 cells/ul, and CD8 counts were 190 cells/ul versus 440 cells/ul for controls.

HIV-1			HIV-1 infection	human	Price2003

Keywords HAART.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ.

- CD4+ and CD8+ T cell responses were analyzed in this longitudinal study (19 mo) of 53 patients with chronic HIV-1 infection receiving continous ART therapy. Three subgroups were compared: one with suppressed viremia and increasing CD4+ T cell counts, one with dectable viral load and declining CD4, and one with detectable viral load with a postive CD4+ T cell slope.
- IFN-γ ELISPOT analysis was performed with peptide s spanning RT, Env, Gag (p24), Gag(p17), Nef, Tat and Rev. The IFN-γ analysis showed the greatest CD4+ as well as CD8+ T cell responses in the group with stable CD4+ T cell responses despiete detectable viurs over a median time course of 9 months.

HIV-1				human	Sindhu2003a, Sindhu2003b

Keywords rate of progression.
Assay type Chromium-release assay.

- In a cross-sectional study of 31 HIV+ people, a correlation was observed between CTL-mediated bystander HLA-unrestricted lysis of primary CD4+-T cells. $\gamma\delta$ CTL are abnormally expanded in HIV+ people, and the Vδ1 subset can deplete bystander CD4+ T-cells and expedite progression. In a sset of 13 patients, an inverse correlation was observed between CD8+ T-cell activation markers and viral load, and suggested to be an indicator of CTL-associated immunopathogenesis in HIV progression.

HIV-1			HIV-1 infection		Vella2003

Keywords review.

- This article reviews the CD8+ T-cell antiviral factor (CAF). CAF contributes to MHC restricted, CD8+ T-cell mediated non-cytolytic suppression of HIV in infected individuals.

HIV-1			Vaccine	human (A11)	Ariyoshi2002

Keywords review, vaccine-specific epitope characteristics, escape.

- This review summarizes issues discussed at a meeting held to discuss options for determining CTL responses to vaccines. Problems are noted: cost for any assay are prohibitive for a Phase III study, Elispot shows interlaboratory variation but could be extended to many samples. HLA-A11 is very common in Thailand – over 30% carry the HLA-A11 allele. Predominant strains may be evolving to evade recognition of A11 restricted epitopes. Few full length CRF01 sequences are available. Epitopes may differ in vaccinees and infected individuals.

HIV-1			HIV-1 infection	human (A11, B8, B40, cW8)	Alter2003

Keywords HAART, acute infection, early treatment.
Assay type cytokine production, CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining.

- Longitudinal study (24 mo) monitoring T-cell immune responses in 4 patient groups: Group 1 (n=6) consists of subjects who underwent HAART preseroconversion, group 2 (n=11)were HAART treated during early postseroconversion, group 3 (n=5) contained patients who started HAART during late postseroconversion, and group 4 (n= 6) commenced with HAART during chronic HIV-1 infection.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The experimental strategey was to test for reactivity levels with sets of peptides that each contain epitopes with known HLA-restriciting elements, making the peptide selection based on the optimal epitope list in this database. The HLA alleles found in the patients were balanced so that the frequency in the groups were comparable. Peptides spanning parts of Gag, Env, Nef, and RT were used for Elispot, and Gag peptides were used for ICS. • All group 1 patients, and 5/11 group 2 patients, maintained the breadth and the magnitude of the immune response throughout the study; those in group 2 that maintained response started therapy earlier. The hierarchy of intensity of responses to different peptides was preserved. Individuals in groups 3 and 4 all showed a decline, and after treatment lost responses. Groups 1 and 2 showed HAART-induced suppression of viremia but maintained resposnes. Groups 3 and 4 both showed viral suppression in association with a decreased immune response in breadth and magnitude after HAART. The authors suggest that preservation of HIV CD4+ responses can be maintained even if HAART is first given beyond the acute phase of infection, and a delay may allow a full CD8 reponse to develop while still allowing CD4 function to be preserved.				
HIV-1			HIV-1 infection	human (A11, B8, B40, cW8)	Alter2003
	Keywords HAART, acute infection, early treatment. **Assay type** cytokine production, CD8 T-cell Elispot - IFNγ, Intracellular cytokine staining. • Longitudinal study (24 mo) monitoring T-cell immune responses in 4 patient groups: Group 1 (n=6) consists of subjects who underwent HAART preseroconversion, group 2 (n=11)were HAART treated during early postseroconversion, group 3 (n=5) contained patients who started HAART during late postseroconversion, and group 4 (n= 6) commenced with HAART during chronic HIV-1 infection. • The experimental strategey was to test for reactivity levels with sets of peptides that each contain epitopes with known HLA-restriciting elements, making the peptide selection based on the optimal epitope list in this database. The HLA alleles found in the patients were balanced so that the frequency in the groups were comparable. Peptides spanning parts of Gag, Env, Nef, and RT were used for Elispot, and Gag peptides were used for ICS. • All group 1 patients, and 5/11 group 2 patients, maintained the breadth and the magnitude of the immune response throughout the study; those in group 2 that maintained response started therapy earlier. The hierarchy of intensity of responses to different peptides was preserved. Individuals in groups 3 and 4 all showed a decline, and after treatment lost responses. Groups 1 and 2 showed HAART-induced suppression of viremia but maintained resposnes. Groups 3 and 4 both showed viral suppression in association with a decreased immune response in breadth and magnitude after HAART. The authors suggest that preservation of HIV CD4+ responses can be maintained even if HAART is first given beyond the acute phase of infection, and a delay may allow a full CD8 reponse to develop while still allowing CD4 function to be preserved.			
HIV-1			Vaccine	human (B27, B8)	McMichael2002
	Keywords binding affinity, review, inter-clade comparisons, epitope processing, escape. • CTL response-eliciting vaccines are reviewed. The natural epitope interactions with the HLA class I presenting molecules and T-cell receptors are described, and the impact of breadth of CTL responses and diversity considered in a vaccine context. • Interesting specific examples are given concerning anchor chain residues. For B27, the B pocket fits Arg (R) but not Lys (K), so even this conservative change is not tolerated. In B8 either R or K can fit in the B pocket, but the substitution will cause conformational shifts in other parts of the epitope.				
HIV-1	gp120 (V3) and p24 (IIIB, MN, BH10)		Vaccine	mouse (H-2^d)	Buonaguro2002
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* A clade UG5.94UG018, B clade IIIB *HIV component:* Gag, gp120 **Keywords** inter-clade comparisons. **Assay type** Chromium-release assay. • Different HIV strains were used for different regions: gp120 A clade UG5.94UG018, and B clade IIIB • BALB/c mice were given intraperitoneal immunization with virus-like particle (VLPs) expressing recombinant subtype A gp120 and Pr55gag in the absence of adjuvants.				

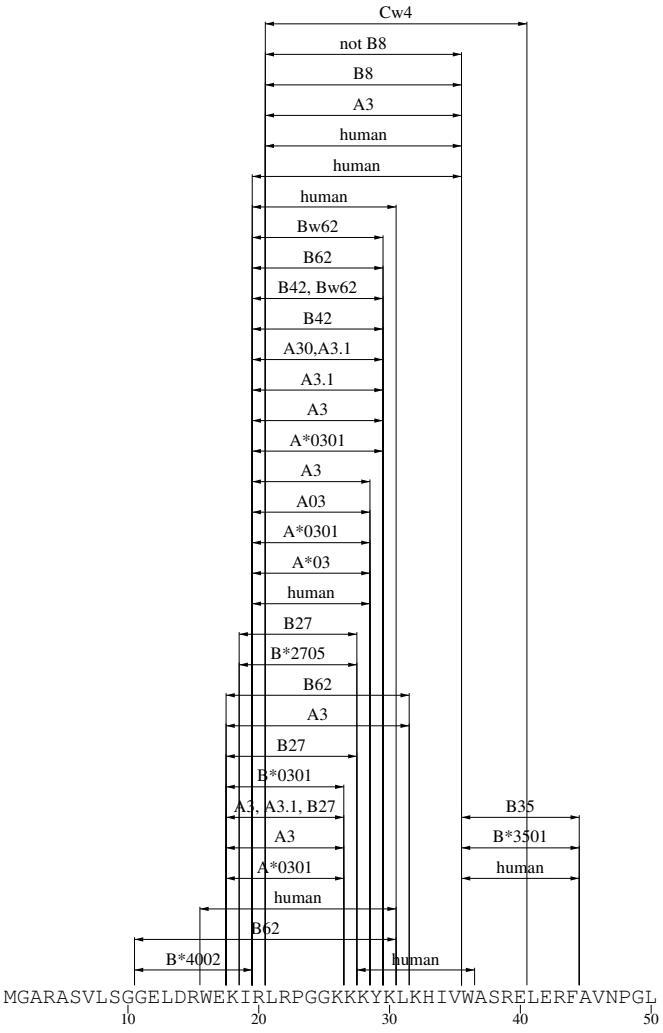
HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• High dose-independent humoral responses against both gp120 and p24 peptides were detected. Antibodies able to elicit 50% neutralization against A clade IIIB and the autologous clade a virus were obtained. • Recombinant rgp120 (clade B, MN) induced T-cell proliferative responses *in vitro* from vaccinated animals. • CTL activity was observed against splenocytes expressing Env (clade A) and Gag (clade B, BH10) from a vaccinia construct.				
HIV-1			Vaccine	mouse (MHC H2d)	Lieberman2002
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* Gag **Keywords** review. • Attenuated Listeria monocytogenes vectors elicit strong persistent CTL responses in vaccinations of BALB/c mice and can protect mice from a vaccinia-gag challenge.				

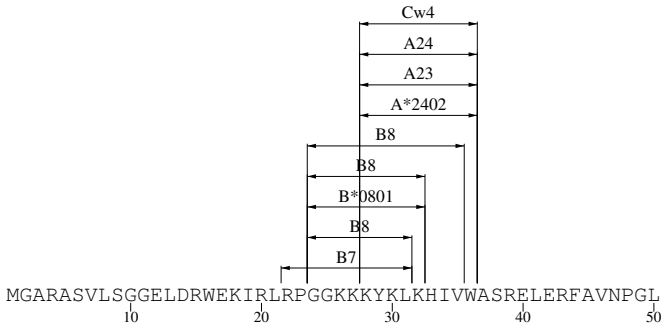
II-C

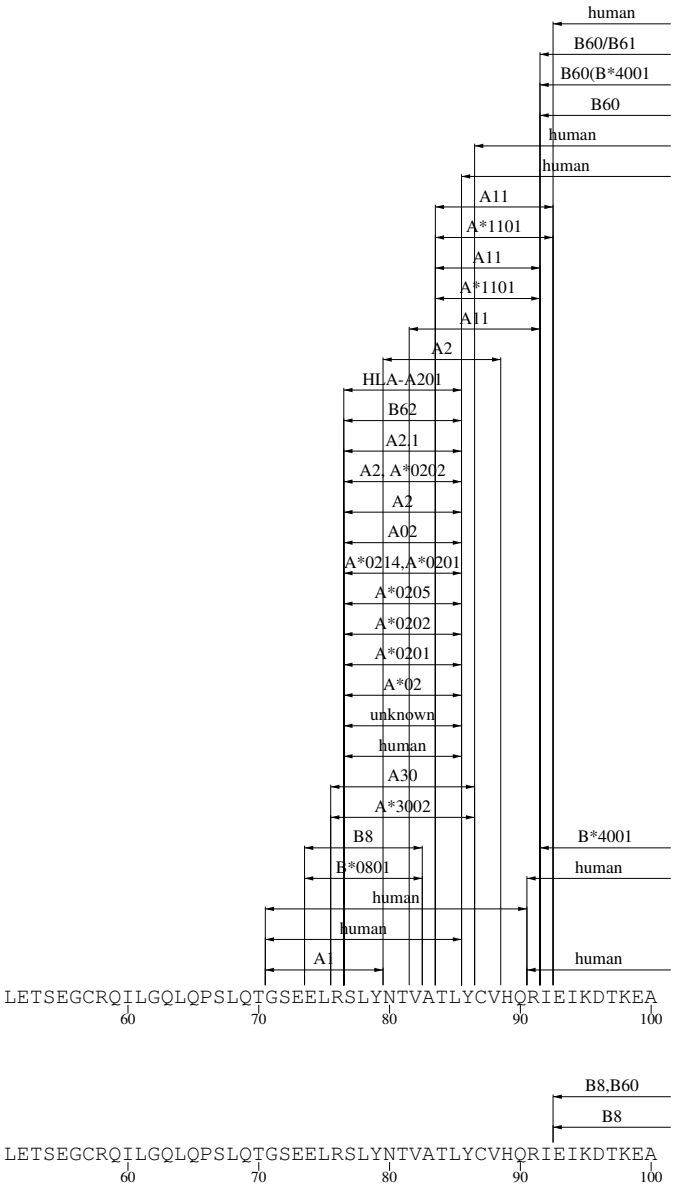
Maps of CTL Epitope Locations Plotted by Protein

Linear CTL epitopes less than twenty-two amino acids long are shown.

II-C-1 p17 CTL epitope map



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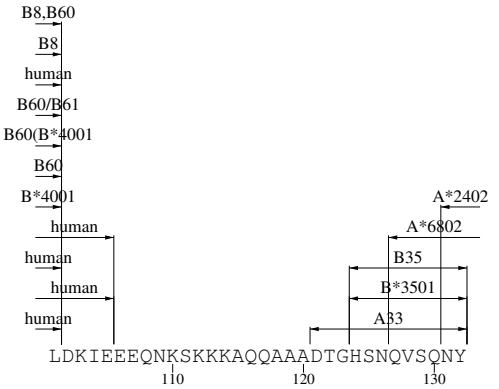
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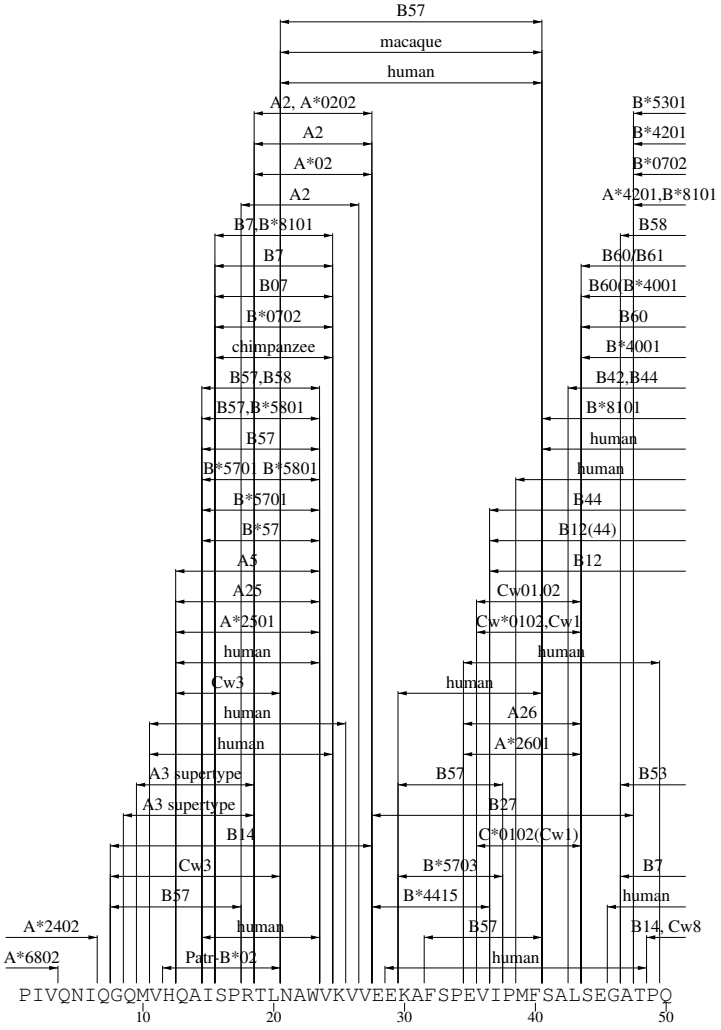
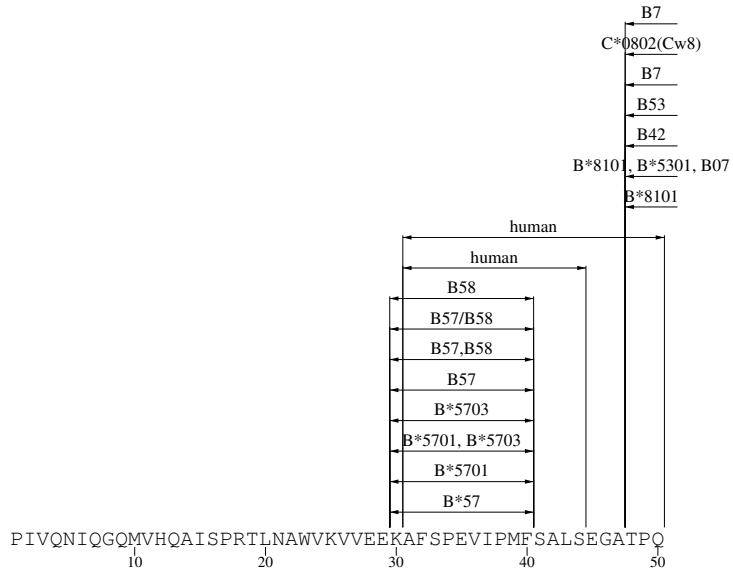
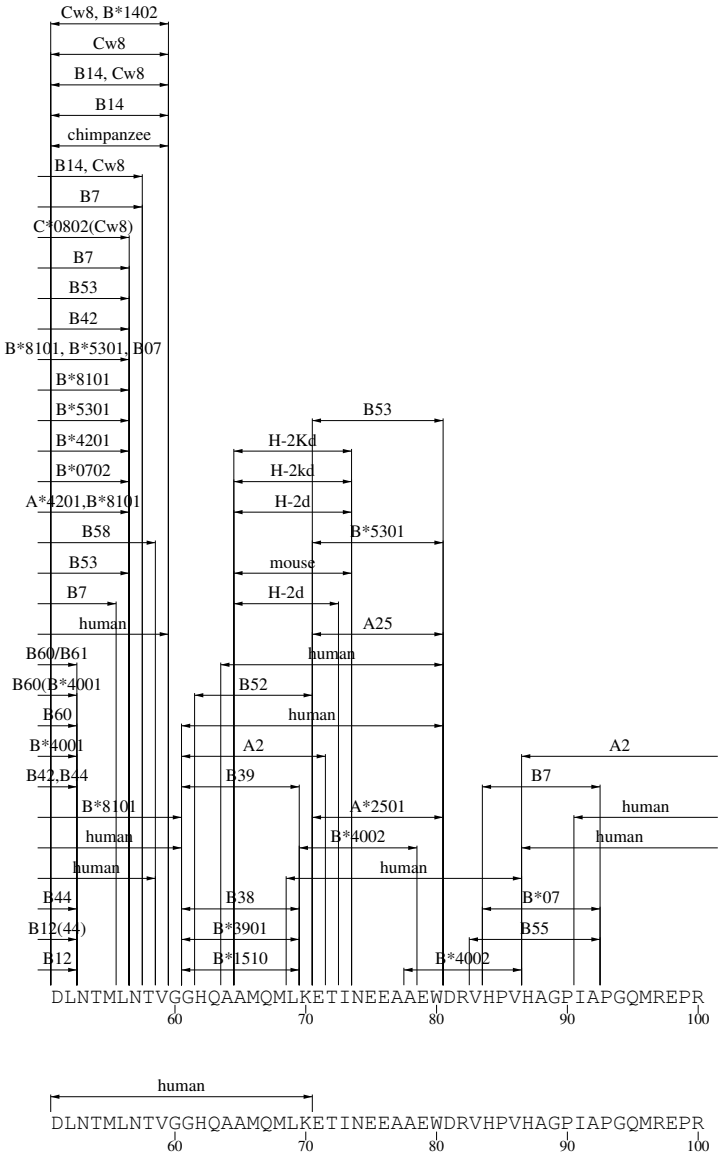
CTL

II-C-2 p24 CTL epitope map



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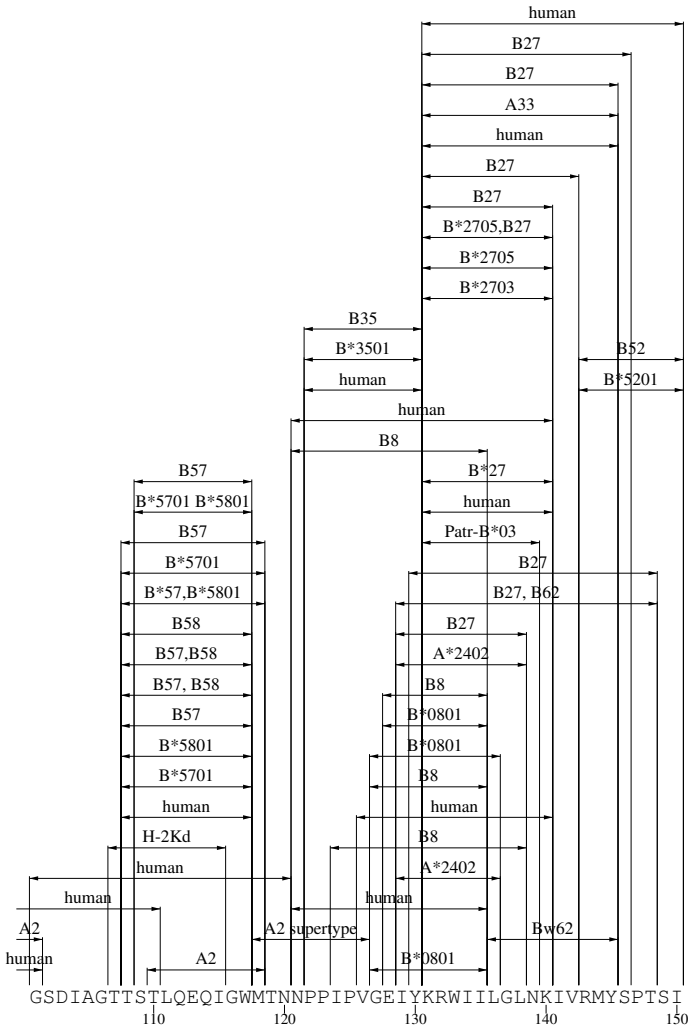
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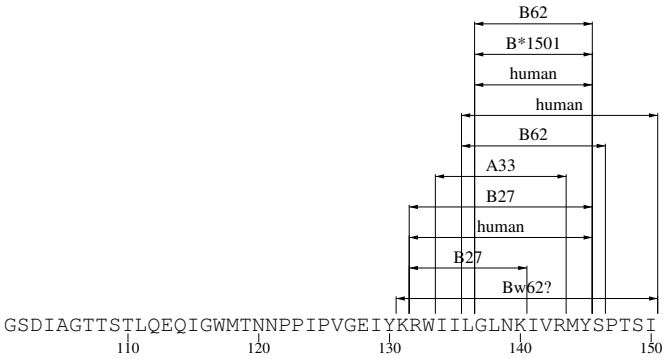
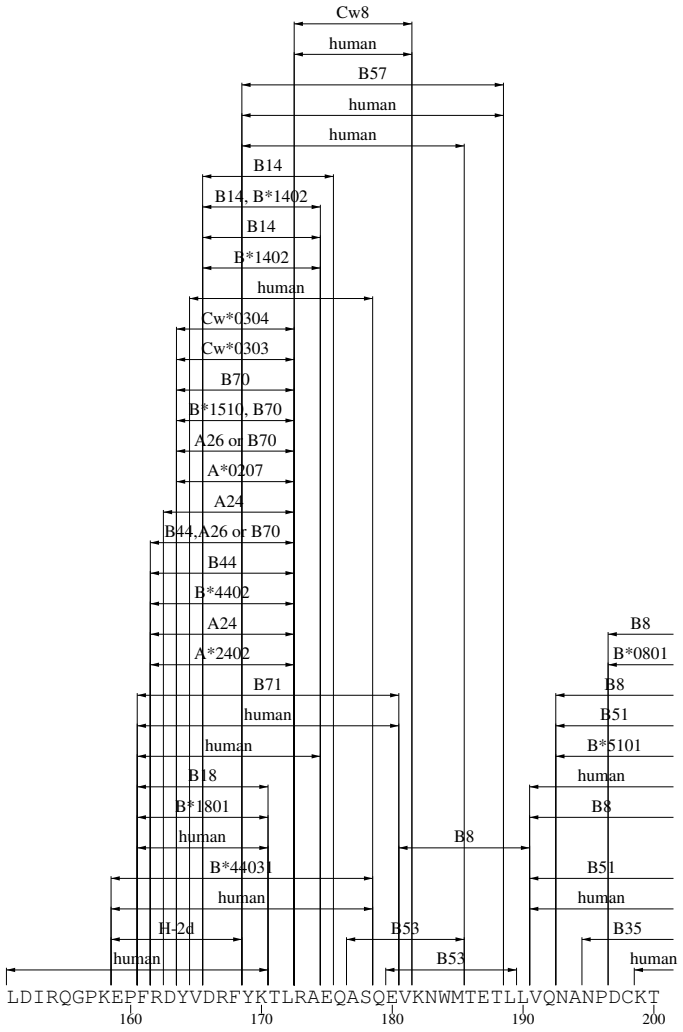
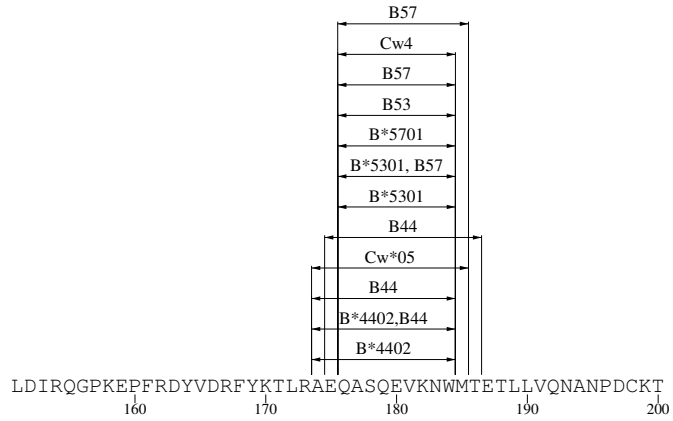
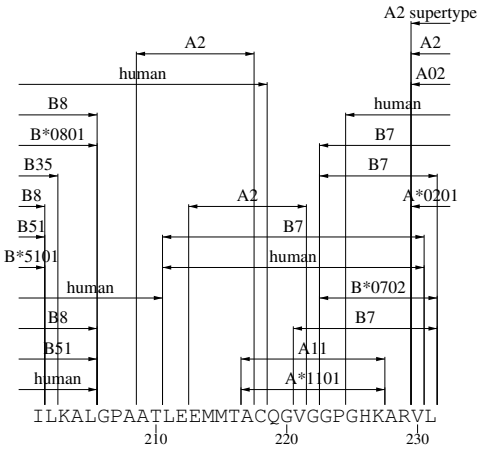
human
B8
B57
B*5701 B*5801
B57
B*5701
B*57,B*5801
B58
B57,B58
B57, B58
B57
B*5801
B*5701
human
H-2Kd
human
A2
human
B52
B*5201
B*27
human
Patr-B*03
B27
B27, B62
B27
A*2402
B8
B*0801
B*0801
B8
human
B8
A*2402
human
A2
A2 supertype
B*0801
Bw62
GSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSI
110
120
130
140
150

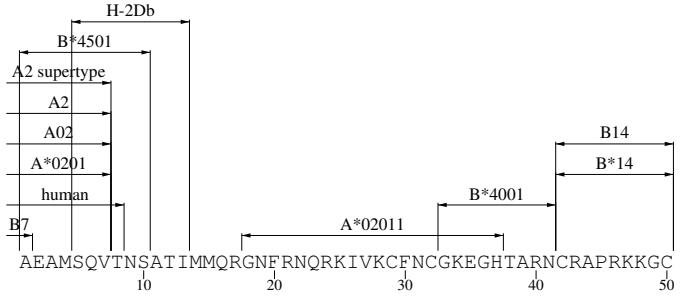

B62
B*1501
human
human
B62
A33
B27
human
B27
Bw62?
GSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSI
110
120
130
140
150

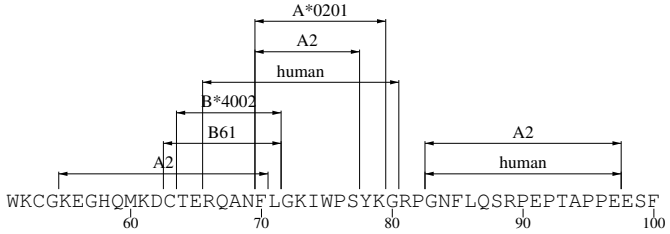

Cw8
human
B57
human
human
B14
B14, B*1402
B14
B*1402
human
Cw*0304
Cw*0303
B70
B*1510, B70
A26 or B70
A*0207
A24
B44, A26 or B70
B44
B*4402
A24
A*2402
B71
human
human
B18
B*1801
human
B*44031
human
H-2d
human
B53
B53
B8
B*0801
B8
B51
B*5101
human
B8
B51
human
B35
human
LDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANPDCKT
160
170
180
190
200

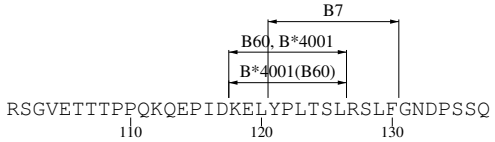




II-C-3 p2p7p1p6 CTL epitope map

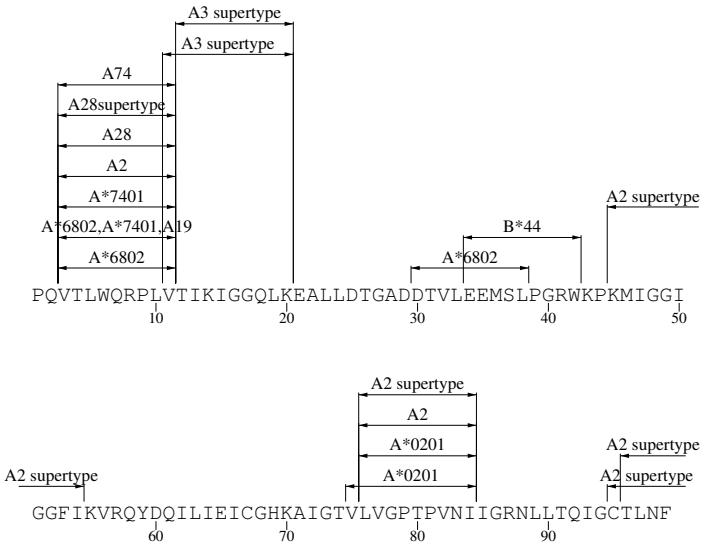




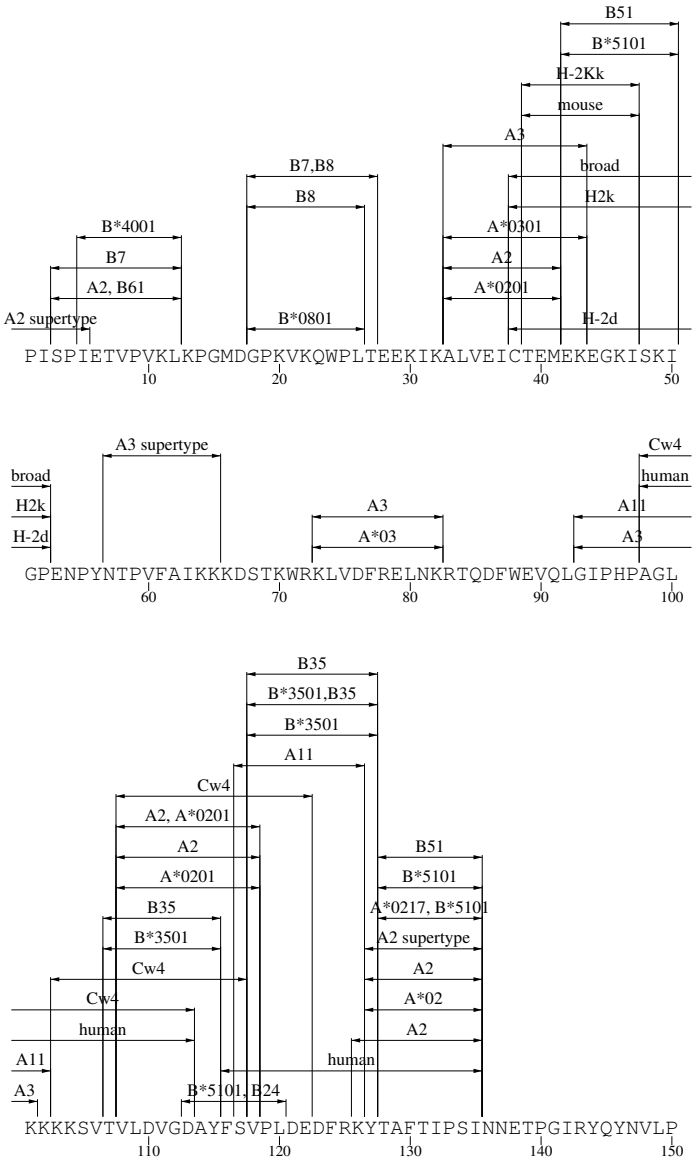


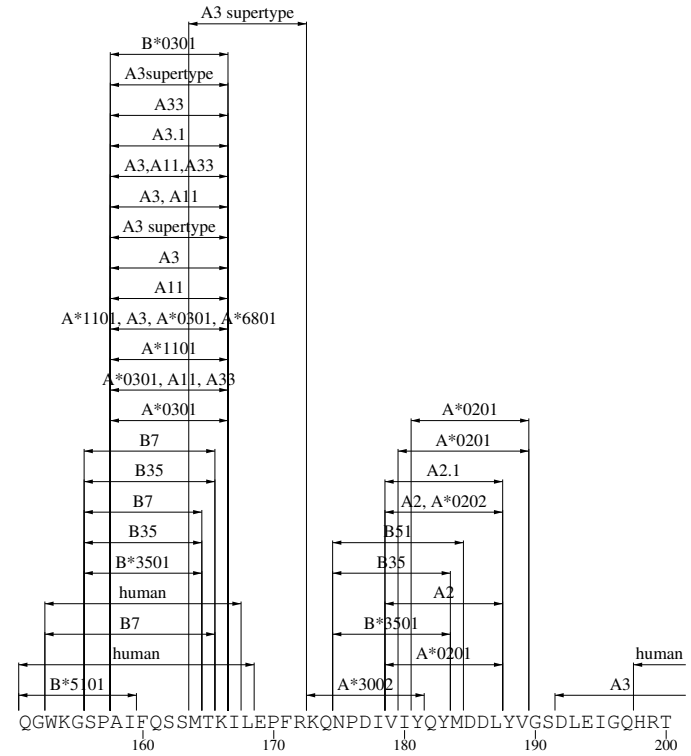
CTL

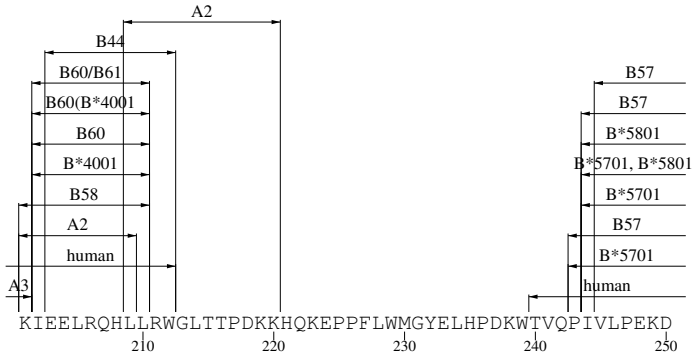
II-C-4 Protease CTL epitope map

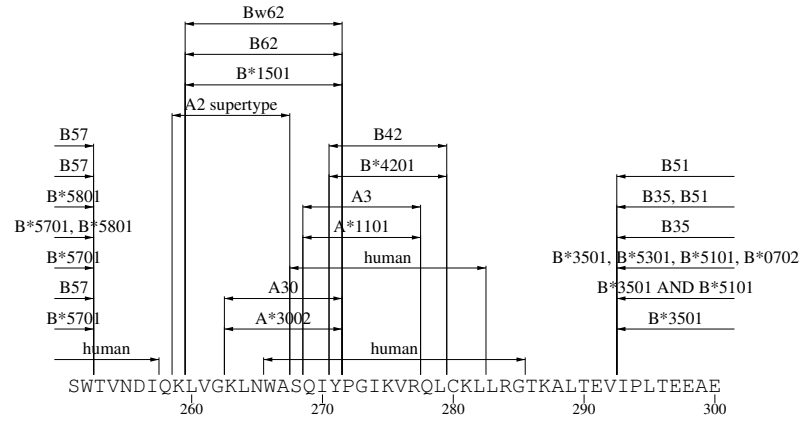


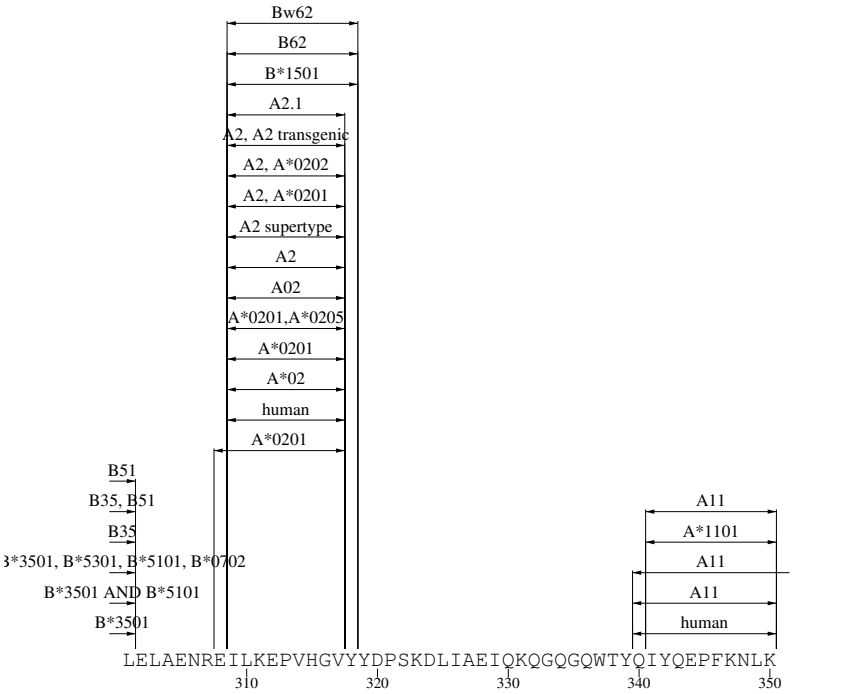
II-C-5 RT CTL epitope map



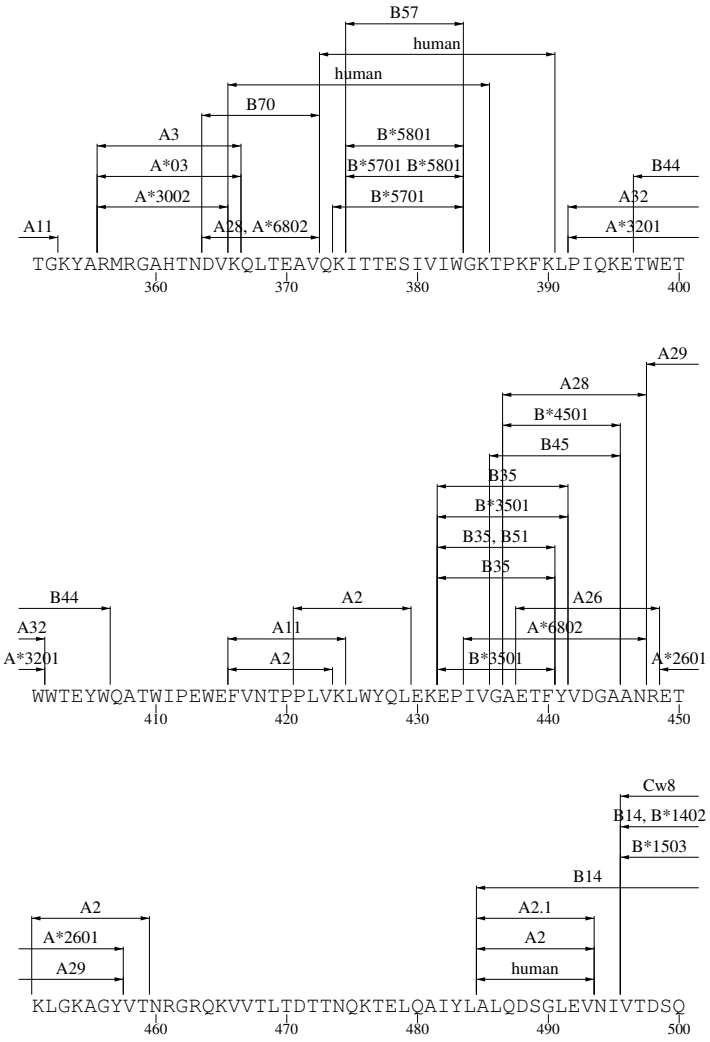

A3 supertype
B*0301
A3supertype
A33
A3.1
A3,A11,A33
A3, A11
A3 supertype
A3
A11
A*1101, A3, A*0301, A*6801
A*1101
A*0301, A11, A33
A*0301
B7
B35
B7
B35
B*3501
human
B7
human
B*5101
A*0201
A*0201
A2.1
A2, A*0202
B51
B35
A2
B*3501
A*0201
A*3002
human
A3
QGWKGSPAIFQSSMTKILEPFRKQNPDIVIYQYMDDLYVGSDLEIGQHRT
160
170
180
190
200

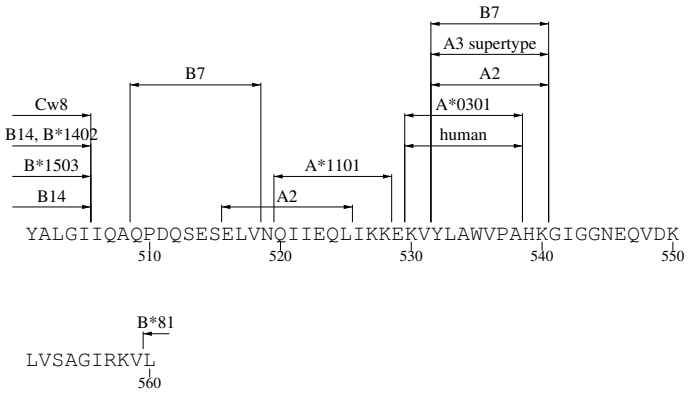

A2
B44
B60/B61
B60(B*4001
B60
B*4001
B58
A2
human
A3
B57
B57
B*5801
B*5701, B*5801
B*5701
B57
B*5701
human
KIEELRQHLLRWGLTTPDKKHQKEPPFLWMGYELHPDKWTVQPIVLPEKD
210
220
230
240
250


Bw62
B62
B*1501
A2 supertype
B57
B57
B*5801
B*5701, B*5801
B*5701
B57
B*5701
human
B42
B*4201
A3
A*1101
human
A30
A*3002
human
B51
B35, B51
B35
B*3501, B*5301, B*5101, B*0702
B*3501 AND B*5101
B*3501
SWTVNDIQKLVGKLNWASQIYPGIKVRQLCKLLRGTKALTEVIPLTEEAE
260
270
280
290
300

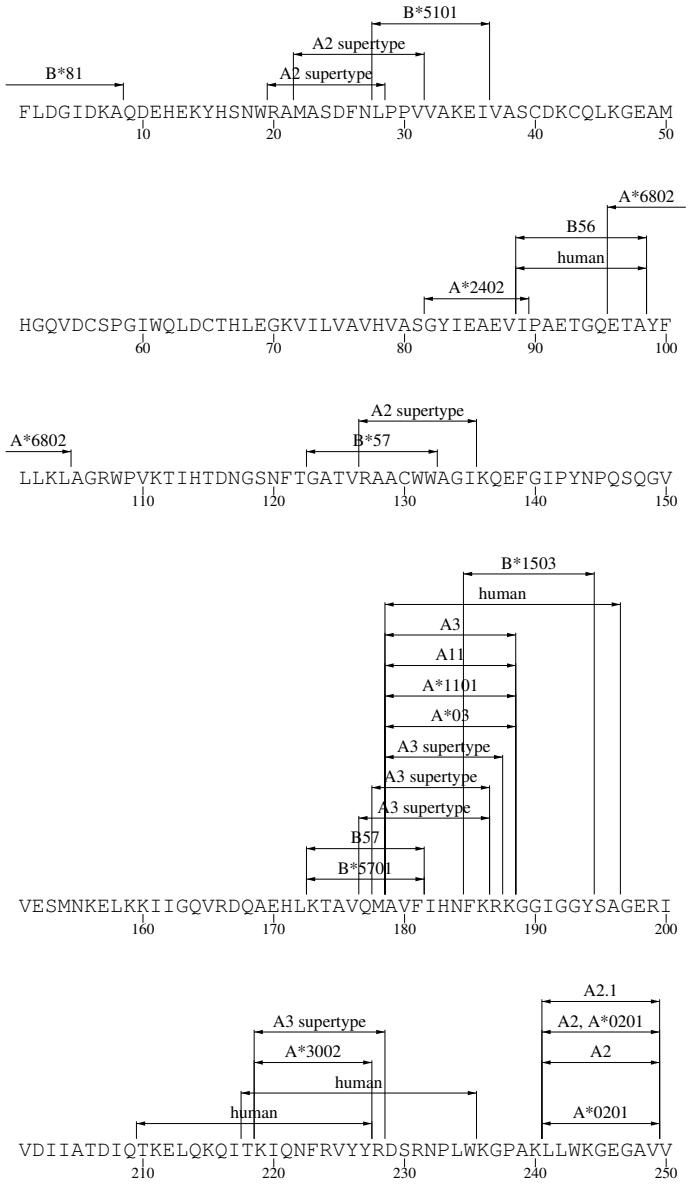

Bw62
B62
B*1501
A2.1
A2, A2 transgenic
A2, A*0202
A2, A*0201
A2 supertype
A2
A02
A*0201,A*0205
A*0201
A*02
human
A*0201
B51
B35, B51
B35
3*3501, B*5301, B*5101, B*0702
B*3501 AND B*5101
B*3501
A11
A*1101
A11
A11
human
LELAENREILKEPVHGVYYDPSKDLIAEIQKQGQGQWTYQIYQEPFKNLK
310
320
330
340
350

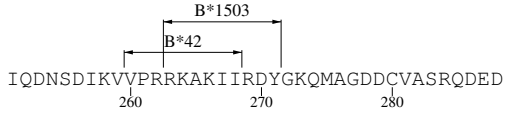
CTL


B57
human
human
B70
A3
B*5801
A*03
B*5701 B*5801
B44
A*3002
B*5701
A32
A11
A28, A*6802
A*3201
TGKYARMRGAHTNDVKQLTEAVQKITTESIVIWGKTPKFKLPIQKETWET
360
370
380
390
400
A29
A28
B*4501
B45
B35
B*3501
B35, B51
B35
B44
A2
A26
A32
A11
A*6802
A*3201
A2
B*3501
A*2601
WWTEYWQATWIPEWEFVNTPPLVKLWYQLEKEPIVGAETFYVDGAANRET
410
420
430
440
450
Cw8
B14, B*1402
B*1503
B14
A2
A2.1
A*2601
A2
A29
human
KLGKAGYVTNRGRQKVVTLTDTTNQKTELQAIYLALQDSGLEVNIVTDSQ
460
470
480
490
500


B7
A3 supertype
B7
A2
Cw8
A*0301
B14, B*1402
human
B*1503
A*1101
B14
A2
YALGIIQAQPDQSESELVNQIIEQLIKKEKVYLAWVPAHKGIGGNEQVDK
510
520
530
540
550
B*81
LVSAGIRKVL
560

II-C-6 Integrase CTL epitope map

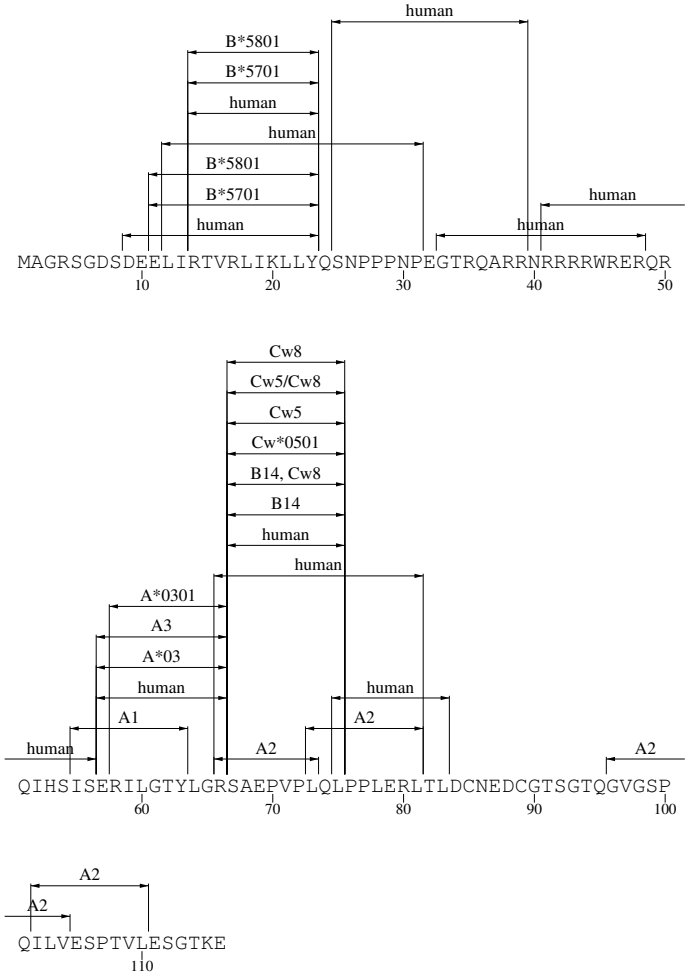




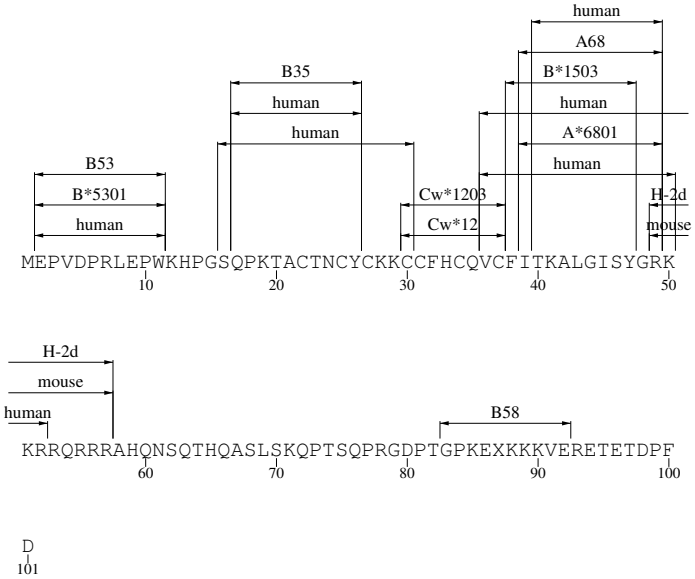
CTL

CTL

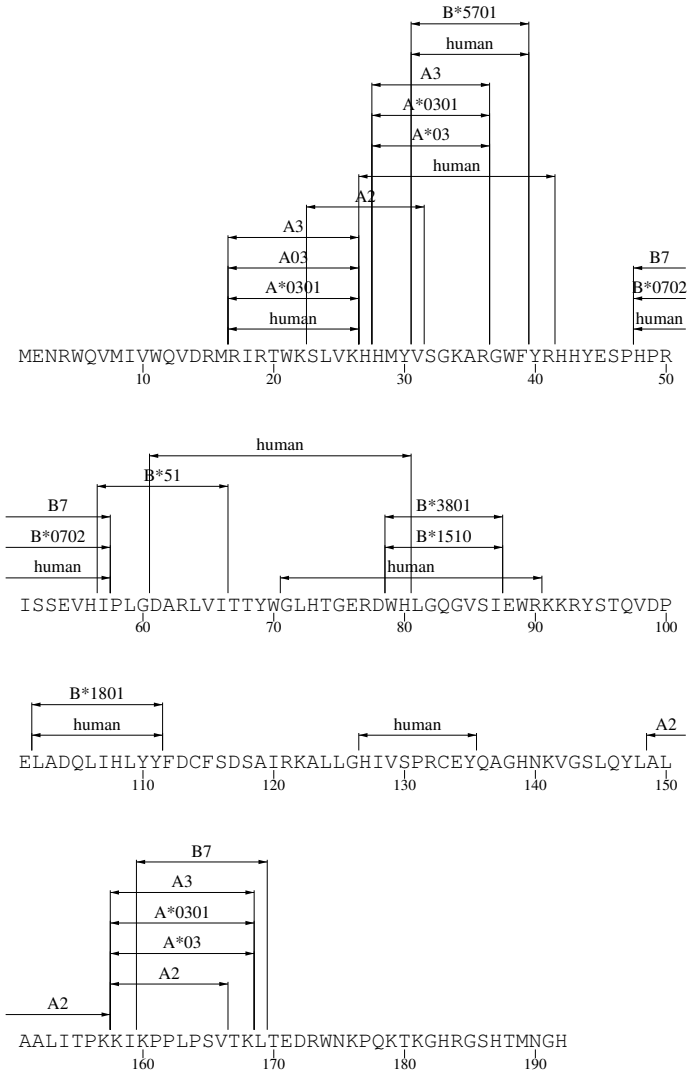
II-C-7 Rev CTL epitope map



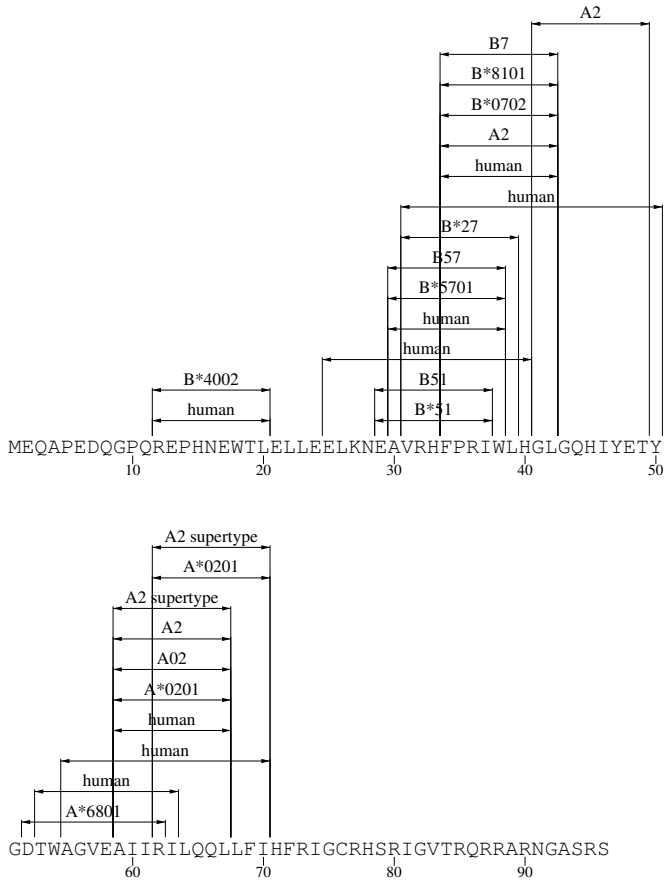
II-C-8 Tat CTL epitope map



II-C-9 Vif CTL epitope map

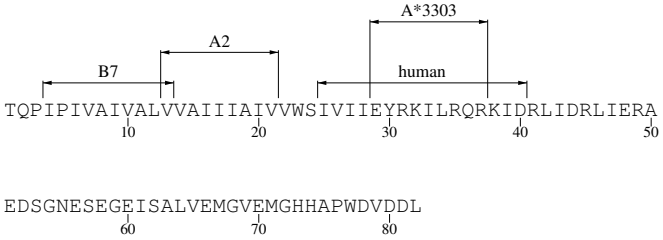


II-C-10 Vpr CTL epitope map

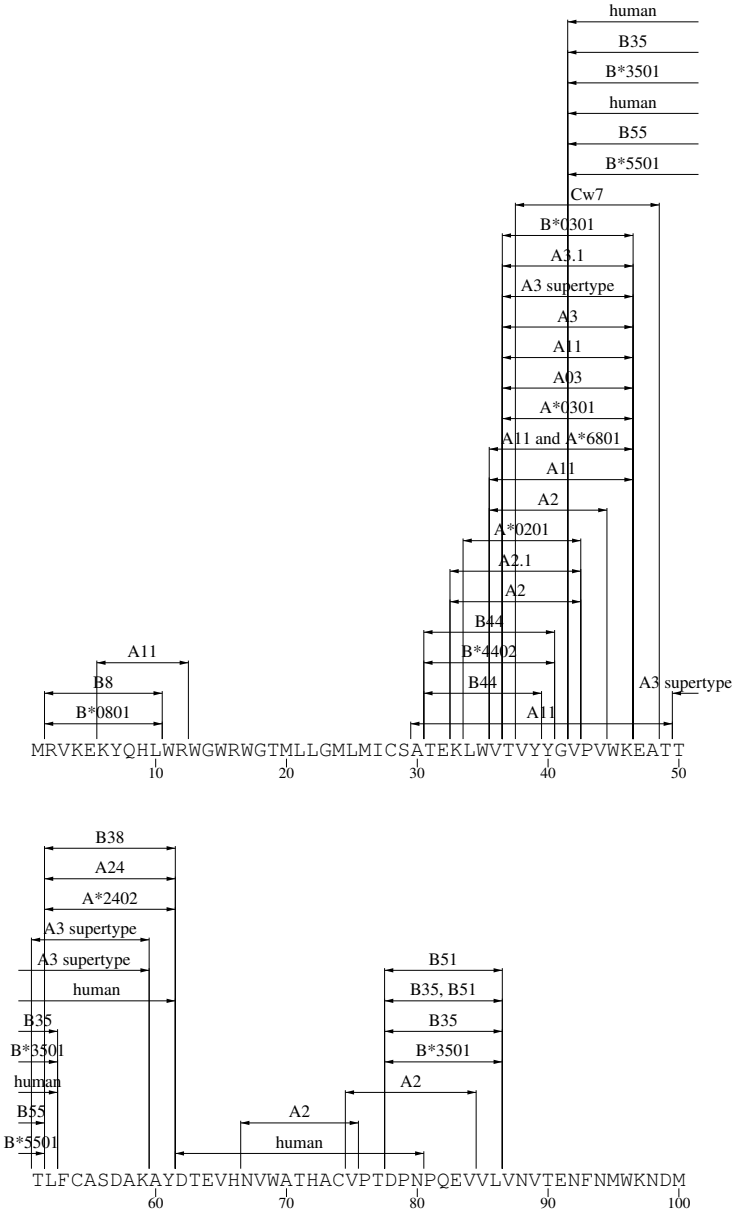


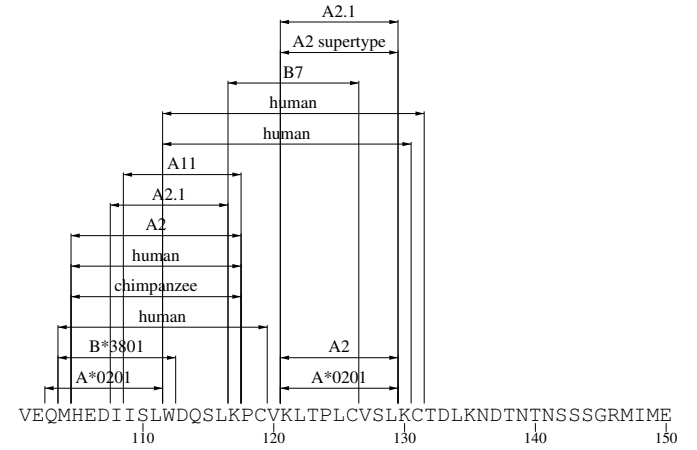
CTL

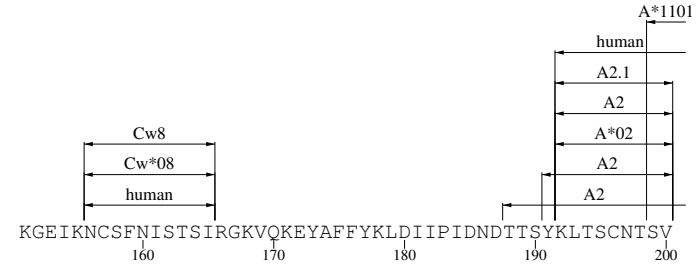
II-C-11 Vpu CTL epitope map

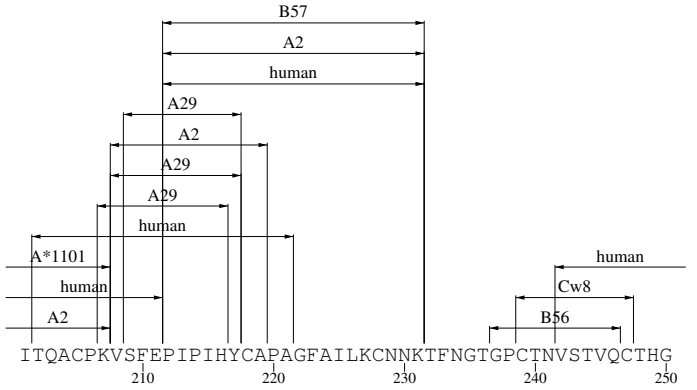


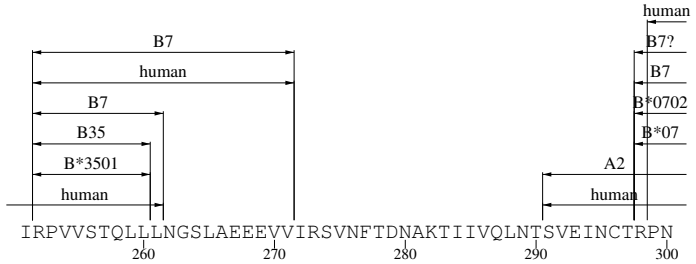
II-C-12 gp160 CTL epitope map

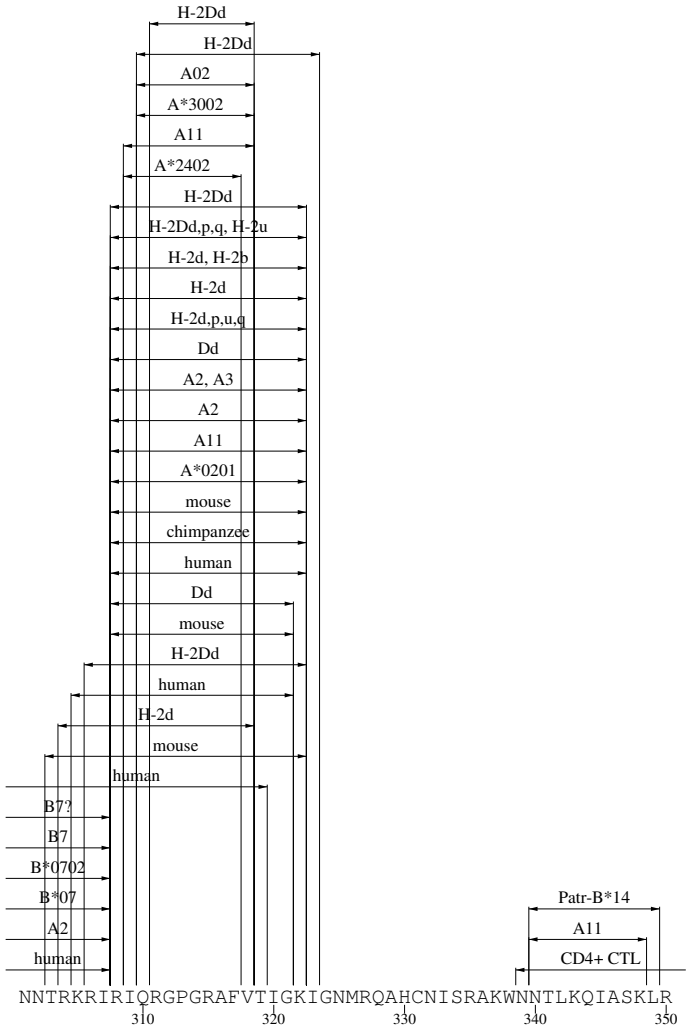


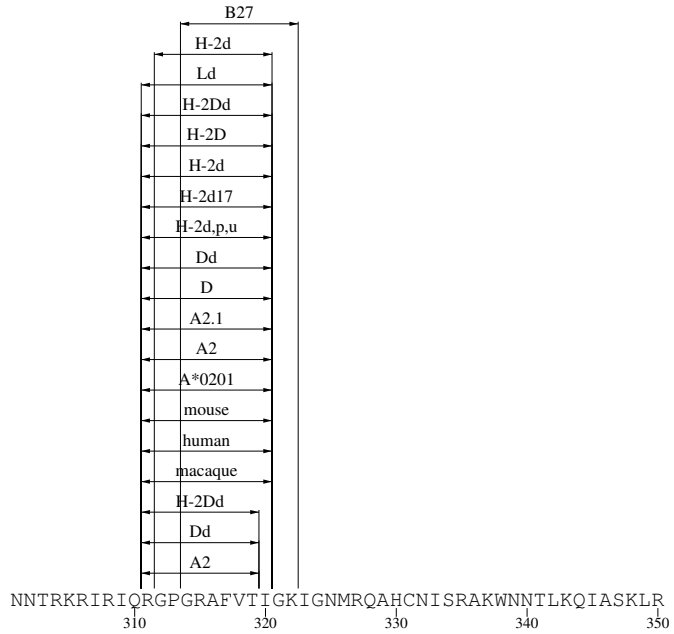

A2.1
A2 supertype
B7
human
human
A11
A2.1
A2
human
chimpanzee
human
B*3801
A*0201
A2
A*0201
VEQMHEDIISLWDQSLKPCVKLTPLCVSLKCTDLKNDTNTNSSSGRMIME
110
120
130
140
150

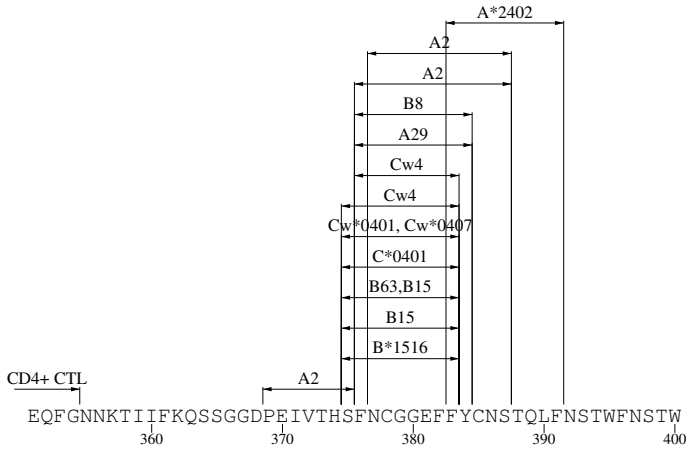

A*1101
human
A2.1
A2
A*02
A2
A2
Cw8
Cw*08
human
KGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSV
160
170
180
190
200

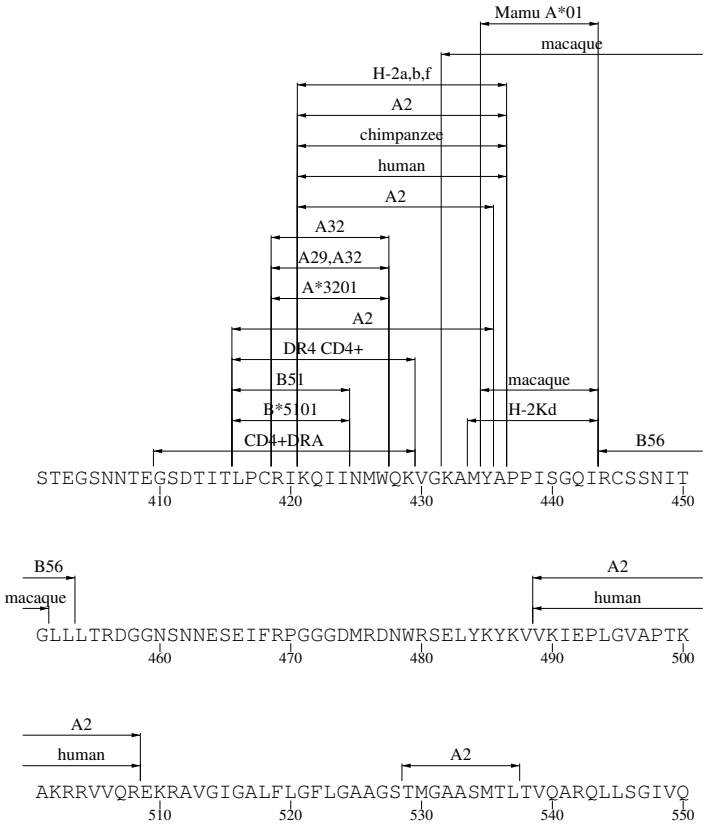

B57
A2
human
A29
A2
A29
A29
human
A*1101
human
A2
human
Cw8
B56
ITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHG
210
220
230
240
250

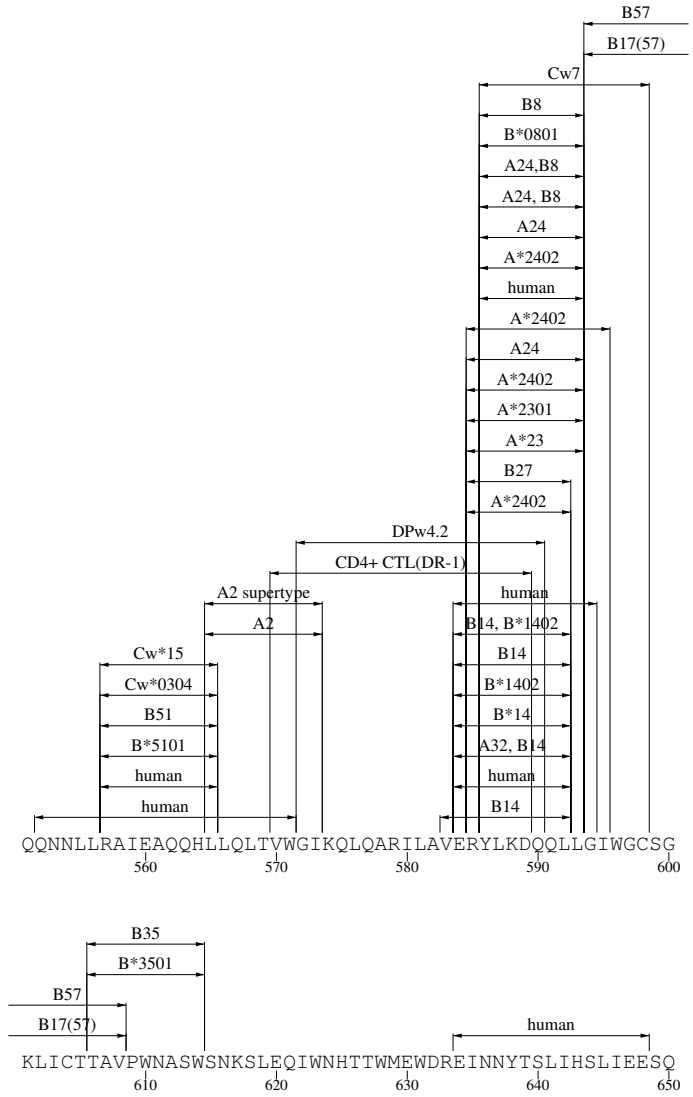

human
B7
B7?
human
B7
B7
B*0702
B35
B*07
B*3501
A2
human
human
IRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPN
260
270
280
290
300


H-2Dd
H-2Dd
A02
A*3002
A11
A*2402
H-2Dd
H-2Dd,p,q, H-2u
H-2d, H-2b
H-2d
H-2d,p,u,q
Dd
A2, A3
A2
A11
A*0201
mouse
chimpanzee
human
Dd
mouse
H-2Dd
human
H-2d
mouse
human
B7?
B7
B*0702
B*07
A2
human
Patr-B*14
A11
CD4+ CTL
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350


B27
H-2d
Ld
H-2Dd
H-2D
H-2d
H-2d17
H-2d,p,u
Dd
D
A2.1
A2
A*0201
mouse
human
macaque
H-2Dd
Dd
A2
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350


A*2402
A2
A2
B8
A29
Cw4
Cw4
Cw*0401, Cw*0407
C*0401
B63,B15
B15
B*1516
CD4+ CTL
A2
EQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
360
370
380
390
400


Mamu A*01
macaque
H-2a,b,f
A2
chimpanzee
human
A2
A32
A29,A32
A*3201
A2
DR4 CD4+
B51
B*5101
CD4+DRA
macaque
H-2Kd
B56
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNIT
410
420
430
440
450
B56
macaque
A2
human
GLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
460
470
480
490
500
A2
human
A2
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQ
510
520
530
540
550


B57
B17(57)
Cw7
B8
B*0801
A24,B8
A24, B8
A24
A*2402
human
A*2402
A24
A*2402
A*2301
A*23
B27
A*2402
DPw4.2
CD4+ CTL(DR-1)
A2 supertype
A2
Cw*15
Cw*0304
B51
B*5101
human
human
human
B14, B*1402
B14
B*1402
B*14
A32, B14
human
B14
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560
570
580
590
600
B35
B*3501
B57
B17(57)
human
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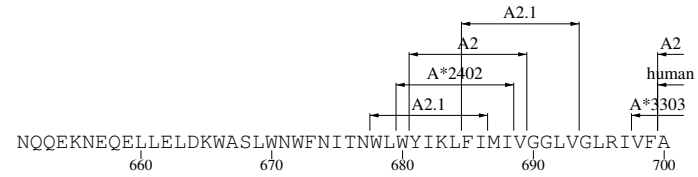
620
630
640
650


A2.1
A2
A2
A*2402
human
A2.1
A*3303
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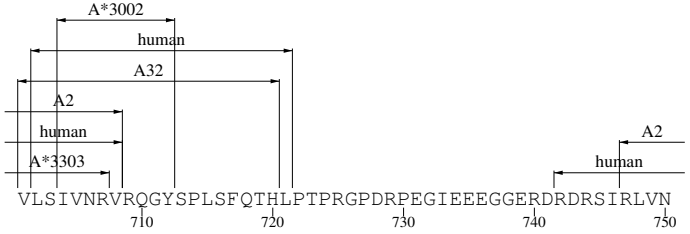
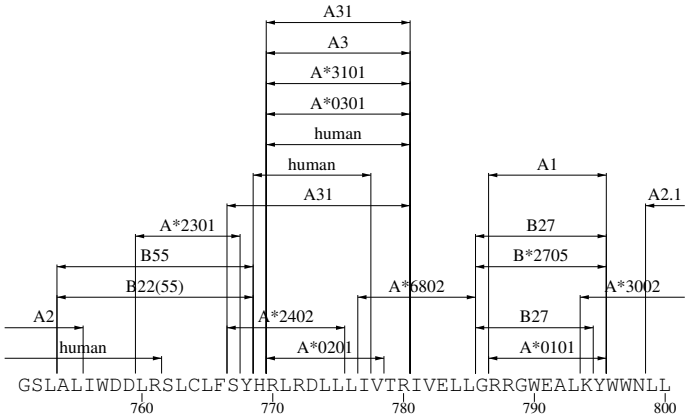
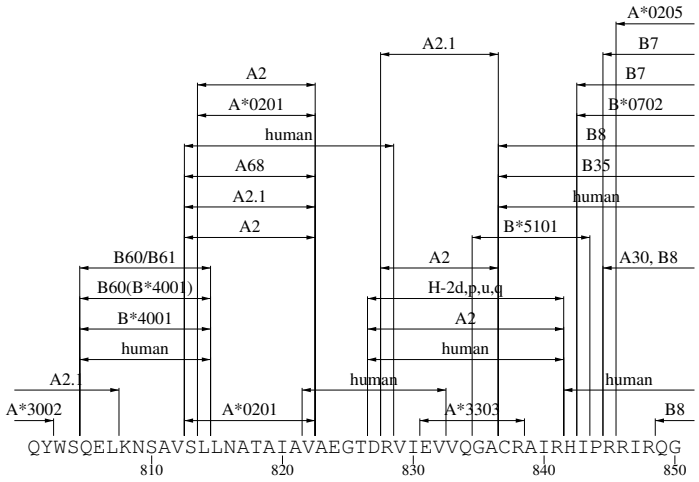
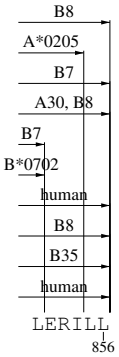
660
670
680
690
700

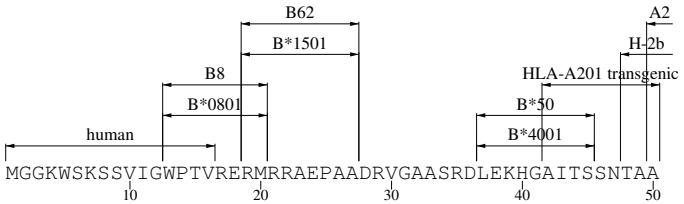

A*3002
human
A32
A2
human
A*3303
A2
human
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710
720
730
740
750

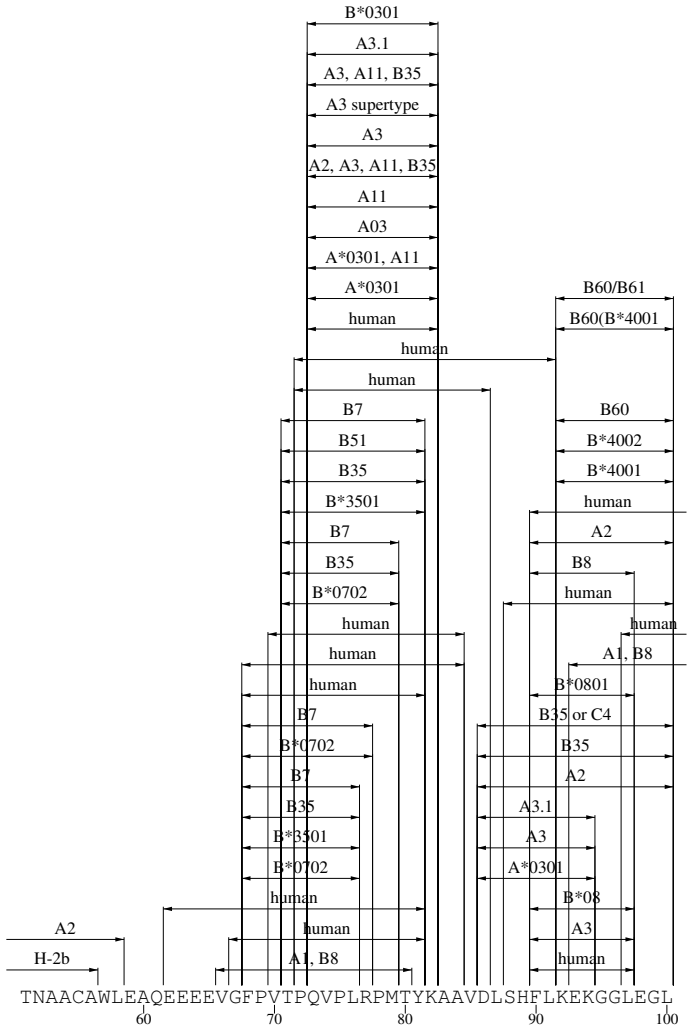

A31
A3
A*3101
A*0301
human
human
A1
A31
A2.1
A*2301
B27
B55
B*2705
B22(55)
A*6802
A*3002
A2
A*2402
B27
human
A*0201
A*0101
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760
770
780
790
800

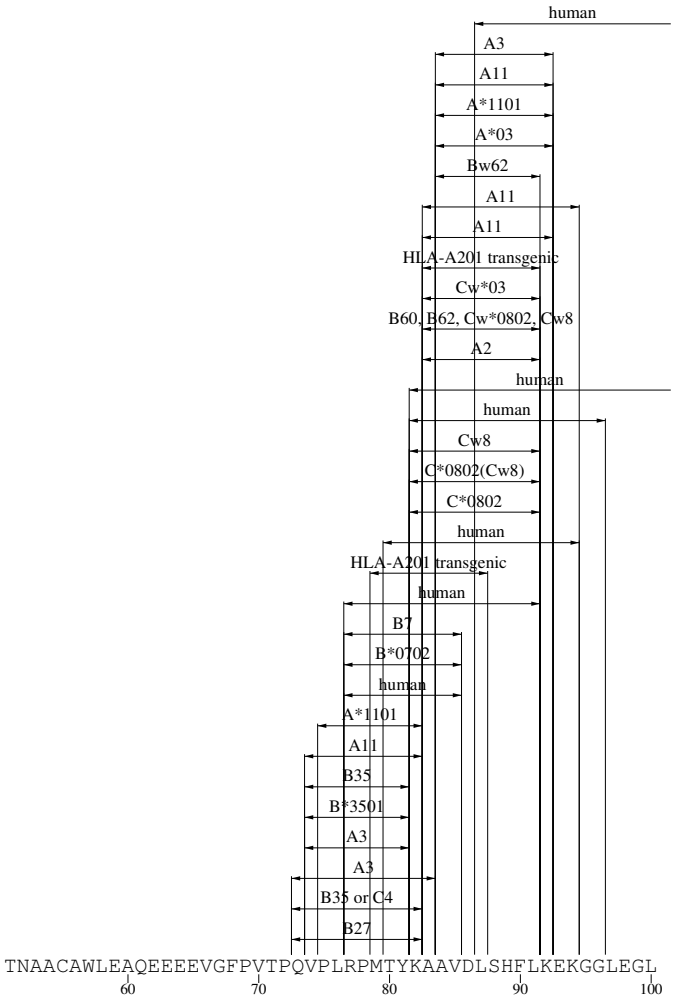

A*0205
A2.1
B7
A2
B7
A*0201
B*0702
human
B8
A68
B35
A2.1
human
A2
B*5101
B60/B61
A2
A30, B8
B60(B*4001)
H-2d,p,u,q
B*4001
A2
human
human
A2.1
human
human
A*3002
A*0201
A*3303
B8
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQG
810
820
830
840
850

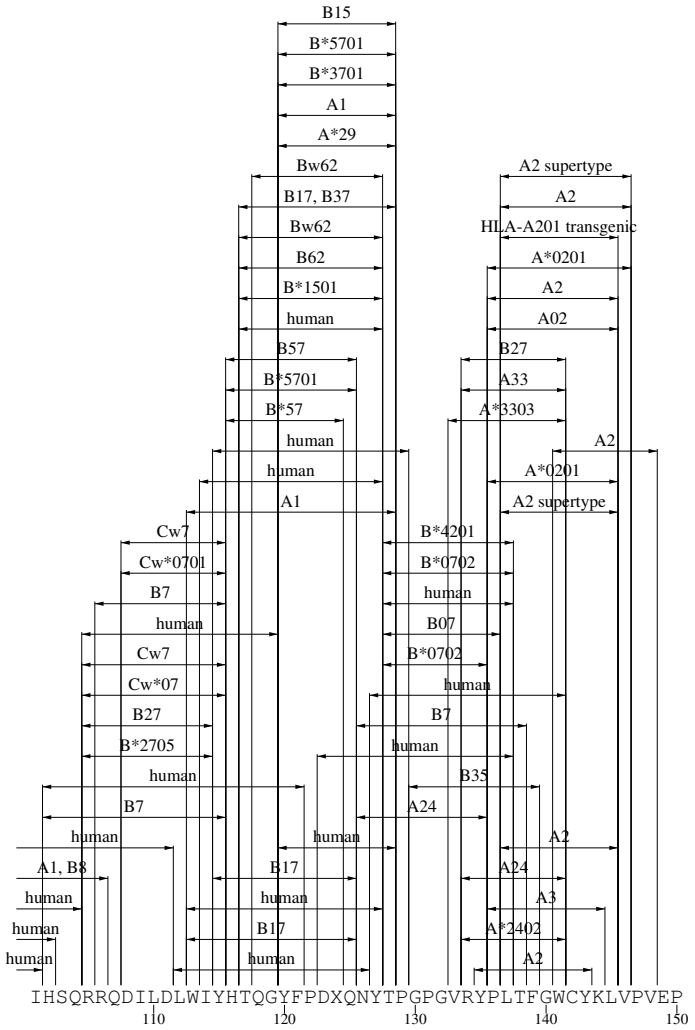

B8
A*0205
B7
A30, B8
B7
B*0702
human
B8
B35
human
LERILL
856

II-C-13 Nef CTL epitope map






human
A3
A11
A*1101
A*03
Bw62
A11
A11
HLA-A201 transgenic
Cw*03
B60, B62, Cw*0802, Cw8
A2
human
human
Cw8
C*0802(Cw8)
C*0802
human
HLA-A201 transgenic
human
B7
B*0702
human
A*1101
A11
B35
B*3501
A3
A3
B35 or C4
B27
TNAACAWLEAQEEEEVGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGLEGL
60
70
80
90
100


B15
B*5701
B*3701
A1
A*29
Bw62
B17, B37
Bw62
B62
B*1501
human
B57
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B*57
human
human
A1
Cw7
Cw*0701
B7
human
Cw7
Cw*07
B27
B*2705
human
B7
A1, B8
human
human
B17
human
B17
human
A2 supertype
A2
HLA-A201 transgenic
A*0201
A2
A02
B27
A33
A*3303
A2
A*0201
A2 supertype
B*4201
B*0702
human
B07
B*0702
human
B7
human
B35
A24
A2
A24
A3
A*2402
A2
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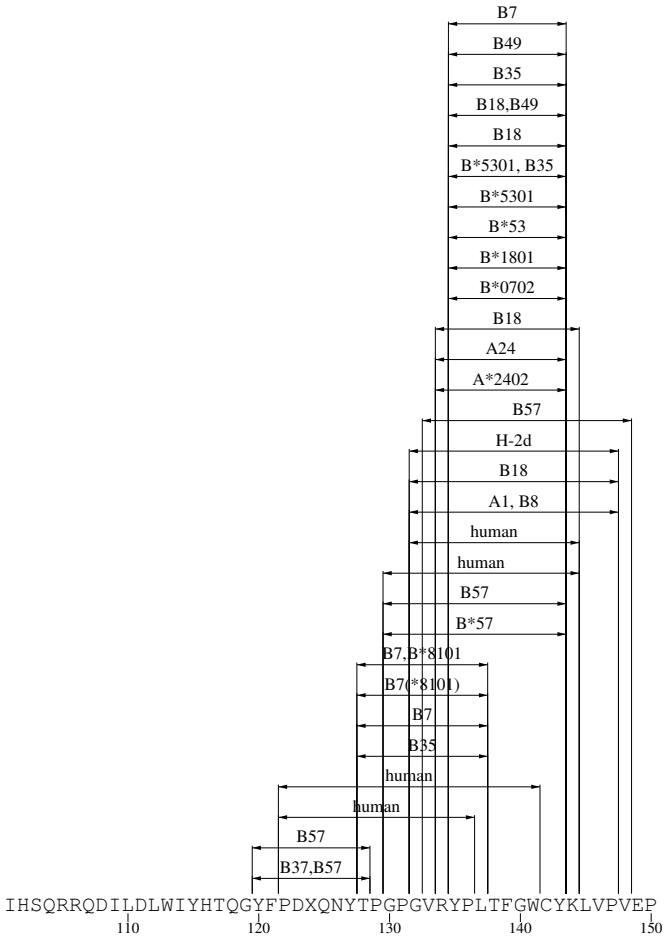
110
120
130
140
150


B7
B49
B35
B18,B49
B18
B*5301, B35
B*5301
B*53
B*1801
B*0702
B18
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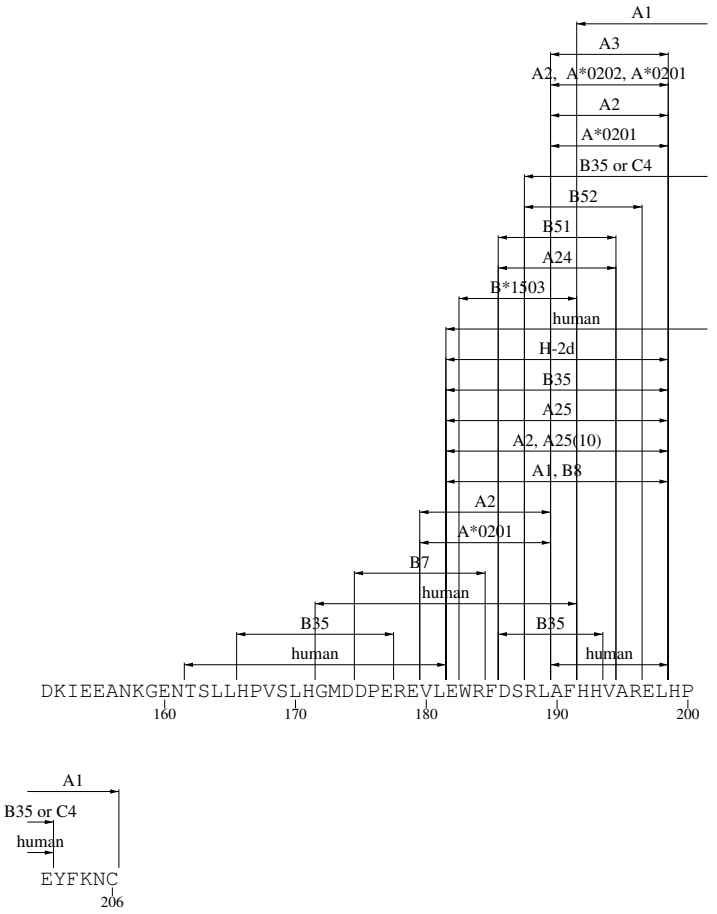
A*2402
B57
H-2d
B18
A1, B8
human
human
B57
B*57
B7,B*8101
B7(*8101)
B7
B35
human
human
B57
B37,B57
IHSQRRQDILDLWIYHTQGYFPDXQNYTPGPGVRYPLTFGWCYKLVPVEP
110
120
130
140
150


A1
A3
A2, A*0202, A*0201
A2
A*0201
B35 or C4
B52
B51
A24
B*1503
human
H-2d
B35
A25
A2, A25(10)
A1, B8
A2
A*0201
B7
human
B35
B35
human
human
DKIEEANKGENTSLLHPVSLHGMDDPEREVLEWRFDSRLAFHHVARELHP
160
170
180
190
200
A1
B35 or C4
human
EYFKNC
206

Part III

HIV Helper T-Cell Epitopes

III-A

Summary

Part III includes tables and maps of HIV-specific helper T-cell (Th) epitopes arranged sequentially according to the location of the proteins in the HIV-1 genome. This part parallels the organization of the CTL part. We attempted to make this part as comprehensive as possible, requiring that the epitope be contained within a region of 30 amino acids maximum, but not that the precise boundaries be defined. The HLA specificity is usually not determined for Th epitopes. For more recent updates, epitope sequence alignments, and useful searching capabilities, please see our web site: `http://www.hiv.lanl.gov/content/immunology`. The same epitope can have multiple entries, as each entry represents a single publication. Helper T-cell responses to proteins with no defined epitope are described at the end of each protein section.

Recent studies utilize multiple functions attributed to T cells to define responses, and the simple distinctions of cytotoxic T-cell and helper T-cells have become blurred as more is learned about the range of responses triggered in CD4 and CD8 positive T-cells responding to antigenic stimulus. When adding the most recent studies to the database, we have tried to place T cell responses in a reasonable manner into our traditional helper T cell and CTL parts, and to specify the assay used to measure the response in each study.

III-A-1 Tables

Each Th epitope has a multi-part basic entry:

HXB2 Location: The viral strain HXB2 (GenBank Accession Number K03455) is used as a reference strain throughout this publication. The position of the defined epitope location relative to the sequence of the HXB2 protein is indicated. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2, rather the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://www.hiv.lanl.gov/content/hiv-db/LOCATE/locate.html`.

Author Location: The amino acid positions of the epitope boundaries and the reference sequence are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases the reference sequence identification was not provided, and in such cases it is not possible to use these numbers to specify precise locations.

Epitope Sequence: The amino acid sequence of the epitope of interest as defined in the reference, based on the reference strain used in the study defining the epitope. On occasions when only the position numbers and not the actual peptide sequence were specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed by a question mark in the table.

Immunogen: The antigenic stimulus of the Th response to the defined epitope. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(HLA): The species responding and HLA specificity of the epitope, when known.

Reference: The primary reference (sometimes two or more directly related studies are included). Details for some of the earlier references are in Part V.

Keywords: Keywords are a searchable field for the web interface that is included in the T-cell sections of the printed version to help identify entries of particular interest.

Following the entry for a given Th epitope are brief comments explaining the context in which the epitope was studied and what was learned about the epitope in a given study.

III-A-2 HIV protein epitope maps

All HIV Th epitopes mapped to within a region of 21 amino acids or less are indicated on the HIV protein epitope maps. The location and HLA restriction elements of Th epitopes are indicated on protein sequences of HXB2. These maps are meant to provide the relative location of defined epitopes on a given protein, but the HXB2 sequence may not actually carry the epitope of interest, as it may vary relative to the sequence for which the epitope was defined. Epitopes with identical boundaries and HLA fields are included in the maps only once. If one laboratory determines HLA presenting molecules at the serotype level (example: A2) and another at the genotype level (example: A*0201) both will be included in the map. MHC specificities are indicative of the host species; when no MHC presenting molecule is defined, the host species is noted.

III-A-3 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the T helper epitope search tool at `http://www.hiv.lanl.gov/content/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site (`http://www.hiv.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html`). The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

III-B

HIV Helper T-Cell Epitope Tables

All HIV Helper T-Cell epitopes arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location within the protein and finally by HLA presenting molecule. Epitopes for which the HXB2 location is unknown appear at the end of the listing of the protein in which they are located.

III-B-1 p17 Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (18–42)	p17 (18–42 PV22)	KIRLRPGGKKKYKLKHIVW-ASRELE	HIV-1 infection	human (DRB1*13)	Lotti2002
	Keywords HAART, Th1, Th2. **Donor HLA** A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13. • 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 6 recognized this peptide sequence restricted by DRB1*13. This clone had a high SI (27.1 to p55, 90.6 to peptide) secreted IFNgamma, indicative of a Th1 response, as well as TNFalpha. Clone 6 was highly cytotoxic, through a perforin-mediated pathway.			
p17 (21–35)	p17 (21–35 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human (DR13.02)	Harcourt1998
	Keywords escape. • 43 asymptomatic HIV+ individuals were screened for proliferative responses to HIV – 12 showed a response, and dominant epitopes were mapped for two individuals, one in p24 and one in p17. • Patient 024's naturally occurring variant LRPGGKKKYQLKHIV also elicited a strong proliferative response. • Naturally occurring variants of this epitope were found within the individual who made this response – several did not stimulate the CD4+ T-cell line that recognized the index peptide, suggestive of immune escape.				
p17 (22–29)	p17 (22–29 LAI)	RPGGKKKY?	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors. • Schrier lists this peptide as p24(22-29), but it appears to be in p17.				
p17 (33–47)	p17 (33–47 IIIB, B10)	HIVWASRELERFAVN?	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• Peptides were identified that commonly evoke T-cell responses – 57% of 90 HIV+ people had a T-cell response to this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p17 (35–59)	p17 (35–49 PV22)	VWASRELERFAVNPGLLET-SEGCRQ	HIV-1 infection	human (DRB1*13)	Lotti2002
	Keywords HAART, Th1, Th2, TCR usage. **Donor HLA** A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13. • 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 25 recognized this peptide sequence restricted by DRB1*13 using TCR Vβ 5.1. This clone had a SI of 4.9 to p55, 13.7 to peptide, secreted low levels of IFNgamma, indicative of a Th1 response. Clone 25 had cytotoxic activity, mediated through both a perforin and a Fas-based pathway.			
p17 (93–107)	p17 (93–107 IIIB, B10)	EIKDTKEALDKIEEE	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p17 (118–132)	p17 (118–132 IIIB, B10)	AAADTGHSSQVSQNY	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				

III-B-2 p24 Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (1–9)	Gag (p24) (133–141 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. • The TCR that recognized this epitope used Vβ5.1.	PIVQNIQGQ	HIV-1 infection	human (DRβ1*0101)	Boritz2003
p24 (1–11)	p24 (1–11 SF2) **Keywords** escape. • 43 asymptomatic HIV+ individuals were screened for proliferative responses to HIV – 12 showed a response, and dominant epitopes were mapped for two individuals, one in p24 and one in p17. • Out of five truncated versions of peptide PIVQNLQGQMVHQAISPRTL, only p24(1-11) elicited a proliferative response. • Nine naturally occurring variants of this epitope were found within the individual who made this response – all bound to HLA-DR1, but three did not stimulate the CD4+ T-cell line that recognized the index peptide, suggestive of immune escape.	PIVQNLQGQMV	HIV-1 infection	human (DR1)	Harcourt1998
p24 (1–15)	p24 (133–147 IIIB, B10) • Peptides were identified that commonly evoke T-cell responses – 62% of 90 HIV+ people had a T-cell response to this peptide.	PIVQNIQGQMVHQAI	HIV-1 infection	human	Wahren1989b, Wahren1989a
p24 (1–22)	p24 (133–154 SF2) • While anti-HIV CD4 Th responses are characteristically undetectable in chronic infections, strong p24-specific proliferative responses were inversely correlated with low viral load in 10 chronically infected people. • The dominant proliferative response in one of two long term survivors was to this peptide.	PIVQNIQGQMVHQAISPRT-LNA	HIV-1 infection	human	Rosenberg1997
p24 (7–21)	Gag (171–185) **Keywords** inter-clade comparisons. **Epitope name** Gag 171. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds to nine HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRBI*0405, DRB1*1302, DRB1*0701, DRB1*0901, DRB5*0101 and DRB4*0101 with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 52% of clade B isolates. • 7/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)	QGQMVHQAISPRTLN	HIV-1 infection	human (DR supermotif)	Wilson2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (7–21)	Gag (171–185)	QGQMVHQAISPRTLN	Vaccine	mouse (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** Gag 171. **Donor HLA** H-2b. • Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice. • Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.				
p24 (11–26)	p24 (143–157)	VHQAISPRTLNAWVKC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors. • Matches 3/3 anchor residues for HLA DR: **V**HQAI**S**PR**T**				
p24 (11–30)	Gag (143–152 SF2)	VHQAISPRTLNAWVKVVEEK	Vaccine	mouse (H-2^d, H-2^b)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade SF2 *HIV component:* p24 Gag **Keywords** immunodominance, Th1. • Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response. • Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice. • Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this epitope is immunodominant in C57BL/6 mice and also can stimulate a BALB/c response. • The proliferative response is due to CD4+, IFNγ producing cells, a Th1 response.				
p24 (11–30)	p24 (143–162 HXB2)	VHQAISPRTLNAWVKVVEEK	Vaccine	mouse (H-2^d, H-2^b)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptides VHQAISPRTLNAWVKVVEEK and FRDYV-DRFYKTLRAEQASQD were recognized in H-2^b and H-2^d mice.				
p24 (21–36)	p24 (153–167)	NAWVKVVEEKAFSPEC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors.				
p24 (28–36)	Gag (p24) (160–168 HXB2)	EEKAFSPEV	HIV-1 infection	human (DRβ1*0101)	Boritz2003
	Keywords HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. • The TCR that recognized this epitope used Vβ2.				
p24 (31–46)	p24 (163–177)	AFSPEVIPMFSALSEC	in vitro stimulation or selectio	human (A*0201)	Bedford1997
	• E elicits a primary proliferative response in PBMC from uninfected donors. • Peptide contains a CTL epitope identified in HIV-positive patients. • Peptide binds to HLA A*0201 and causes regulation of class I expression on T2 cells. • Matches 3/3 anchor residues for HLA DR: **V**IPMF**S**AL**S**				
p24 (31–52)	p24 (163–184 SF2)	AFSPEVIPMFSALSEGATP-QDL	HIV-1 infection	human	Rosenberg1997
	• Low viral load correlated with strong HIV-1-specific proliferative response. • A proliferative response to this epitope was detected in two long term survivors.				
p24 (35–44)	Gag (p24) (167–176 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51.	EVIPMFSALS	HIV-1 infection	human (DRβ1*0101)	Boritz2003
	• HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.				
p24 (41–56)	p24 (173–187)	SALSEGATPQDLNTMC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors.				
p24 (48–62)	p24 (180–194)	TPQDLNTMLNTVGGH	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of proliferative response to p24. • Homology to an SIV epitope recognized by macaque T-cells. • T-cells from 8 of 19 HIV+ individuals responded to this epitope. • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.				
p24 (51–66)	p24 (183–197)	DLNTMLNTYGGHQAAC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors.				
p24 (51–82)	Gag (183–214 LAI) **Vaccine** *Vector/Type:* lipopeptide	DLNTMLNTVGGHQAAMQML-KETINEEAAEWDR	Vaccine	human	Gahery-Segard2000
	• Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 2/10 reacted to this peptide. • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual. • None of the 12 tested had an IgG response to this peptide.				
p24 (69–88)	Gag (p24) (201–220 IIIB) **Keywords** immunodominance, Th1, Th2, TCR usage. **Epitope name** P21. **Donor HLA** DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 85 recognized this peptide using TCR Vβ 8 and 18; the two TCR receptors indicates this limiting dilution represents a mixed population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.	LKETINEEAAEWDRVHPVHA	in vitro stimulation or selectio	human (DR)	Venturini2002
p24 (71–86)	p24 (203–220) • Epitope elicits a primary proliferative response in PBMC from uninfected donors.	ETINEEAAEWDRVHPC	in vitro stimulation or selectio	human	Bedford1997
p24 (71–88)	p24 **Epitope name** 17. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51.	ETINEEAAEWDRVHPVHA		(DRβ1*0101)	
p24 (71–88)	(203–220) **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51.	ETINEEAAEWDRVHPVHA		human (DRβ1*0101)	
p24 (71–88)	**Epitope name** 17. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51.	ETINEEAAEWDRVHPVHA		(DRβ1*0101)	
p24 (71–88)	Gag (p24) (203–220 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. • The Th clone that recognized this epitope utilized TCR Vβ17.	ETINEEAAEWDRVHPVHA	HIV-1 infection	human (DRβ1*0101)	Boritz2003
p24 (71–92)	Gag (p24) (203–224 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining.	ETINEEAAEWDRVHPVHAG-PIA	HIV-1 infection	human (DRβ1*0101)	Boritz2003

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.				
p24 (73–97)	p24 (205–229 PV22)	INEEAAEWDRVHPVHAGPI-APGQMR	HIV-1 infection	human (DRB1*03)	Lotti2002
	Keywords HAART, Th1, Th2, TCR usage. **Donor HLA** A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13. • 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 12 recognized this peptide sequence restricted by DRB1*03 using TCR Vβ 22. This clone had a SI of 12.4 to p55, 49.6 to peptide, secreted low levels of IFNgamma, indicative of a Th1 response. Clone 12 had cytotoxic activity, mediated through both a perforin and a Fas-based pathway.				
p24 (76–85)	p24 (208–217)	EAAEWDRVHP	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of the proliferative response to p24. • T-cells from 11 of 24 HIV+ individuals responded to this epitope. • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.				
p24 (76–90)	p24 (208–222 IIIB, B10)	EAAEWDRVHPVHAGP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (79–88)	Gag (p24) (211–220 HXB2)	EWDRVHPVHA	HIV-1 infection	human (DRβ1*0101)	Boritz2003
	Keywords HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were also recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. Two clones recognized this epitope.				
p24 (81–95)	p24 (215–229 SF2)	DRVHPVHAGPIAPGQ	Vaccine	macaque	Mills1990
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade SF2 *HIV component:* p24 Gag • Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (81–102)	p24 (213–234 SF2)	DRVHPVHAGPIAPGQMREP-RGS	HIV-1 infection	human	Rosenberg1997
	• While anti-HIV CD4 Th responses are characteristically undetectable in chronic infections, strong p24-specific proliferative responses were inversely correlated with low viral load in 10 chronically infected people. • The dominant proliferative response in one of two long term survivors was to this peptide.				
p24 (86–94)	p24 (NY5)	VHAGPIAPG	HIV-1 infection	human (DQ7)	Norris2001b
	Keywords HAART, supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection, cross-presentation by different HLA, early treatment, TCR usage. • Gag-specific CD4+ helper T-cell clones were derived from one long-term non-progressor (LTNP) (CTS-01), and three individuals given therapy during acute infection, two before (AC-01 and AC-36) and one after (AC-25) STI. Gag peptide recognition induced proliferation, IFNgamma production and perforin-mediated cytotoxicity in all CD4+ T-cell clones isolated. • 3/23 p24-derived peptides tested induced proliferative p24-specific T-helper cell responses in the LTNP CDT-01. The immunodominant response was to the peptide DRVHPVHAGPIAPGQMREPRGS (81-102), and 9/10 CD4+ T-cell clones reacted with it. One was characterized in detail and used a Bβ4 TCR. • The minimum peptide recognized by the clones from CDT-01 was VHAGPIAPG and it was restricted by HLA-DQ7.			
p24 (87–101)	p24 (219–233 BRU)	HAGPIAPGQMREPRG	in vitro stimulation or selectio	mouse (H-2^b)	Vaslin1994
	• Peptide G2: could prime for *in vitro* immunoproliferative responses and for subsequent IgG responses.				
p24 (96–103)	p24 (228–235 LAI)	MREPRGSD	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
p24 (96–110)	p24 (228–242 IIIB, B10)	MREPRGSKIAGTTST	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (99–118)	Gag (p24) (231–250 IIIB)	PRGSDIAGTTSTLQEQIGWM	in vitro stimulation or selectio	human (DR4)	Venturini2002
	Keywords immunodominance, Th1, Th2, TCR usage. **Epitope name** P24. **Donor HLA** DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 6 recognized three peptides including this one with a Th1 response using TCR Vβ 6 (6s5A1N1). Sequencing TCR Vβ regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide does not carry the main epitope of this clone.			
p24 (101–115)	p24 (235–249 SF2)	GSDIAGTTSTLQEQI	Vaccine	macaque	Mills1990
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade SF2 *HIV component:* p24 Gag • Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques – epitope response defined by T-cell clone.				
p24 (101–116)	p24	GSDIAGTTSTLQEQIC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p24 (109–128)	Gag (p24) (241–260 IIIB)	STLQEQIGWMTNNPPIPVGE	in vitro stimulation or selectio	human	Venturini2002
	Keywords immunodominance, Th1, Th2, TCR usage. **Epitope name** P25. **Donor HLA** DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 50 recognized this peptide with a Th0 response (Th0 means that cytokines characteristic of both Th1 and Th2 responses were stimulated), using TCR Vβ 17, and was a homogeneous T-cell population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.				
p24 (111–132)	p24 (243–264 SF2)	LQEQIGWMTNNPPIPVGEI-YKR	HIV-1 infection	human	Rosenberg1997
	• Low viral load correlated with strong HIV-1-specific proliferative response. • A proliferative response to this epitope was detected in two long term survivors.				
p24 (119–133)	p24 (251–265)	TNNPPIPBGEIYKRW	HIV-1 infection	human (DRB1*1301)	Blankson2001b, Malhotra2001
	Keywords binding affinity, HAART. • The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months. • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment. • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (LTNPs) (it was in 9/18 versus, versus 21% of the general population) • This epitope was mapped with truncated peptides using the Elispot assay. • Two distinct DRB1*13 epitopes were defined in the peptide region spanning 251 to 270, and this 20-mer bound with very high affinity to DRB1*1302 – DRB1*1301 and DRB1*1302 would be expected to have very similar binding properties.				
p24 (121–136)	p24 (253–267)	NPPIPVGEIYKRWIIC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors.				
p24 (121–140)	Gag (253–272 SF2)	NPPIPVGEIYKRWILGLNK	Vaccine	mouse (H-2^d)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade SF2 *HIV component:* p24 Gag **Keywords** immunodominance, Th1. • Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response. • Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice. • Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this epitope is immunodominant in BALB/c mice and did not stimulate a C57BL/6 response. • The proliferative response is due to CD4+, IFNγ producing cells, a Th1 response.				
p24 (121–140)	p24 (253–272 HXB2)	NPPIPVGEIYKRWIILGLNK	Vaccine	mouse (H-2^d)	Mata1999
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag **Keywords** immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptide MPPIPVGEIYKRWIILGLNK gave the immunodominant response for the H-2^d haplotype, but was not recognized in H-2^b mice.				
p24 (121–152)	Gag (183–214 LAI)	NPPIPVGEIYKRWIILGLN-KIVRMYSPTSILD	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 9/10 reacted to this peptide. • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees. • All of the 12 tested had an IgG response to this peptide.				
p24 (127–141)	Gag (294–308)	GEIYKRWIILGLNKI	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Gag 294. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicted proliferative responses from multiple HIV-infected donors. • This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101 with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 95% of clade B isolates. • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
p24 (128–137)	p24 (260–269)	EIYKRWIILG	HIV-1 infection	human (DRB1*1301, DRB1*1302)	Blankson2001b, Malhotra2001
	Keywords binding affinity, HAART, Th1. • The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months. • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment. • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population) • The truncated peptide that gave the optimal proliferative response for a Th1 phenotype clone was this nine-mer. • This region, shared by 2 overlapping peptides, was the reactive region for clones from two DRB1*13 patients, one carried DRB1*1301 and one DRB1*1302. • Two distinct epitopes were defined in the peptide region spanning 251 to 270, and this 20-mer bound with very high affinity to DRB1*1302 – DRB1*1301 and DRB1*1302 would be expected to have very similar binding properties.				
p24 (129–148)	Gag (p24) (261–280 IIIB)	IYKRWIILGLNKIVRMYSPT	in vitro stimulation or selectio	human	Venturini2002
	Keywords immunodominance, Th1, Th2, TCR usage. **Epitope name** P27.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 74 recognized two peptides including this one with a Th1 response using TCR Vβ 13 (13s1); it required 200 ng/ml (100 nM) and 1 µg/ml (0.5 µM) for stimulation by peptides 480-500 and 261-280, respectively. Sequencing TCR Vβ regions of colonies from clone 74 suggested this was a clonal population.				
p24 (131–145)	p24 (265–279 SF2)	KRWIILGLNKIVRMY	Vaccine	macaque	Mills1990
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade SF2 *HIV component:* p24 Gag • Responses to 3 T-cell and multiple linear B-cell epitopes were found in vaccinated macaques – epitope response defined by T-cell clone.				
p24 (131–145)	Gag (298–312)	KRWIILGLNKIVRMY	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Gag 298. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds thirteen HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0802, DRB1*0701, DRB1*1302, DRB1*1201, DRB1*1101, DRB1*0405, DRB1*0401, DRB*0301, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 94% of clade B isolate. • 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
p24 (131–152)	p24 (263–284 SF2)	KRWIILGLNKIVRMYSPTS-ILD	HIV-1 infection	human	Rosenberg1997
	• Low viral load correlated with strong HIV-1-specific proliferative response. • A proliferative response to this epitope was detected in two long term survivors.				
p24 (135–154)	p24 (267–286)	ILGLNKIVRMYSPTSILDIR	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of the proliferative response to p24. • 8 of 24 HIV+ individuals responded to this epitope. • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.				
p24 (139–157)	Gag (p24) (271–290 IIIB)	NKIVRMYSPTSILDIRQGP	in vitro stimulation or selectio	human (DR4)	Venturini2002
	Keywords immunodominance, Th1, Th2, TCR usage. **Epitope name** P28. **Donor HLA** DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 6 recognized three peptides including this one with a Th1 response using TCR Vβ 6 (6s5A1N1). Sequencing TCR Vβ regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide, 271-290, contains the main epitope of this clone. Upon activation, clone 6 was observed to induce a cytopathic effect in the adherent layer of fibroblasts expressing HLA DR4W14 and -W15. Clone 6 was activated in response to vaccinia virus Gag-infected B-LCL, so it could recognize naturally processed epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Clone 37 recognized this peptide sequence with a Th2 response using TCR Vβ 3, and was a homogeneous T-cell population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL. • Clone 97 recognized this peptide sequence with a using TCR Vβ 9 and 14; the two TCR receptors used indicates this limiting dilution represents a mixed population. This clone was only activated by peptide, not by processed protein from vaccinia virus Gag-infected B-LCL.				
p24 (140–148)	Gag (p24) (272–280 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. • The Th clone that recognized this epitope utilized TCR Vβ 5.2.	KIVRMYSPT	HIV-1 infection	human (DRβ1*0101)	Boritz2003
p24 (141–156)	p24 (273–287) • Epitope elicits a primary proliferative response in PBMC from uninfected donors. • Matches 3/3 anchor residues for HLA DR: **I**VRMY**S**PT**S**	IVRMYSPTSILDIRQC	in vitro stimulation or selectio	human	Bedford1997
p24 (146–160)	p24 (278–292 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	SPTSILDIRQGPKEP	HIV-1 infection	human	Wahren1989b, Wahren1989a
p24 (149–168)	Gag (p24) (281–300 IIIB) **Keywords** immunodominance, Th1, Th2, TCR usage. **Epitope name** P29. **Donor HLA** DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA clas II DR restricted. • Clone 6 recognized three peptides including this one with a Th1 response using TCR Vβ 6 (6s5A1N1). Sequencing TCR Vβ regions of colonies from clone 6 suggested this was a clonal population. Assays using different peptide concentrations suggest that this peptide does not carry the main epitope of this clone.	SILDIRQGPKEPFRDYVDRF	in vitro stimulation or selectio	human (DR4)	Venturini2002
p24 (150–169)	p24 (282–301) • Stimulates T-cell proliferation in HIV-infected donors.	ILDIRQGPKEPFRDYVDRFY	HIV-1 infection	human	Schrier1989
p24 (151–166)	p24 (283–297) • Epitope elicits a primary proliferative response in PBMC from uninfected donors.	LDIRQGPKEPFRDYVC	in vitro stimulation or selectio	human	Bedford1997
p24 (155–177)	p24 (287–309) **Vaccine** *Vector/Type:* peptide	QGPKEPFRDYVDRFYKTLR-AEQA	Vaccine	mouse	Nakamura1997

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mice immunized with this peptide generated proliferative responses, CTLs and antibodies. • This immunogenic domain is from a highly conserved region of p24.				
p24 (156–170)	p24 (288–302 IIIB, B10)	GPKEPFRDYVDRFYK	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
p24 (156–174)	p24 (287–306)	QPKEPFRDYVDRFYKTLRA	HIV-1 infection	human	Adams1997
	• One of four immunogenic Gag peptides used in study of the proliferative response to p24. • T-cells from 5 of 21 HIV+ individuals responded to this epitope. • Improved assay system (increase in culture time to 8 days and addition of IL-2 to cultures) gave increased detection of proliferative response.				
p24 (157–165)	Gag (p24) (289–297 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects.	PKEPFRDYV	HIV-1 infection	human (DQ5)	Boritz2003
p24 (161–180)	Gag (293–312 SF2) **Vaccine** *Vector/Type:* Listeria monocytogenes *Strain:* B clade SF2 *HIV component:* p24 Gag **Keywords** Th1. • Listeria moncytogenes is an intracellular bacterium that lives in the cytoplasm and generates a cell-mediated immune response. • Listeria moncytogenes vaccine expressing HIV-1 p24 protein (Lm-Gag) was used to stimulate gag specific CD4+ T cell proliferative responses in BALB/c(H-2d) and C57BL/6(H-2b) mice. • Two of three reactive p24 peptides (out of 22 overlapping peptides that span p24) were recognized by both murine strains – this peptide stimulated a response in both BALB/c and C57BL/6 mice. • The proliferative response is due to CD4+, IFNγ producing cells, a Th1 response.	FRDYVDRFYKTLRAEQASQD	Vaccine	mouse (H-2^d, H-2^b)	Mata1999
p24 (161–180)	p24 (293–312 HXB2) **Vaccine** *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • The class II T helper response was probed using 20 mer peptides that overlapped by 10, and the peptides VHQAISPRTLNAWVKVVEEK and FRDYV-DRFYKTLRAEQASQD were recognized in H-2^b and H-2^d mice.	FRDYVDRFYKTLRAEQASQD	Vaccine	mouse (H-2^d, H-2^b)	Mata1999
p24 (163–175)	Gag (295–307) **Keywords** HAART, supervised treatment interruptions (STI). **Assay type** cytokine production, proliferation, Tetramer binding, CD4 T-cell Elispot - IFNγ.	DYVDRFYKTLRAE	HIV-1 infection	human (DR0101)	Iyasere2003

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Fifteen patients recieving HAART with strong CD4+ proliferative responses to HIV antigens while on therapy were examined, to see the effects of viremia on these responses during treatment interuptions. Increased viremia occurred in 12/15 patients during at least one treatment interuption. Anti-HIV proliferative responses were inhibited during viremia, but IFNgamma production to Gag, Pol, and Nef peptide pools were maintained. • IL-2 production diminished during viremia, and exogenous IL-2 revived *in vitro* proliferation of HIV-specific T cells to a Gag or Pol DR0101 epitopes in a tetramer as well as Gag-specific total CD4 T-cell responses.				
p24 (163–177)	p24 (295–309)	DYVDRFYKTLRAEQA	HIV-1 infection	human (DRB1*1302)	Blankson2001b, Malhotra2001
	Keywords HAART. • The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months. • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment. • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population) • This epitope was mapped with truncated peptides using the Elispot assay, and is highly conserved.				
p24 (163–177)	p24 (295–309)	DYVDRFYKTLRAEQA	HIV-1 infection	human (DRB1*1302)	Blankson2001b, Malhotra2001
	Keywords HAART. • The DRB1*13-DQB1*06 haplotype is associated with maintained viral suppression after HAART – 7/7 early-treated DRB1*13-DQB1*06 positive people, but only 3/14 (21%) of those who did not have DRB1*13-DQB1*06, maintained viral suppression for 18 months. • PBMC from individuals with the haplotype DRB1*13-DQB1*06 displayed increased IFNγ secretion and stronger proliferative responses against p24 80 weeks post treatment. • DRB1*13-DQB1*06 was also found to be enriched among long-term non-progressors (it was in 9/18 versus, versus 21% of the general population) • This epitope was mapped with truncated peptides using the Elispot assay, and is highly conserved.				
p24 (175–199)	p17 (307–331 PV22)	EQASQEVKNWMTETLLVQN-ANPDCK	HIV-1 infection	human (DRB1*03)	Lotti2002
	Keywords HAART, Th1, Th2, TCR usage. **Donor HLA** A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13. • 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage, and some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production). 5/10 CD4+ clones could also induce cytotoxicity. • 4/10 clones from patient F45 had their epitopes mapped using overlapping peptides. Clone 26 recognized this peptide sequence restricted by DRB1*03. This clone had a SI of 4.1 to p55, 5.3 to peptide, secreted high levels of IFNγ, indicative of a Th1 response, but also IL-4 and IL-5. Clone 26 had no cytotoxic activity.				
p24 (181–196)	p24 (313–327)	VKNWMTETLLVQNANC	in vitro stimulation or selectio	human	Bedford1997
	• Epitope elicits a primary proliferative response in PBMC from uninfected donors. • Matches 3/3 anchor residues for HLA DR: **V**KNWM**T**ET**L**				

III-B-3 p2p7p1p6 Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
p2p7p1p6 (18–37)	Gag (p24) (384–400 HXB2) **Keywords** HAART. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. **Donor HLA** DRβ1*0101, DRβ1*1501, DQ5, DQ1, DR51. • HIV infected individuals with advanced disease often have only weak or undetectable HIV specific Th responses, and HAART can sometimes restore Th HIV recognition in such cases. The repertoire of Th responses to p24 in an individual who responded to HAART after having a CD4+ T-cell count of 0 cells/ul was determined. Eleven clonotypes were found among 13 clones, recognizing eight distinct epitopes, with a range of MHC affinities and functional avidities. Multiple Gag p24 peptides were recognized using CD4 Elispot assays based on samples from six additional HAART-treated CD4 T-cell-reconstituted subjects. • The two Th clones that recognized this epitope utilized TCR Vβ2 and Bβ8.1.	GNFRNQRKIVKCFNCGKEGH	HIV-1 infection	human (DR15/51)	Boritz2003
p2p7p1p6 (30–44)	p15 (393–407 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	FNCGKEGHTARNCRA	HIV-1 infection	human	Wahren1989b, Wahren1989a
p2p7p1p6 (55–69)	p15 (418–432 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	KEGHQMKDCTERQAN	HIV-1 infection	human	Wahren1989b, Wahren1989a
p2p7p1p6 (60–74)	p15 (423–437 IIIB, B10) • 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.	MKDCTERQANFLGKI	HIV-1 infection	human	Wahren1989b, Wahren1989a
p2p7p1p6 (76–83)	p24 (439–446 LAI) • Stimulates T-cell proliferation in HIV-infected donors. • Schrier lists this peptide as p24(439-446), but because of the numbering used for Gag epitopes, we placed it in p2p7p1p6.	PSYKGRPG	HIV-1 infection	human	Schrier1989
p2p7p1p6 (83–97)	p15 (446–460 BRU) • Peptide G4: could prime for *in vitro* immunoproliferative responses and for subsequent IgG responses.	GNFLQSRPEPTAPPA	in vitro stimulation or selectio	mouse (H-2^b)	Vaslin1994
p2p7p1p6 (98–112)	p15 (473–487 IIIB, B10) • Peptides were identified that commonly evoke T-cell responses – 50% of 90 HIV+ people had a T-cell response to this peptide.	ESFRSGVETTTPPQK	HIV-1 infection	human	Wahren1989b, Wahren1989a
p2p7p1p6 (103–110)	p24 (466–473 LAI) • Stimulates T-cell proliferation in HIV-infected donors. • Schrier lists this peptide as p24(466-473), but it is in p2p7p1p6.	REETTTPS	HIV-1 infection	human	Schrier1989
p2p7p1p6 (117–137)	Gag (p6) (480–500 IIIB) **Keywords** immunodominance, Th1, Th2, TCR usage. **Donor HLA** DR4, DR7 DQ2 and DQ3. • PBMC from a seronegative donor, the healthy brother of a pair of monozygotic twins discordant for HIV-1 infection, were used to generate HIV-1 Gag-specific CD4+ T-cell clones by *in vitro* immunization with HIV-1 overlapping 20mer peptides spanning p55. Six clones were generated by limiting dilution. All reacted with p24 except one which recognized a p24 peptide and a p6 peptide. All CD4+ T cell clones were HLA class II DR restricted.	DKELYPLTSLRSLFGNDPS-SQ	in vitro stimulation or selectio	human	Venturini2002

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Clone 74 recognized two peptides, including this one, with a Th1 response using TCR Vβ 13 (13s1); it required 200 ng/ml (100 nM) and 1 µg/ml (0.5 µM) for stimulation by peptides 480-500 and 261-280, respectively. Sequencing TCR Vβ regions of colonies from clone 74 suggested this was a clonal population. Clone 74 was activated in response to vaccinia virus Gag-infected B-LCL, so it could recognize naturally processed epitopes.				

III-B-4 Gag Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24		HIV-1 infection, Vaccine	human	Kelleher1998b
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* p17 Gag, p24 Gag • Immunization of HIV+ people with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre. • Immunization with p24-VLP showed a modest, short-lived increased proliferative response to p24.				
Gag	p24		HIV-1 infection, Vaccine	human	Maino2000
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)), protein *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus, p24 Gag • 18 HIV-1-seropositive patients with a low frequency or no detectable CD4+ T cell response to HIV-1 antigen received an HIV-1 immunogen consisting of 10 units of native p24 and 100 ug of HZ321, a gp120 depleted antigen. • Using flow-cytometric methods, HIV-1 specific CD4+ T cells were shown to increase in response to immunization – in many patients significant enhancement was observed after a single immunization. • The frequency of CD4+ T cells expressing cytokines in response to antigen by FACS was correlated with a lymphoproliferation assay.				
Gag	p24		HIV-1 infection	human	Ruiz2000
	Keywords HAART, supervised treatment interruptions (STI). • Structured treatment interruption in chronically infected patients allowed recovery of p24 Th proliferative responses after HAART therapy discontinuation in 2/12 patients. • The Th response to p24 was identified during peak viremia in one patient, while in the second it was noted when viremia was controlled after restarting antiviral therapy.				
Gag	p24		HIV-1 infection	human	Lori1999
	• Ten patients with acute, pre-seroconversion HIV-1 infections were treated with didanosine, indinavir and hydroxyurea – this treatment is associated with normalization of immune parameters. • A vigorous HIV-specific Th response (stimulation index greater than 8) was observed in 7/8 patients treated before complete WB seroconversion, but in only 1/5 controls treated after seroconversion. • Vigorous Th responses were detected as early as 34 days after treatment begin. • Patients treated prior to seroconversion had no loss of naive CD4 T lymphocytes, recovery of up to 35% of the naive CD8 cells in several weeks, and a reduced latent viral reservoir.				
Gag	p24		HIV-1 infection	human	Haslett2000
	Keywords HAART, supervised treatment interruptions (STI), Th1. • 11/22 adult patients on HAART showed strong CD4+ T-cell IFNγ producing Th1 responses to HIV p24. • The magnitude of the Th1 response correlated with previous interruptions in HAART, suggesting the interruptions primed or boosted the response. • In contrast, the magnitude of the CD8+ CTL response did not correlate with interruptions in therapy, although a greater breadth in response was associated with interruptions in HAART.				
Gag	p24		HIV-1 infection, Vaccine	human	Klein1997
	Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* p17 Gag, p24 Gag • Immunization of HIV+ people with a HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Two of four subjects that received 500 or 1000 ug of p24-VLP had an increase in gag-specific CTL.				
Gag	p24		Vaccine	human	Moss1998
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus **Keywords** inter-clade comparisons. • Immunization with gp120 depleted HZ321 virus (REMUNE^{TM}) triggered an increase in lymphocyte proliferative response to native p24, a clade B virus and clade E viral antigens – Z321 is clade A in env and clade G in gag. [Moss1998]				
Gag	p24		HIV-1 infection	human	Rosenberg1999
	Keywords HAART. • This paper reviews the role of T-cells in viral control and HIV disease outcome. • Strong anti-p24 lymphoproliferative responses were found in seven persons who were treated with potent anti-viral therapy during acute HIV-1 infection syndrome. • This suggests that Th cells are part of the normal response to HIV-1 infection, but their numbers are rapidly diminished by either being infected during the peak viremia or by activation-induced cell death – if peak viremia can be controlled, a robust anti-p24 Th response can be maintained.				
Gag	p24		HIV-1 infection	human	Rosenberg1998
	Keywords HAART. • Strong Th responses have been found in rare individuals who effectively maintain low viral loads. • If aggressive anti-retroviral therapy is given prior to sero-conversion, strong helper responses can be maintained.				
Gag	p17		Vaccine	mouse	Birk1998a
	Vaccine *Vector/Type:* protein *HIV component:* p17 Gag • Different p17 genes derived from the same quasispecies and expressed and purified in E. coli primed different Th 1 and Th 2 subsets in mice, depending on their H-2 type.				
Gag	Gag		HIV-1 infection	human	Schiller2000
	• Study of parameters that might influence the performance or reproducibility of clinical Th proliferative assays. • HIV-1 replication *in vitro* is unlikely to influence the assay. • Gag proteins including p17 and possibly p7 as well as p24 perform better than p24 alone. • Frozen samples can be used in T-proliferative assays, but with lower radiolabled thymidine incorporation.				
Gag	Gag		HIV-1 infection	human	Pitcher1999
	Keywords HAART. • In contrast to earlier studies suggesting that HIV-1 specific Th responses were eliminated in the early stages of infection in most HIV+ individuals, this paper shows using flow cytometric detection of antigen-induced cytokines that Th-1 CD4+ memory gag-specific Th cells are detectable in most HIV+ subjects. • Effective anti-viral therapy reduces the frequency of these cells, presumably due to reduced antigenic stimulus.				
Gag	Gag		HIV-1 infection	human	Plana1998
	Keywords HAART. • Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses.				
Gag	Gag		HIV-1 infection	human	Kelleher1998a
	Keywords HAART.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses.				
Gag	Gag (LAI)		Vaccine	macaque	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag **Keywords** Th1, Th2. • Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone. • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env – The Th response happened despite a fall in Ab titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.				
Gag			Vaccine	macaque	Heeney1999
	Vaccine *Vector/Type:* DNA, protein, virus-like particle (VLP), ISCOM **Keywords** Th1, Th2. • Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge. • Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response. • DNA, protein+adjuvant, VLP and ISCOM vaccines were tested. • HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production.				
Gag	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86 • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.				
Gag	Gag/Pol (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease • A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers.				
Gag	p55 (IIIB)		HIV-1 infection	human	Zhang2001b
	Keywords HAART. • T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient. • Untreated patients showed a negative correlation between plasma viral load and HIV p24-specific T-cell responses, and the responses could be detected after extended HAART therapy with viremia below the detection limit.				
Gag	p24		HIV-1 infection	human	Carcelain2001
	Keywords HAART, supervised treatment interruptions (STI), kinetics, Th1. • Repeated structured HAART therapy interruptions (STI) in 3 chronically HIV infected patients induced rapid but transient (< 3 weeks) HIV-1 specific CD4+ Th1 responses concurrently with viral rebound, as measured by proliferation assays and by IFNγ production by CD8-depleted PBMC. • Kinetics suggest that viral replication leads to rapid destruction of the HIV-specific Th1 cell response. • HIV-specific CD8+ T-cell responses were delayed relative to the Th1 responses and were not sustained.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	Gag		HIV-1 infection	human	Blankson2001a
	Keywords HAART. • 5/10 chronically HIV infected patients with low CD4+ counts who received HAART therapy and experienced immune reconstitution displayed p24, p17 and p66 T-helper CD4 proliferative responses, in contrast to 0/8 chronically HIV infected patients with high CD4+ counts at the initiation of antiretroviral treatment. • This surprising result could be due to the low CD4 nadir patients being more likely to have thymic regeneration or a peripheral expansion of T cells.				
Gag	p24		HIV-1 infection	human	Angel2001
	Keywords HAART. • Prolonged viral suppression resulting from potent anti-retroviral therapy allowed a T helper response to Gag p24 and PHA to develop in many HIV+ patients. • At baseline, 2/41 (4.9%) subjects had a proliferative response to Gag p24, and 7/41 (17.1%) had a response to PHA, but by week 72 of therapy, 53% had a detectable response to p24 and 94% to PHA.				
Gag	p24		HIV-1 infection	human	Blazevic2000
	Keywords HAART. • Prolonged viral suppression resulting from potent anti-retroviral therapy did not allow an HIV T helper response to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients.				
Gag	Gag (SF2)		HIV-1 infection	human	Altfeld2001b
	Keywords HAART, acute infection. • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection. • The breadth and specificity of the CTL response was determined using Elispot by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef. • Individuals who were given HAART during acute or early in infection had significantly stronger proliferative responses than individuals who were chronically infected.				
Gag	p24		HIV-1 infection	human	Oxenius2000
	Keywords HAART. • Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable. • In 3/4 responders tested p24 gave the strongest T helper response.				
Gag	p24		Vaccine	rat	Moss2001
	Vaccine *Vector/Type:* gp120 depleted whole killed virus *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA), CpG immunostimulatory sequence (ISS) • Different HIV strains were used for different regions: subtype A env, subtype G gag • Lewis rats simultaneously immunized with HIV-1 antigen and with immunostimulatory sequences CpG had increased Th proliferative responses, but when CpG was given as a prime prior to the injection of HIV-1 antigen it was not as effective.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24		Vaccine	rat	Moss2000
Vaccine *Vector/Type:* gp120 depleted whole killed virus *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA), CpG immunostimulatory sequence (ISS) • Different HIV strains were used for different regions: subtype A env, subtype G gag • Lewis rats co-immunized with HIV-1 antigen in Freund's and with immunostimulatory sequences CpG stimulated increased IFNγ expressing CD4+ and CD8+ T cells and anti-p24 antibodies relative to antigen in Freund's without CpG.					
Gag	p24		HIV-1 infection	human	Kalams1999a
Keywords rate of progression, Th1. • The strength of p24 specific Gag proliferative responses (SIs) were inversely correlated with viral load in 21 ARV naive patients. The responses were Th1, IFNγ producing. Proliferative responses against gp160 were rarely observed (only 4 cases). • Gag specific CTL levels were correlated with Gag proliferative responses but were not correlated with viral load. 8 subjects lacked p24 specific Gag proliferative responses, and 4/8 had no CTLp to any HIV-1 antigen tested.					
Gag	p24		HIV-1 infection	human	Kalams1998
Keywords HAART, review, rate of progression. • This paper reviews the role of specific T cell help in many viral infections, and covers the interplay between Th, CTL and survival, and discusses briefly advantages of HAART during acute HIV infection to prevent the early decimation of the Th response in HIV infections.					
Gag	p24		HIV-1 infection	human	Wilson2000b
Keywords rate of progression, Th1, Th2. • Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease. • Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses. • None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction. • Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1+ LTNP, progressors, and HIV-1 controls.					
Gag	p24		HIV-1 infection	human	Alatrakchi2002
Keywords rate of progression, Th1. • LTNP co-infected with HCV and HIV showed higher frequencies of Th1 response to both HIV-1 p24 and HCV antigens. • HIV-1 CD4 Th1 responses in untreated LTNP were inversely correlated with viral load.					
Gag	p24		HIV-1 infection	human	Lange2002
Keywords HAART. • Cross-sectional study compares CD4 T-cell count and age matched untreated HIV-1+ patients (N = 14) with patients undergoing HAART therapy (N = 14). • The fractions of naive and memory T-cells were comparable for both groups, as were proliferative responses to non-HIV antigens. Lymphocyte proliferation responses to HIV-1 p24 were of greater magnitude in the group treated with HAART (5/10 had SI >10, versus 1/12 in the untreated group), suggesting that ongoing viral replication impairs the anti-Gag response, and the response can be improved and restored through HAART. • DTH responses to recall antigens were tested, and responses to C. albicans and Trichophyton were comparable in both treated and untreated patients, although patients on therapy had higher responses to mumps.					
Gag	p24		HIV-1 infection	human	Fidler2002
Keywords HAART, inter-clade comparisons, escape, acute infection.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 37/45 patients with primary HIV infection underwent a short course of antiretroviral therapy (SCART). 29/37 patients received triple ART therapy and eight patients received four ART drugs. Initiation of SCART was effective in controlling HIV replication by ten weeks in all patients and preserving CD4+ T cell responses for up to 64 weeks after therapy. • No induction of drug escape mutations was observed, although two individuals had escape mutations in their infecting virus at baseline. • 34 UK infected patients were clade B infected. 11/45 subjects had non-UK acquired HIV infection, 2 were clade A, 1 was A/E, 1 was C, 1 was "untypable", the rest were B. • Recombinant HIV-1 derived gp120, p24, p66 and overlapping peptide pools spanning Tat and Nef were employed to measure CD4 T-cell frequencies in ELISPOT assays. The strongest preservation of T helper responses 12 weeks off SCART was seen for p24-specific CD4+ T-cell responses. • 6/8 of the untreated individuals were tested for CD4+ T-cell responses. 1 had no detectable response. 1 had detectable responses to all HIV-1 proteins tested at baseline, but this narrowed to p24 and gp120, then became undetectable by 52 weeks. 3 had detectable and persistent responses, but only to p24. • Post-therapy, the average spot forming cells for all proteins tested in 17/37 with 24 weeks of follow up had not declined, although the plasma viral RNA was increasing. SFU using p24 were measurable following SCART and preserved at levels comparable to baseline.			
Gag			Vaccine	human	Klein1997, Lindenburg2002
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* B clade IIIB *HIV component:* p17 Gag, p24 Gag *Adjuvant:* aluminum hydroxide **Keywords** rate of progression. • HIV-1 p17/p24:Ty virus-like particles therapeutic vaccination of 56 HIV-1 infected patients had no effect on disease progression, AIDS and CD4+ T-cell decline in a longitudinal study, despite some evidence suggesting it can enhance Th anti-Gag proliferative responses in HIV+ individuals [Klein1997]				
Gag	p24 (NY5)		HIV-1 infection	human	Norris2001b
	Keywords HAART, supervised treatment interruptions (STI), rate of progression, immunodominance, acute infection, cross-presentation by different HLA, early treatment. • Gag-specific CD4+ helper T-cell clones were derived from one long-term non-progressor (LTNP) (CTS-01), and three individuals given therapy during acute infection, two before (AC-01 and AC-36) and one after (AC-25) STI. • The immunodominant response in LTNP CTS-01 was to peptide 9, and 9/10 clones derived from this patient reacted with it. Three, two, and one clones were obtained from the three patients given therapy. These six clones all reacted with different p24 peptides, and all had peptide induced proliferative responses, IFNgamma production, and cytotoxic responses. The implications of cytoxic responses in CD4+ T-helper cells are discussed.				
Gag	p24		HIV-1 infection	human	Palmer2002
	Keywords HAART. • CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication *in vivo* specifically reduces proliferation responses. • No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.				
Gag	p24 (SF2)		HIV-1 infection	human	Imami2002b
	Keywords rate of progression, Th1, Th2. • 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. • SF2 p24 20mer peptides overlapping by 10 were used to assess the response in the different groups. At least 1/10 and up to 7/10 nonprogressors had a proliferative response with every one of the 22 p24 overlapping peptides. All peptides produced an IL-2 (Th1) response in at least one of the 10 nonprogressors. IL-4 (Th2) responses were strong, but somewhat less comprehensive as 6/22 peptides elicited no IL-4 production, and fewer IL-4 responses were see per peptide. In contrast, only 1/10 progressors had a clear proliferative and IL-2 response to 2/22 peptides, and neither one made an IL-4 response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The results taken together suggest that a balanced Th1/Th2 response to HIV is important for viral control in long-term non-progression. • One immunologically discordant progressor became symptomatic while on the study. He showed a rapid decline in proliferative activity at that point, and a shift from a Th1 to a Th2 IL-4 producing response.				
Gag	(BRU)		Vaccine	mouse	Haas1991
	Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade BRU *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA) • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				
Gag	Gag (III-B)		Vaccine	mouse	Bojak2002a
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Gag **Keywords** vaccine-specific epitope characteristics, Th1. **Donor HLA** H-2^d. • Codon-optimized gag gene DNA vaccines were compared to wild type by vaccination of BALB/c mice. Codon optimized DNA gave a Th1 polarized Th response, a strong antibody response that persisted from more than 20 weeks, and CTL responses, while wild-type DNA induced weak and inconsistent immune respones.				
Gag	Gag (MN)		HIV-1 infection	human	Malhotra2003
	Keywords HAART, acute infection. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy.				
Gag	Gag (p24)		HIV-1 infection, Vaccine	human	Moss2003
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)), protein *Strain:* AG recombinant HZ321 *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** HAART, supervised treatment interruptions (STI), immunotherapy. **Assay type** cytokine production, proliferation, T-cell Elispot. • Structured treatment interruptions (STIs) were compared in individuals that had been given prior therapeutic vaccines, and those that had not. Therapeutic immunization increased gag p24 stimulated proliferative responses and MIP-1β responses prior to STIs, although total CD4 counts viral RNA levels were unchanged. Proliferative responses and chemokine induction in the vaccinated group correlated with the control of viremia during subsequent STIs.				
Gag			HIV-1 infection	human	Papasavvas2003
	Keywords supertype. **Assay type** proliferation, T-cell Elispot, Intracellular cytokine staining. • Children with full or partial viral supression along with stable CD4+ T cell counts had significantly increased levels of anti-HIV CD4+ T cell proliferative responses, and decreased CD38+ T-cells. • Preservation of high levels of CD4+ T-cells was associated with a high percentage of CD4+ naive T-cells relative to memory T-cells.				
Gag	Gag (p24)		HIV-1 infection, Vaccine	human	Robbins2003
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** HAART, immunotherapy.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type proliferation, T-cell Elispot, Delayed-type hypersensitivity (DTH). • Augmented Th cell responses to Gag p24 were seen in five out of five chronically infected individuals who had virological control with HAART, after therapeutic immunization with REMUNE (gp120 depleted inactived virus). The magnitude of responses ranges from a five-fold to a 200 fold incresase, with fluctuation in magnitude over time. • There was no change in the magnitude and breadth of CTL responses, CD4 counts or percentages, or DTH responses. • , and intermittently negative for some.				
Gag	Gag (p24)		HIV-1 infection	human	Wang2002a
	Keywords rate of progression, immunodominance. **Assay type** cytokine production, proliferation, CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. **Donor HLA** A1, A2, B8, B44, DR4, DR15; LTNP S24: A2, A11, B55, B57, DR4, DR13; LTNP C135: A1, A33, B50, B57, DR7, DR13. • A 51 year old male, infected presumably in 1988, diagnosed seropositive in 1993, has remained asymptomatic and is a long term non-progressor. He had very low proviral copy number in his PBMCs with high levels of G-A hypermutation, resulting in multiple stop codons, and viral replication was not evident. He was heterozygous for the CCR5 delta 32 allele, and has undergone a variety of treatments through the years. T cell responses in this patient and in two additional LTNPs were described, and this patient had particularly intense CD4+ Th responses. • PBMC from this patient resisted infection from CCR5, CXCR4 and dual-tropic HIV-1 strains. Purified CD4+ T cells became infected, however, without detectable cytopathic effect. CD8+ T cells were shown to protect PBMCs from infection, and this protection was not mediated by IFNgamma. Undefined CD8 T-cell secreted factors were stimulated by Gag, Pol and Nef genes introduced into target cells with vaccinia and processed through a class I pathway were responsible for the protective effect. This factor resembled CAF, the CD8+ cell antiviral factor described in Mackewicz and Levy (ARHR 8:1039, 1992) • The CD4+ and CD8+ T-cell populations were both strongly skewed toward the CD45RO+ phenotype, many of which were terminally differentiated CD28- and expressed the activation markers CD38+ and HLA-DR+. Cell turnover, however, wasn't much elevated as measured by apoptosis or Ki-67+ and Bcl-2 dim expression. • Vigorous p24-specific Th proliferative responses were observed, and 50% of CD4+ T-cells proliferated in response to p24 Gag, an extraordinary percentage. Responses were also detected against other regions in Gag, gp120 and Nef. It remains unclear how such vigorous Th responses are maintained with undetectable ongoing viral replication. • Strong CD4+ T-cell IFNgamma Elispot responses were mapped to many peptides in Gag for this patient. T-cells from two other LTNPs were tested here, and they did not react with as many Gag peptides as the main study subject of the paper. NIH reference Gag peptide set was used, but the sequences of the reactive peptides and the precise strain was not indicated in the paper, so we could not record them in the database. • CD8+ T cell Elispot responses to Gag, Env, Nef, and Pol were detected as well, although CTL were not prominent, consistent with undetectable viremia. • This subject had strong NAb responses when tested using the X4 primary isolate 228 200.				
Gag	Gag (p24)		HIV-1 infection		Sullivan2003
	Keywords HAART. **Assay type** proliferation. • Lymphoproliferative responses to HIV antigens p24, gp120 and Nef were enhanced in eight patients who were switched from protease inhibitors to non-nucleoside reverse transcriptase inhibitors.				
Gag	Gag (p24)		HIV-1 infection	human	Hardy2003
	Keywords HAART. **Assay type** cytokine production, proliferation. • Upon initiating HAART, CD4+ T cell proliferative responses in 36 patients were restored to specific antigens, mitogens, and IL-2. Restored recall responses were largely to persistent antigens, and not to HIV-1 or new antigens, and recall responses were associated with IL-2, not IL-4 production.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	p24 (IIIB)		in vitro stimulation or selectio	human (A*0201)	Engelmayer2001
	Keywords dendritic cells. • Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors. • Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific IFNγ CD4+ helper T cell responses to Gag from bulk or purified CD4+ T cells.				
Gag	p55		HIV-1 infection	human (DRB1*13, DRB1*03)	Lotti2002
	Keywords HAART, Th1, Th2, TCR usage. **Donor HLA** A29(19)/A30(19), B8/B35, DRB1*03/DRB1*13. • 10/49 chronically HIV-1 infected patients had low p55-Gag-specific CD4+ T cell responses prior to therapy, and these responses remained unchanged 3 and 6 months after initiation of HAART. There was no difference in level of response in those with or without a detectable p55 response. • For one individual, patient F45 CDC stage A2, CD4+ p55 responding clones were generated. Her response was consistently strong and heterogeneous in terms of HLA restriction and Vβ usage. Two clones were DRB1*13 restricted and used TCR Vβ 17+19 or 5.1. Three clones were DRB1*03 restricted and used TCR Vβ 22. Some clones had a Th1 cytokine secretion profile (high IFNgamma production) while some had a Th2 profile (high IL-4 and IL-5 production).				
Gag	p24		Vaccine	mouse (H-2^d)	Qiu2000
	Vaccine *Vector/Type:* DNA *HIV component:* Gag • Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein. • Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors. • IFNγ levels were increased compared to an undetectable IL-4 response. • CTL levels were also increased in secreted Gag expression vaccination studies.				
Gag	Gag		Vaccine	mouse (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18 **Keywords** Th1, Th2. • DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 showed lymphoproliferative responses 7 weeks post immunization. • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime + DNA boost was more effective than DNA prime + protein boost. • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine resulted in Th1 cytokines production (IL-2 and IFNγ) in spleen cell cultures stimulated by Tat and Gag, while Th2 cytokines IL-4 and IL-10 production was not detectable. • Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.				
Gag	p24		Vaccine	mouse (H-2^d)	Halim2000
	Vaccine *Vector/Type:* coxsackievirus *HIV component:* p24 Gag • An avirulent rec coxsackievirus (CB4-P) construct was generated that can express p24 Gag sequences – CB4-P is attenuated even in immunodeficient mice and T help responses can be elicited from peptides embedded in a surface loop of the VP1 capsid. • This paper describes the vaccine strategy and generation of constructs, and employs amino-terminal fusion of Gag sequences to the viral polyprotein with subsequent cleavage to elicit CTL responses via MHC class I presentation in BALB/c mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Gag	gp120 (V3) and p24 (IIIB, MN, BH10)		Vaccine	mouse (H-2^d)	Buonaguro2002
	Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* A clade UG5.94UG018, B clade IIIB *HIV component:* Gag, gp120 **Keywords** inter-clade comparisons. • Different HIV strains were used for different regions: gp120 A clade UG5.94UG018, HIV-1 IIIB • BALB/c mice were given intraperitoneal immunization in the absence of adjuvants with virus-like particles (VLPs) expressing recombinant subtype A gp120 and Pr55gag. • High dose-independent humoral responses were elicited against both gp120 and p24 peptides, and CTL responses were observed against target cells carrying vaccinia expressed gp120 and Gag.				
Gag	Gag (HXB2)		Vaccine	mouse (H-2^d, H-2^b)	Mata2001
	Vaccine *Vector/Type:* Listeria monocytogenes *Strain:* B clade HXB2 *HIV component:* Gag **Keywords** Th1. • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • CD4+ Th1 T-cells mediated the Gag specific immunological protection in mice immunized with Lm-Gag and challenged with vaccinia-Gag. • Gag-specific CTL may enhance viral clearance via IFNγ secretion, but are not essential for immunity.				
Gag	Gag		Vaccine	mouse (H-2^d, H-2^b)	Mata2000
	Vaccine *Vector/Type:* Listeria monocytogenes *HIV component:* Gag **Keywords** review, Th1. • BALB/c and C57BL/6 mice were immunized with rec Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag and mice were challenged with vaccinia expressing Gag. • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways. • This article is a review of L. monocytogenes biology and its potential as a vaccine vector for HIV, comparing to other vector systems, and discussing CD4+ Th1 T-cells mediated Gag specific immunological protection in mice and the Gag CTL response.				

III-B-5 RT Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT (36–52)	RT (36–52 BRU)	EICTEMEKEGKISKIGP	HIV-1 infection	human	De Groot1991
	• 9 out of 17 humans can make strong IL2 responses to this epitope.				
RT (38–52)	RT (38–52 BRU)	CTEMEKEGKISKIGP	Vaccine	mouse (H-2^k)	De Groot1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide.				
RT (39–53)	RT (194–208)	TEMEKEGKISKIGPE	in vitro stimulation or selectio	human	Manca1995a
	• Protein priming induced T-cells that recognize peptide, 4 clones from a single donor recognized this peptide.				
RT (48–62)	RT (48–62 BRU)	SKIGPENPYNTPVFA	Vaccine	mouse (H-2^k)	De Groot1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide.				
RT (62–77)	RT (62–77 BRU)	AIKKKDSTKWRKLVDF	Vaccine	mouse (H-2^k)	De Groot1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide.				
RT (88–102)	RT (88–102 BRU)	WEVQLGIPHPAGLKK	Vaccine	mouse (H-2^{t4})	De Groot1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT				
	• T-cells from RT immunized mice have enhanced proliferative response with peptide.				
RT (124–138)	Pol (303–317)	FRKYTAFTIPSINNE	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons.				
	Epitope name Pol 303.				
	• Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.				
	• This epitope binds seven HLA-DR alleles: DRB1*0901, DRB1*0802, DRB1*0701, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM.				
	• This epitope sequence is conserved in 68% of clade B isolates.				
	• 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (124–138)	Pol (303–317)	FRKYTAFTIPSINNE	Vaccine	mouse (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	Keywords vaccine-specific epitope characteristics, immunodominance.				
	Epitope name Pol 303.				
	Donor HLA H-2b.				
	• Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.				
RT (133–147)	RT (133–147 BRU)	PSINNETPGIRYQYN	Vaccine	mouse (H-$2^{k, i5}$)	De Groot1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT • T-cells from RT immunized mice have enhanced proliferative response with peptide.				
RT (144–158)	RT (144–158 BRU)	YQYNVLPQGWKGSPA	Vaccine	mouse (H-2^{t4})	De Groot1991
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* RT • T-cells from RT immunized mice have enhanced proliferative response with peptide.				
RT (156–170)	Pol (335–349)	SPAIFQSSMTKILEP	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 596. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds nine HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0901, DRB5*0101 and DRB3*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 79% of clade B isolates. • 7/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (156–170)	Pol (335–449)	SPAIFQSSMTKILEP	Vaccine	mouse (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** Pol 335. **Donor HLA** H-2b. • Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice. • Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination.				
RT (171–189)	Pol (171–189 HXB2)	FRKQNPDIVIYQYMDDLYV	HIV-1 infection	human (DR0101)	Iyasere2003
	Keywords HAART, supervised treatment interruptions (STI). **Assay type** cytokine production, proliferation, Tetramer binding, CD4 T-cell Elispot - IFNγ. • Fifteen patients recieving HAART with strong CD4+ proliferative responses to HIV antigens while on therapy were examined, to see the effects of viremia on these responses during treatment interuptions. Increased viremia occurred in 12/15 patients during at least one treatment interuption. Anti-HIV proliferative responses were inhibited during viremia, but IFNgamma production to Gag, Pol, and Nef peptide pools were maintained.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• IL-2 production diminished during viremia, and exogenous IL-2 revived *in vitro* proliferation of HIV-specific T cells to a Gag or Pol DR0101 epitopes in a tetramer as well as Gag-specific total CD4 T-cell responses.				
RT (171–190)	RT (171–190 HXB2)	FRKQNPDIVIYQYMDDLYVG	HIV-1 infection	human (DR1, 2 or 3, 4 and 7)	vanderBurg1999
	Keywords Th1. • T-cells specific for this epitope from the three donors were stimulated when presented with target cells pulsed with whole RT, indicating that the peptide is naturally processed for multiple HLA-DR molecules. • Epitope binds to HLA-DR1, -DR2, -DR3, -DR4, and DR7, and can elicit Th1 cells that recognize peptide, protein, and HIV pulsed stimulator cells in the context of DR1, 2 or 3, 4 and 7 – these HLA types cover more than half of the general population.				
RT (171–190)	RT (171–190 HXB2)	FRKQNPDIVIYQYMDDLYVG	HIV-1 infection, in vitro stimulation or selectio	human (DR1, DR2, DR3, DR4, DR7)	vanderBurg1999
	Keywords binding affinity, cross-presentation by different HLA, Th1. • The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, and but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors. • This highly conserved epitope binds with high affinity to HLA-DR1, -DR2, -DR3, -DR4, and -DR7 but not HLA-DR5, and stimulated proliferation in 3/3 PBMC individuals with the appropriate HLA alleles. • This epitope was able to be naturally processed in protein pulsed stimulator cells, and responding clones had a Th1 cytokine profile. • This epitope is highly conserved and spans the highly conserved YMDD motif, and showing only minor variability in clades A, B, and D.				
RT (195–209)	RT (IIIB)	IGQHRTKIEELRQHL	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (196–215)	RT (351–370)	GQHRTKIEELRQHLLRWGLT	in vitro stimulation or selectio	human	Manca1995a
	• Protein priming induced T-cells that recognize peptide, 4 clones from a single donor recognized this peptide.				
RT (249–263)	RT (IIIB)	KDSWTWNDIQKLVGK	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming did not induce T-cells that recognize whole protein.				
RT (249–263)	RT (248–262)	KDSWTVNDIQKLVGK	in vitro stimulation or selectio	human	De Berardinis1999
	• PBMC from donors GD (HLA DR 11; DRB52) and LD (HLA DR 11, 13; DRB52) recognized this epitope (pep23) • A subset of T-cell lines generated from these donors were capable of recognizing pep23 expressed on the surface of filamentous phage fd, fused to the major coat protein gVIIIp. • This peptide was selected to study phage presentation of peptide sequences because it was known to serve as a T-cell helper determinant which could induce proliferation from a naive repertoire [Manca1995a]				
RT (249–263)	RT (249–263)	KDSWTVNDIQKLVGK	Vaccine, in vitro stimulation or selectio	human (DR5)	De Berardinis2000
	Vaccine *Vector/Type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT **Keywords** epitope processing. **Epitope name** RT2. • Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses in PBMC from HIV negative individuals and *in vivo* in immunization of HLA-A2 transgenic mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors. • HIV-1 peptides were displayed in filamentous bacteriophage fd virion major coat protein pVIII.				
RT (249–263)	RT (249–263)	KDSWTVNDIQKLVGK	Vaccine, in vitro stimulation or selectio	human, transgenic mouse (DR5)	Domingo2003
	Vaccine *Vector/Type:* peptide presented on icosahedral protein scaffold *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Epitope name** pep23. **Assay type** cytokine production, T-cell Elispot, Th support of CTL response. • A virus-like protein scaffold, called E2DISP, derived from pyruvate dehydrogenase multienzyme from Bacillus stearothermophilus has been engineered to display 60 copies of one or more epitopes on a single molecule. An E2DISP scaffold which displayed pep23, a 15-residue B and T helper epitope from the reverse transcriptase of HIV-1 elicited a pep23-specific elicited a T-helper response *in vitro*. • The E2DISP scaffold displaying pep23 to stimulate a Th responses, and peptide RT2, which is a CTL epitope from HIV-1 reverse transcriptase, was able to elicit a CD8+ T cell response *in vitro* and in a vaccinated HLA-A2 transgenic mouse. Thus the E2DISP scaffold allows cell-entry and access to the class I and class II processing pathways. • The Th response in vaccinated mice was also able to support Pep23 specific IgG response.				
RT (249–263)	RT (248–262)	KDSWTVNDIQKLVGK	in vitro stimulation or selectio	human (DR5-11.01)	Moschella2003
	Keywords binding affinity, epitope processing, vaccine-specific epitope characteristics, escape. **Assay type** proliferation. **Donor HLA** DR5,DR6. • Two helper T-cell clones specific for this epitope presented in the context of HLA-DR5-11.01 have been characterized. They have different T cell receptor usage. Residue 11 (kdswtvndiqKlvgk)is a natural variant, and K11A, K11G, K11I, and K11L variants were synthesized and studied in two presentation contexts, one as simple peptides, the other embedded in a recombinant protein, GST. • The two Th clones and the two presentation contexts gave different outcomes with the peptides. K11I was not stimulatory, and was an antagonist in GST, an agonist as a peptide. K11L retained reactivity when presented in the fusion antigen, and had no acitivity as a peptide. K11G stimualted in both contexts, but the concentrations required for half maximal reactivity were different. K11A cuold not bind to the MHC in the processed form and could only stimulate when given as a peptide. • In conclusion, substitutions in epitopes have different effects on Th stimulation depending on the mode of processing, and this should be considered when interpreting Th escape studies and vaccine development.				
RT (249–263)	RT (248–262)	KDSWTVNDIQKLVGK	in vitro stimulation or selectio	human (DR5-11.01)	Bonomi2000
	Keywords binding affinity, epitope processing, vaccine-specific epitope characteristics, escape, TCR usage. **Assay type** proliferation. **Donor HLA** DR5,DR6. • Two helper T-cell clones specific for this epitope presented in the context of HLA-DR5-11.01 have been characterized. One of them used TCR Vβ15, the other used Vβ2. The substituions D2A, W4A, D8A, I9A, and K15A were generated and only D8A, I9A failed to react with one clone, while W4A, D8A, I9A were all critical for a reaction with the other clone, showing the TCRs focused on different but overlapping residues. • Moving the epitope to different contexts in recombinant proteins for presentation by APCs, as well as adding polyanalanine and polyserine strings to either side of the epitope, influenced reactivity, suggesting processing context can influence the structure of the presentation complex.				
RT (249–263)	RT (248–262 HXB2)	KDSSTVNDIQKLVGK	in vitro stimulation or selectio	human (DRS)	Fenoglio1999
	• RT pep23 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end.				
RT (251–261)	RT (250–260)	SSTVNDIQKLV	in vitro stimulation or selectio	human (DR5(11.01))	Manca1996
	• This peptide was the minimal stimulatory sequence. • One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein. • Constructs linking GST to the KDSSTVNDIQKLVGK peptide at the N-term end of GST stimulated Th cells, but not constructs linking at the C-term end. • The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see FAILKCNNK for contrast)				
RT (258–272)	RT (IIIB)	QKLWGKLNWASQIYP	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming did not induce T-cells that recognize whole protein.				
RT (271–290)	RT (271–290 HXB2)	YPGIKVRQLCKLLRGTKALT	HIV-1 infection	human	vanderBurg1999
	• Epitope can bind to at least 5 different HLA-DR molecules, and peptide on target cells can elicit Th responses from PBMC cultures from healthy donors, however it does not seem to be processed properly from whole RT or virus.				
RT (271–290)	RT (271–290 HXB2)	YPGIKVRQLCKLLRGTKALT	HIV-1 infection, in vitro stimulation or selectio	human (DR1, DR2, DR3, DR5, DR7)	vanderBurg1999
	Keywords binding affinity, cross-presentation by different HLA. • The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors. • This epitope binds with high affinity to HLA-DR1, -DR2, -DR3, -DR5, and -DR7 but not HLA-DR4, and stimulated proliferation in 3/4 individuals with the appropriate HLA alleles. • This epitope was not able to be naturally processed in protein-pulsed stimulator cells.				
RT (276–290)	RT (IIIB)	WRQLCKLLRGTKALT	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (285–299)	RT (IIIB)	GTKALTEVIPLTEEA	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (294–308)	RT (IIIB)	PLTEEAELELAENRE	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (303–317)	RT (IIIB)	LAENREILKEPVHGV	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (384–398)	RT (IIIB)	GKTPKFKLPIQKETW	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (414–428)	Pol (596–610)	WEFVNTPPLVKLWYQ	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 596. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This epitope binds eleven HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 84% of clade B isolates. • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (429–443)	RT (IIIB)	LEKEPIVGAETFYVD	in vitro stimulation or selectio	human	Manca1995b
	• Protein priming induced T-cells that recognize peptide.				
RT (432–450)	RT (431–450 HXB2)	EPIVGAETFYVDGAANRET	HIV-1 infection, in vitro stimulation or selectio	human (DR1, DR2, DR3, DR4)	vanderBurg1999
	Keywords binding affinity, cross-presentation by different HLA. • The goal of this study was to identify Th epitopes that could be cross-presented by multiple class II HLA molecules. 5 RT peptides were identified that could bind to more than one HLA class II protein, and but only 2/5 could stimulate strong proliferation responses in PBMC derived from multiple healthy donors. • This epitope binds with high affinity to HLA-DR1, -DR2, -DR3, and -DR4, but stimulated a strong proliferation response in only 1/4 individuals tested so was not considered broadly cross-presented.				
RT (526–540)	RT (526–540 BRU)	IKKEKVYLAWVPAHK	Vaccine	mouse (Ad or Dd)	Haas1991
	Vaccine *Vector/Type:* peptide, protein, inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA) **Epitope name** W9. • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses. • The peptide KEKVYLAWVPAHKG was one of two RT peptides with Th cells recognition.				
RT (528–540)	RT (528–540)	KEKVYLAWVPAHK	Vaccine	mouse (H-2b, H-2d, H-2k)	Loleit1996
	Vaccine *Vector/Type:* lipopeptide *Strain:* B clade BRU *HIV component:* RT *Adjuvant:* P3CSS **Assay type** proliferation. • BALB/c, C3H/Hej, and C57BL/6 mice were immunized with 22-mer lipopetide tripeptide conjugates P3CSS-[RT-(522-543)] and P3CSS-[RT-(528-549)] of HIV-1 RT, which included the optimal T-helper epitope [RT-(528-540)]. P3CSS conjugated RT epitopes resulted in a specific Th responses, and mice were primed for secondary recognition of native RT. A proximal B cell epitope was also active, containing the motif EQVD.				
RT (528–541)	RT (528–543 BRU)	KEKVYLAWVPAHKG	Vaccine	mouse (Ad and Dd)	Haas1991
	Vaccine *Vector/Type:* peptide, protein, inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA) **Epitope name** A3. **Donor HLA** H-2d, H-2f, H-2k. • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses. • The peptide KEKVYLAWVPAHKG was one of two RT peptides with Th cells recognition. It could by itself prime different strains of mice for RT-specific Th responses, and the C-term half of the peptide is highly conserved in HIV-1, HIV-2 and SIV strains.				
RT (528–543)	RT (528–543 BRU)	KEKVYLAWVPAHKGIG	Vaccine	mouse ($H\text{-}2^{f, k, d}$)	Haas1991
	Vaccine *Vector/Type:* peptide *Strain:* B clade BRU				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• T-cells from peptide-primed mice could be restimulated by native RT.				
RT (529–543)	Pol (711–725)	EKVYLAWVPAHKGIG	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 711. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 94% of clade B isolates. • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				
RT (529–543)	Pol (711–725)	EKVYLAWVPAHKGIG	Vaccine	mouse (I-Ab and HLA-DR)	Livingston2002
	Vaccine *Vector/Type:* DNA with CMV promotor, peptide *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, immunodominance. **Epitope name** Pol 711. **Donor HLA** H-2b. • Four Th HIV epitopes presented by HLA-DR molecules were identified that also could be presented my murine class II molecule I-Ab, enabling testing of vaccine strategies of in H-2b mice. • Responses to pooled peptides, polyepitope peptides in a linear construct or in a branched MAP construct, and a DNA polyepitope construct with a CMV promotor were compared. A linear arrangement in polyepitope construct created a junctional epitope that could be disrupted with the addition of GPGPG spacers. The linear polyepitope construct with the GPGPG spacer worked well in terms of eliciting responses to all four peptides, using either DNA or protein for the vaccination. • Although responses to this peptide indicated it was immunodominant, responses to all four peptides were made upon vaccination with linear constructs when GPGPG spacers were used.				
RT (530–544)	Pol (712–726)	KVYLAWVPAHKGIGG	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 712. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds ten HLA-DR alleles: DRB1*0101, DRB1*1501, DRB1*0401, DRB1*0405, DRB1*1101, DRB1*0701, DRB1*0802, DRB1*0901, DRB5*0101 and DRB4*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 89% of clade B isolates. • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)				

III-B-6 RT-Integrase Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
RT-Integrase (553–3)	RT (720–730 LAI) • Stimulates T-cell proliferation in HIV-infected donors.	SAGIRKVLFLD	HIV-1 infection	human	Schrier1989

III-B-7 Integrase Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Integrase (16–30)	Pol (758–772)	HSNWRAMASDFNLPP	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 758. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds eight HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0701, DRB1*1101, DRB1*0405, DRB1*0401 and DRB1*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 68% of clade B isolates. • 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)			
Integrase (172–186)	RT (899–913 LAI)	LKTAVQMAVFIHNFK	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
Integrase (173–187)	Pol (915–929)	KTAVQMAVFFIHNFKR	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 915. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds seven HLA-DR alleles: DRB5*0101, DRB1*1302, DRB1*1101, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 94% of clade B isolates. • 6/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)			
Integrase (196–210)	RT (923–937 LAI)	AGERIVDIIATDIQT	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
Integrase (214–228)	Pol (956–970)	QKQITKIQNFRVYYR	HIV-1 infection	human (DR supermotif)	Wilson2001
	Keywords inter-clade comparisons. **Epitope name** Pol 956. • Eleven peptides were identified that had the HLA-DR supermotif, all were found to bind to MHC class II DR molecules and all elicited proliferative responses from multiple HIV-infected donors. • This epitope binds twelve HLA-DR alleles: DRB4*0101, DRB5*0101, DRB1*0901, DRB1*0802, DRB1*0701, DRB1*1302, DRB1*1201, DRB1*1101, DRB1*0405, DRB1*0401, DRB1*1501 and DRB1*0101, with an IC_{50} threshold below 1,000 nM. • This epitope sequence is conserved in 95% of clade B isolates. • 8/22 HIV infected individuals responded to this epitope (13/22 responded to some of the DR supermotif epitopes, the 9 non-responder peptides tended to also not have recall responses to rec HIV-1 whole proteins)			
Integrase (215–227)	RT (942–954 LAI)	KQITKIQNFRVYY	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				

III-B-8 Pol Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	Gag/Pol		Vaccine	mouse	Kim1997b
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, Pol, Vif *Adjuvant:* B7, IL-12				
	• A gag/pol DNA vaccine delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12 gives a dramatic increase in both the cytotoxic and proliferative responses in mice.				
Pol	Gag/Pol		Vaccine	mouse	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, gp160, Pol *Adjuvant:* CD86				
	• A gag/pol DNA vaccine delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86 gives an increase in proliferative responses to Pr55 in mice.				
Pol	Gag/Pol (MN)		Vaccine	chimpanzee	Kim1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86				
	• Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.				
Pol	Pol		HIV-1 infection	human	Blankson2001a
	Keywords HAART.				
	• 5/10 chronically HIV infected patients with low CD4+ counts who received HAART therapy and experienced immune reconstitution displayed p24, p17 and p66 T-helper CD4 proliferative responses, in contrast to 0/8 chronically HIV infected patients with high CD4+ counts at the initiation of antiretroviral treatment.				
	• This surprising result could be due to the low CD4 nadir patients being more likely to have thymic regeneration or a peripheral expansion of T cells.				
Pol	p66		HIV-1 infection	human	Oxenius2000
	Keywords HAART.				
	• Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.				
Pol	p66		HIV-1 infection	human	Palmer2002
	Keywords HAART.				
	• CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication *in vivo* specifically reduces proliferation responses.				
	• No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.				
Pol	(BRU)		Vaccine	mouse	Haas1991
	Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	• Of 5 mouse inbred lines tested DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus.				
	• B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Pol	RT (248–256 HXB2)		in vitro stimulation or selectio	human (DR5)	Manca1995b
	• CD4+ T-cell lines from uninfected individuals by stimulation with p66-pulsed APC. • TcR Vβ Dβ Jβ sequences were obtained from p66-specific T-cell clones. • There were multiple responses to peptides throughout p66, but because of uncertain locations, they have not been mapped. • Response to peptide 248-256 was associated with DR5.				
Pol	RT		Vaccine	mouse (H-2^{d})	Kim2000
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* IFN-gamma, IL-2, IL-4 **Keywords** Th1. • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFNγ drove Th1 immune responses and enhanced CTL responses.				
Pol	RT		Vaccine	mouse (H-2^{d})	Burnett2000
	Vaccine *Vector/Type:* Salmonella *HIV component:* RT • A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV RT gene in the Lpp-OmpA-HIV fusion protein, induced a lymphoproliferative Th response in BALB/c mice.				

III-B-9 Vif Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vif (65–76)	Vif (65–80)	VITTYWGLHTGE	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion.				
Vif (81–96)	Vif (81–96)	LGQGVSIEWRKQRYST	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion.				
Vif	Vif		Vaccine	mouse (H-2^d)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Vif, Vpu **Keywords** inter-clade comparisons, Th1. • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFNγ levels. • Antigen stimulation increased IFNγ production in pVVN-P immunized mice, indicating a Th1 response. • IL-4 production was not significantly changed after antigen stimulation compared to control levels. • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.				

III-B-10 Vpr Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpr (66–80)	Vpr (66–80 IIIB)	QLLFIHFRIGCRHSR	HIV-1 infection	human	Sarobe1994
	• This peptide was found to stimulate proliferative responses in 37.5% of HIV-1 positive individuals.				
Vpr (66–80)	Vpr (66–80 IIIB)	QLLFIHFRIGCRHSR	Vaccine	mouse (H-2^d)	Sarobe1994
	Vaccine *Vector/Type:* peptide				
	• Included as a Th stimulatory component of peptide vaccines that also incorporated B-cell epitopes.				

III-B-11 Tat Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Tat (1–20)	Tat (1–20 LAI)	MEPVDPRLEPWKHPGSQPKT	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Tat (16–35)	Tat (16–35 LAI)	SQPKTACTTCYCKKCCFHCQ	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Tat (17–32)	Tat (17–32)	QPKTACTNCYCKRCCF	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion.				
Tat (17–32)	Tat (17–32 HXB2)	QPKTACTNCYCKKCCF	HIV-1 infection	human (DR5? plus others)	Blazevic1993
	Keywords immunodominance. **Epitope name** D26. • 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production. • 3/12 peptides were recognized. • This immunodominant, highly conserved and most frequently recognized peptide was recognized by 57% of the HIV-1 infected patients. A beta-sheet secondary structure was predicted at aa residues 21-28, but no amphipathic helix structure, suggested to be most favorable for T-cell epitopes, was indicated. • This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR5 was enriched (3/6) among the patients that recognized the peptide.				
Tat (31–50)	Tat (31–50 LAI)	CFHCQVCFTTKALGISYGRK	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Tat (33–48)	Tat (33–48)	HCQVCFMTKGLGISYG	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion.				
Tat (33–48)	Tat (33–48 HXB2)	HCQVCFITKALGISYG	HIV-1 infection	human (DR5? plus others)	Blazevic1993
	Epitope name D28. • 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production. • 3/12 peptides were recognized. • 4/14 HIV+ people recognized this peptide. • An alpha-helix structure was predicted at residues 39-44, but charge patterns did not indicate it was an amphipathic helix, suggested to be most favorable for T-cell epitopes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR5 was enriched (2/4) among the patients that recognized the peptide.				
Tat (36–50)	Tat (36–50 HTLV IIIB)	VCFITKALGISYGRK?	Vaccine	mouse (H-2^d)	Borsutzky2003
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2) **Keywords** Th1, Th2, mucosal immunity. **Assay type** cytokine production, proliferation, T-cell Elispot, Th support of CTL response. • BALB/c mice that were vaccinated intranasally with Tat protein plus mucosal adjuvant macrophage-activating lipopeptide-2 (MALP-2) had increased proliferative, antibody, and IFNγ producing T-cell responses than did with Tat+IFA delivered by the i.p. route. • IFA as adjuvant stimulated a Th2-dominant response pattern, and MALP-2 as adjuvant shifted to a Th1 response. Anti-Tat IgG1 dominated the Ab response with IFA, IgG2b dominated with MALP-2. In animals vaccinated with Tat+MALP-2, IFNγ and IL-2 were the most prominent cytokines, with some IL-6. In contrast, in mice vaccinated with Tat+IFA, IL-6 was the dominant cytokine. Secreted IL-4, IL-5 and IL-10 were below the detection limit in both cases. • The strongest proliferation of spenocytes was observed was after re-stimulation with residues 36-50 and 56-70.				
Tat (46–65)	Tat (46–65 LAI)	SYGRKKRRQRRRPPQGSQTH	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Tat (56–70)	Tat (56–70 HTLV IIIB)	RRAHQNSQTHQASLS?	Vaccine	mouse (H-2^d)	Borsutzky2003
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2) **Keywords** Th1, Th2. **Assay type** cytokine production, proliferation, T-cell Elispot, Th support of CTL response. • BALB/c mice that were vaccinated intranasally with Tat protein plus mucosal adjuvant macrophage-activating lipopeptide-2 (MALP-2) had increased proliferative, antibody, and IFNγ producing T-cell responses than did with Tat+IFA delivered by the i.p. route. • IFA as adjuvant stimulated a Th2-dominant response pattern, and MALP-2 as adjuvant shifted to a Th1 response. Anti-Tat IgG1 dominated the Ab response with IFA, IgG2b dominated with MALP-2. In animals vaccinated with Tat+MALP-2, IFNγ and IL-2 were the most prominent cytokines, with some IL-6. In contrast, in mice vaccinated with Tat+IFA, IL-6 was the dominant cytokine. Secreted IL-4, IL-5 and IL-10 were below the detection limit in both cases. • The strongest proliferation of spenocytes was observed was after re-stimulation with residues 36-50 and 56-70.				
Tat (61–80)	Tat (61–80 LAI)	GSQTHQVSLSKQPTSQPRGD	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally; rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Tat (65–80)	Tat (65–80 HXB2)	HQASLSKQPTSQPRGD	HIV-1 infection	human (DR2? plus others)	Blazevic1993
	Epitope name D32. • 9/14 (64%) of HIV-1 positive patients had proliferative T-cell responses associated with IL-2 production against at least one Tat-derived synthetic peptides of twelve overlapping 15-16 mer peptides spanning Tat. T cell proliferation was associated with IL-2 production. • 3/12 Tat peptides were recognized. • 3/14 HIV+ people recognized this peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• An alpha-helix structure was predicted at residues 65-72, but charge patterns did not indicate it was an amphipathic helix, suggested to be most favorable for T-cell epitopes.. • This peptide contained epitopes restricted by several HLA DR alleles, although the frequency of DR2 was enriched (2/3) among the patients that recognized the peptide.				
Tat (67–86)	Tat (67–86 LAI)	VSLSKQPTSQPRGDPTGPKE	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Tat	Tat		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat **Keywords** HAART. • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated. • The nef DNA immunization induced the highest and most consistent CTLp activity, IFNγ production, and IL-6 and IgG responses. • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.				
Tat	Tat		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS) **Keywords** review, Th1. • This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals.				
Tat	Tat		in vitro stimulation or selectio	human	Corinti2002
	Keywords dendritic cells, Th1, Th2. • In vitro delivery of recombinant Tat protein conjugated to red blood cells (RBCs) via avidin-biotin bridges (RBC-Tat) to human dendritic cells was compared to dendritic cells pulsed with rec Tat. • Dendritic cells pulsed with RBC-Tat elicited specific and significantly stronger CD4+ and CD8+ T-cell responses and required 1250-fold less antigen than DCs stimulated with soluble Tat. • Dendritic cells which were maturated in the presence of IFNgamma induced elevated IL-12 and TNF-alpha secretion. IFNgamma upregulated IP-10 and down regulated TARC, chemokines which attract Th1 and Th2 cells, respectively.				
Tat	Tat (IIIB, BH10)		in vitro stimulation or selectio	human	Fanales-Belasio2002b
	Keywords epitope processing, vaccine-specific epitope characteristics, dendritic cells, Th1. • Biologically active HIV-1 Tat is readily taken up by monocyte-derived dendritic cells (MDDC) (and activated endothelial cells), but not other APCs. Tat must be in a native, non-oxidized conformation for efficient uptake. Tat upregulates MHC molecules, IL-12, TNFα, RANTES and MIP-1-α and MIP-1-β production which drives Th1 immune responses and enhances antigen presentation. • Native Tat enhanced the antigen presentation of MDDC and boosted proliferative recall and allogeneic antigen responses, and the authors propose it could be used as an adjuvant to drive the immune response as well as an antigen.				
Tat	Tat		Vaccine	macaque	Fanales-Belasio2002a
	Vaccine *Vector/Type:* DNA, protein *HIV component:* Tat *Adjuvant:* aluminum hydroxide, Ribi adjuvant (MPL+TDM) (RIBI) **Keywords** review, early-expressed proteins, Th1. **Assay type** cytokine production, Delayed-type hypersensitivity (DTH).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• HIV-1 Tat protein has several virtues vaccine component. It is an early expressed protein, and though variable, contains consverved T-cell and B-cell epitopes that allow cross-clade recognition. It is efficiently taken up by monocyte-derived dendritic cells (MDDCs) and in this context can stimulate Th1 immune responses. A Tat based vaccine can elicit an immune response that can control primary infection in monkeys that are in early stage of in infection with SHIV89.6P.				
Tat	Tat		Vaccine	mouse (H-2^d)	Billaut-Mulot2001
	Vaccine *Vector/Type:* DNA, DNA with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18 **Keywords** Th1, Th2. • DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 gave lymphoproliferative responses 7 weeks post immunization. • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime + DNA boost was more effective than DNA prime + protein boost. • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine resulted in Th1 cytokines production (IL-2 and IFNγ) in spleen cell cultures stimulated by Tat and Gag, while Th2 cytokines IL-4 and IL-10 production was not detectable. • Co-administration of IL18 increased T-cell responses but decreased anti-HIV antibody levels.				

III-B-12 Rev Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev (9–23)	Rev (9–23 HXB2)	DEELIRTVRLIKLLY	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.				
Rev (16–35)	Rev (16–35 LAI)	VRLIKFLYQSNPPPNPEGTR	Vaccine	mouse (H-2^{d})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Rev (25–39)	Rev (25–39 HXB2)	SNPPPNPEGTRQARR	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.				
Rev (31–50)	Rev (31–50 LAI)	PEGTRQARRNRRRRWRERQR	Vaccine	mouse (H-2^{d})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Rev (33–48)	Rev (33–48 HXB2)	GTRQARRNRRRRWRER	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.				
Rev (41–56)	Rev (41–56 HXB2)	RRRRWRERQRQIHSIS	HIV-1 infection	human	Blazevic1995
	• One of four peptides that stimulates in PBLs from HIV-1+ donors both CD4+ Th cell proliferation and CTL to autologous targets incubated with peptide were stimulated.				
Rev (76–95)	Rev (76–95 LAI)	PPLERLTLDCNEDCGTSGTQ	Vaccine	mouse (H-2^{b})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Rev (96–116)	Rev (96–116 LAI)	GVGSPQILVESPTVLESGT-KE	Vaccine	mouse (H-2^{d})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat				
	• Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.				
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Rev	Rev		Vaccine	mouse	Chan1998
	Vaccine *Vector/Type:* DNA *HIV component:* Rev				
	Keywords HAART.				
	• Rev M10 is a construct that was introduced into mice through a genetic vaccination.				
	• Rev was used to test for down-regulation of HIV-1 in infected cells as a method for gene therapy – in the course of this study, Rev-specific IL-2 producing Th cells developed in the mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Rev	Rev		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat **Keywords** HAART. • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated. • The nef DNA immunization induced the highest and most consistent CTLp activity, IFNγ production, and IL-6 and IgG responses. • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.				
Rev	Rev		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS) **Keywords** review, Th1. • This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals.				
Rev	Rev		Vaccine	human	MacGregor2002
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade MN *HIV component:* Env, Rev *Adjuvant:* Bupivacaine **Keywords** early-expressed proteins. • A phase I clinical trial of a HIV-1 Env and Rev DNA vaccine with a CMV promoter was conducted and Th proliferative, CTL and Elispot responses monitored. The construct was modified for safety and included no LTRs or packaging signals. The vaccine strategy was safe, and elicited strong CD4-T cell responses, but not CD8 T-cell responses. Rev elicited strong Th responses, and is a early produced protein so may confer advantages. • With a 300 ug dose, 4/6 individuals had a lymphocyte proliferation (LP) responses to gp120, 3/6 to Rev. • With a 1000 ug dose, 4/6 individuals had a LP and 2/6 had IFNgamma Elispot responses to gp160; 3/6 had LP, and 4/6 had IFNgamma Elispot responses to Rev. • No responses to three specific CTL epitopes were observed by Elispot in individuals with appropriate HLA. Some cytoxic activity against whole protein was observed that was CD4+ T-cell mediated.				

III-B-13 Vpu Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Vpu (19–34)	Vpu (19–34) • T-cell response to this epitope persisted after seroreversion.	AIVVWSIVLIEYRKIL	HIV-1 infection	human	Ranki1997
Vpu	Vpu **Vaccine** *Vector/Type:* DNA *HIV component:* Nef, Vif, Vpu **Keywords** inter-clade comparisons, Th1. • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFNγ levels. • Antigen stimulation increased IFNγ production in pVVN-P immunized mice, indicating a Th1 response. • IL-4 production was not significantly changed after antigen stimulation compared to control levels. • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.		Vaccine	mouse (H-2^d)	Ayyavoo2000

III-B-14 gp160 Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (30–51)	gp120 (30–51 IIIB)	ATEKLWVTVYYGVPVWKEA-TTT?	HIV-1 infection	human	Geretti1994
	Epitope name A1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, mean SI = 4.6.				
gp160 (32–44)	gp120 (39–51)	EQLWVTVYYGVPV	Vaccine	mouse (H-2^{bxk})	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (38–48)	Env (45–55)	VYYGVPVWKEA	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.				
gp160 (38–48)	Env (45–55)	VYYGVPVWKEA	HIV-1 infection	human, chimpanzee	Nehete1998b
	• Seven out of nine HIV-infected chimpanzees and eight out of seventeen HIV-positive humans exhibited positive proliferative responses to this conserved peptide (peptide 104) – no HIV negative individuals showed a response. • This peptide, along with 4 other peptides from conserved regions of envelope, can induce proliferative responses to HIV and may be useful for vaccines. • Peptide 104 elicited proliferative responses in inbred mouse strains and outbred rhesus monkeys in previous study by same group.				
gp160 (38–48)	gp120 (45–55)	VYYGVPVWKEA	Vaccine	mouse (H-$2^{bxk, sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (41–54)	Env (48–60)	GVPVWKEATTLFC	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • Despite the proliferative response to this peptide in mice, no response was observed in 3 rhesus monkeys.				
gp160 (41–54)	gp120 (48–61)	GVPVWKEATTLFC	Vaccine	mouse (H-2^{sxd})	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (41–60)	gp120 (40–59 89.6)	GVPVWREATTTLFCASDAKA	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 2. **Donor HLA** H-2k, H-2d.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 10/10 BALB/c mice tested, but only in 5/10 CBA/J mice.				
gp160 (41–60)	gp120 (40–59 89.6)	GVPVWREATTTLFCASDAKA	Vaccine	mouse (H-2^d)	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** immunodominance. • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 10/10 BALB/c with an average SI of 6.4, the strongest reaction among BALB/c mice, but not by CBA/J mice, but recognized well not by CBA/J mice, so is considered to be uniquely immunodominant for H-2^d • Uniquely immunodominant sequences tended to be in the inner domain of the protein.				
gp160 (42–61)	gp120 (42–61 IIIB)	VPVWKEATTTLFCASDAKA-Y?	HIV-1 infection	human	Geretti1994
	Epitope name A2. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, mean SI = 6.6.				
gp160 (52–71)	gp120 (52–71 IIIB)	LFCASDAKAYDTEVHNVWA-T?	HIV-1 infection	human	Geretti1994
	Epitope name A3. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, mean SI = 4.3.				
gp160 (61–80)	gp120 (60–79 89.6)	YDTEVHNVWATHACVPTDPN	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 4. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• This peptide was highly reactive in 4/10 BALB/c mice tested, but only in 1/10 CBA/J mice.				
gp160 (62–80)	gp120 (62–80 IIIB)	DTEVHNVWATHACVPTDPN?	HIV-1 infection	human	Geretti1994
	Epitope name A4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.5.				
gp160 (62–81)	gp120 (MN)	DTEVHNVWATQACVPTDPNP	HIV-1 infection	human (DR)	Malhotra2003
	Keywords HAART, acute infection, cross-presentation by different HLA. **Epitope name** DP20. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy. • This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. The CD4+ clones showed MHC-restricted cytotoxicity and secreted high levels of cytokines when stimulated. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintainted in Env. • This peptide showed bound to HLA-DRB1*0101.				
gp160 (65–75)	gp120 (72–82)	AHKVWATHACV	Vaccine	mouse (H-$2^{bxk, sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (74–85)	gp120 (74–85 LAI)	CVPTDPNPQEVV	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (74–85)	gp120 (81–92)	CVPTNPVPQEVV	Vaccine	mouse (H-$2^{bxk, sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (80–99)	gp120 (51–70 HXB2)	NPQEVVLVNTENFNMWKND	in vitro stimulation or selectio	human	Li Pira1998
	Keywords TCR usage. • Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 13 usage. • Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 7.				
gp160 (81–100)	gp120 (80–99 89.6)	PQEVVLGNVTENFNMWKNNM	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 6.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA H-2k. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was not reactive in any BALB/c mice tested (0/10), but was highly reactive in all (10/10) CBA/J mice.				
gp160 (81–100)	gp120 (80–99 89.6)	PQEVVLGNVTENFNMWKNNM	Vaccine	mouse (H-2^k)	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** immunodominance. • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 10/10 CBA/J with an average SI of 8.2, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k • Uniquely immunodominant sequences tended to be in the inner domain of the protein.				
gp160 (81–101)	gp120 (81–101 IIIB)	PQEVVLVNVTENFNMWKND-MV?	HIV-1 infection	human	Geretti1994
	Epitope name B1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, mean SI = 5.1.				
gp160 (92–101)	gp120 (90–100 W6.ID)	YFNMWKNNMV	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21 • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated. • One T-cell clone reacts with two overlapping peptides, and the region of overlap is: YFNMWKNNMV. • The first 20-mer peptide that this clone reacts with is PQEVVLGNVTEYFNMWKNNMV, and the IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version: IIIB: pqevvlVnvteNfDmwknDmv.				
gp160 (92–111)	gp120 (92–111 W6.ID)	YFNMWKNNMVDQMHEDIISL	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21 • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated. • The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide NfDmwknDmvEqmhediisl. • Six T-cell lines react with this peptide, but some of these can also be stimulated by other gp120 peptides located in different regions of gp120.				
gp160 (101–126)	gp120 (101–126)	VEQMHEDIISLWDQSLKPC-VKLTPLC	Vaccine	mouse (H-2^k)	Sjolander1996
	Vaccine *Vector/Type:* protein *HIV component:* gp160 • Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein.				
gp160 (102–114)	gp120 (109–121)	EQMHEDIISLWDQ	Vaccine	mouse (H-2^{bxk})	Sastry1991
	Vaccine *Vector/Type:* peptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (102–116)	gp120 (109–123 IIIB)	EQMHEDIISLWDQSL	Vaccine	mouse (H-$2^{d, i5}$)	Hale1989
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (102–116)	gp160 (109–123 IIIB)	EQMHEDIISLWDQSL	Vaccine	mouse (H-2^{d}, H-2^{b})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • B10.D2 (H-$2A^{d}$, E^{d}) and B10.A(R5) (H-$2A^{b}$, E^{b}) mice immunized with rec gp160 showed a proliferative response to EQMHEDIISLWDQSL. • EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (102–121)	gp120 (102–121 IIIB)	EQMHEDIISLWDQSLKPCV-K?	HIV-1 infection	human	Geretti1994
	Epitope name B3. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 5.9.				
gp160 (102–121)	gp160 (109–128 IIIB)	EQMHEDIISLWDQSLKPCVK	HIV-1 infection, Vaccine	human, mouse (H-2^{k}, H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide. • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people. • This cluster peptide elicited proliferative responses in cells from vaccinated B10.BR mice (H-$2A^{k}$, E^{k}) and B10.S(9R) mice (H-$2A^{s}$, E^{s}), while shorter peptides from within this region stimulated H-2^{k}, H-2^{d} and H-2^{b} responses, but not H-2^{s} • IL-2 production was observed in response to this peptide in 64% (23/36) of asymptomatic HIV-infected individuals.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Clerici1997
	Epitope name T2. • Used in a study of pentoxifylline's influence on HIV specific T-cells.				
gp160 (105–117)	gp120 (112–124 BH10)	HEDIISLWDQSLK	Vaccine	human	Berzofsky1988
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T2. • Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Clerici1989
	Epitope name T2. • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Clerici1991a
	Epitope name T2. • Peptides stimulate Th cell function and CTL activity in similar patient populations.				
gp160 (105–117)	gp120 (112–124)	HEDIISLWDQSLK	Vaccine	human	Clerici1991b
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T2. • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK		human	Clerici1992
	Epitope name T2. • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	Vaccine	macaque	Hosmalin1991
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T2. • Peptide priming to induce T-cell help enhances antibody response to gp160 immunization.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK		human	Pinto1995
	Epitope name T2. • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human	Kaul1999
	Epitope name T2. • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]				
gp160 (105–117)	gp120	HEDIISLWDQSLK	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001a
	Keywords inter-clade comparisons, responses in children, mother-to-infant transmission. **Epitope name** T2. • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4. • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (105–117)	Env (112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection, HIV-1 exposed seronegative		Clerici1993a
	Keywords mother-to-infant transmission.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name T2. **Assay type** cytokine production. • Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected. • PBL from 10/21 of the mothers showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.				
gp160 (105–117)	Env (IIIB)	HEDIISLWDQSLK	HIV-1 exposed seronegative		Clerici1994a
	Epitope name T2. **Assay type** cytokine production. • Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection. • Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.				
gp160 (105–117)	HIV-1 (IIIB)	HEDIISLWDQSLK	HIV-1 infection		Clerici1994b
	Epitope name T2. **Assay type** cytokine production. • IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.				
gp160 (105–117)	Env (112–124)	HEDIISLWDQSLK	HIV-1 infection	human	Kuhn2001b
	Keywords responses in children, mother-to-infant transmission. **Epitope name** T2. **Assay type** proliferation. • T helper proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery. • The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).				
gp160 (105–117)	gp120 (112–124 BH10)	HEDIISLWDQSLK	computer prediction	mouse (H-$2^{k, s}$)	Cease1987
	Epitope name T2. • 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm.				
gp160 (105–117)	gp120 (112–124 IIIB)	HEDIISLWDQSLK	Vaccine	mouse (H-2^{k})	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T2. • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (105–117)	gp160 (112–124 IIIB)	HEDIISLWDQSLK	Vaccine	mouse (H-2^k)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • B10.BR (H-2A^k, E^k) mice immunized with rec gp160 showed a strong proliferative response to three overlapping peptides, QMHEDIISLWDQSL, HEDIISLWDQSLK, and DIISLWDQSLKPCVK, and HEDIISLWDQSLK is common to between them. • EQMHEDIISLWDQSLKPCVK encompasses several murine Th epitopes including HEDIISLWDQSLK and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (105–123)	gp120 (112–130 IIIB)	HEDIISLWDQSLKPCVKLT		human	Furci1997
	• 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope.				
gp160 (108–119)	gp120 (108–119 LAI)	IISLWDQSLKPC	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (110–125)	gp120 (110–125)	SLWDQSLKPCVKLTPL	HIV-1 infection	human	Caruso1997
	Keywords rate of progression. • As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71. • The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost. • This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.				
gp160 (111–123)	gp120 (118–130)	LWDQSLKPCVKLT	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.				
gp160 (112–130)	gp120 (112–130 IIIB)	WDQSLKPCVKLTPLCVSLK?	HIV-1 infection	human	Geretti1994
	Epitope name B4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 4.4.				
gp160 (112–141)	gp120 (112–141 NL43)	WDQSLKPCVKLTPLCVSLK-CTDLGNATNTN	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients. • Over 35% of vaccinees had a stimulation index of greater than 5 to this peptide.				
gp160 (115–126)	gp120 (115–126 LAI)	SLKPCVKLTPLC	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (115–129)	gp120 (115–129 LAI)	SLKPCVKLTPLCVSL	Peptide-HLA interaction	human (HLA-DR)	Gaudebout1997
	Keywords binding affinity. • Peptide bound to both HLA-DR*1101 and HLA-DR*0401 with high affinity. • Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding.				
gp160 (121–140)	gp120 (120–139 89.6)	KLTPLCVTLNCTNLNITKNT	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 10. **Donor HLA** H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 5/10 BALB/c mice tested, but not in and (0/10) CBA/J mice.			
gp160 (121–141)	gp120 (131–151 IIIB)	KLTPLCVSLKCTDLKNDTN-TN?	HIV-1 infection	human	Geretti1994
	Epitope name C1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 3.9.			
gp160 (122–141)	gp120 (121–140 MN)	LTPLCVTLNCTDLRNTTNTN	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, Th1. **Epitope name** 1931. • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 3/5 animals vaccinated with rec gp120 responded by DTH to this peptide, while 0/6 vaccinated with plasmid gp120 DNA responded.			
gp160 (122–141)	gp120 (122–141 IIIB)	LTPLCVSLKCTDLKNDTNT-N?	HIV-1 infection	human	Geretti1994
	Epitope name B5. • • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • 1/15 responders recognized this peptide, SI = 3.1.				
gp160 (136–155)	gp120 (141–160 MN)	NSTAWNNSNSEGTIKGGEMK	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, Th1. **Epitope name** 1932. • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 2/6 vaccinated with plasmid gp120 DNA.				
gp160 (138–159)	gp120 (141–160 W6.ID)	TTSNGWTGEIRKGEIKNCSF	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21 • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated. • The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide: IIIB: ttsnSSGR-MIMEgeikncsf.				
gp160 (142–161)	gp120 (142–161 IIIB)	SSSGRMIMEKGEIKNCSFN-I?	HIV-1 infection	human	Geretti1994
	Keywords immunodominance. **Epitope name** C2. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 4.3.				
gp160 (147–168)	gp120 (152–173 NL43)	MMMEKGEIKNCSFNISTSI-RGK	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients. • Over 50% of vaccinees had a stimulation index of greater than 5 to this peptide.				
gp160 (152–171)	gp120 (152–171 IIIB)	GEIKNCSFNISTSIRGKVQ-K?	HIV-1 infection	human	Geretti1994
	Keywords immunodominance. **Epitope name** C3.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 4.4.				
gp160 (155–169)	Env (UG92005)	KNCSFNITTELIDKK	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the V2 region of UG92005 (UG, clade D) and the hybridoma that recognized it used Vβ5. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (155–169)	gp120 (160–174 LAI)	KNCSFNISTSIRGKV		human (HLA-DR)	Gaudebout1997
	Keywords binding affinity. • Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity. • Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding.				
gp160 (159–178)	gp120 (160–179 89.6)	FYITTSIRNKVKKEYALFNR	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 14. **Donor HLA** H-2k, H-2d.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 6/10 BALB/c mice tested, and in 4/10 CBA/J mice.				
gp160 (162–181)	gp120 (162–181 IIIB)	STSIRGKVQKEYAFFYKLDI	Vaccine	macaque	Lekutis1997b
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Env • HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkeys.				
gp160 (162–182)	gp120 (162–182 IIIB)	STSIRGKVQKEYAFFYKLD-II?	HIV-1 infection	human	Geretti1994
	Epitope name C4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.3.				
gp160 (166–185)	gp120 (MN)	RDKMQKEYALLYKLDIVSID	HIV-1 infection	human	Malhotra2003
	Keywords HAART, acute infection. **Epitope name** RD20. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy. • This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail.These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintainted in Env.				
gp160 (169–189)	gp120 (141–160 W6.ID)	VQKEYALFYNLDVVPIDDD-NA	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21 • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated. • The IIIB version of this peptide does not induce proliferation in the T-cell line that responds to the W61D version of the peptide ——F–K–II—N-TT vqkeyaFfyKldIIpidNdTT. • Two T-cell lines react specifically with this peptide.				
gp160 (172–191)	gp120 (172–191 IIIB)	EYAFFYKLDIIPIDNDTTSY	Vaccine	macaque	Lekutis1997b
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Env • HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (172–191)	gp120 (172–191 IIIB)	EYAFFYKLDIIPIDNDTTS-Y?	HIV-1 infection	human	Geretti1994

Keywords immunodominance.
Epitope name C5.
- Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.
- After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.
- IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.
- Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops.
- 4/15 responders recognized this immunodominant peptide, average SI = 7.4.

gp160 (175–189)	Env (UG92005)	LFYKLDVVQIDNSTN	Vaccine	mouse (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Keywords inter-clade comparisons, epitope processing, TCR usage.
- This epitope is located in the V2 region of UG92005 (UG, clade D) and the Vβ usage of the TCR was not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

gp160 (186–215)	gp120 (191–220 NL43)	NDTTSYTLTSCNTSVITQA-CPKVSFEPIPI	Vaccine	human	Sitz1999

Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160
- There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.
- Over 30% of vaccinees had a stimulation index of greater than 5 to this peptide.

gp160 (188–207)	gp120 (89.6)	NTKYRLISCNTSVITQACPK	Vaccine	mouse	Dai2001

Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Keywords epitope processing, immunodominance.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name Peptide 17. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in only 1/10 BALB/c mice tested, but was one of the most reactive in CBA/J mice, reacting with 9/10 mice.				
gp160 (188–207)	gp120 (190–209 89.6)	NTKYRLISCNTSVITQACPK	Vaccine	mouse (H-2^k)	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** immunodominance. • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 9/10 CBA/J with an average SI of 9.8, one of the two immunodominant peptides in CBA/J mice, and not by BALB/c mice, so is considered to be uniquely immunodominant for H-2^k • Uniquely immunodominant sequences tended to be in the inner domain of the protein.				
gp160 (192–211)	gp120 (192–211 IIIB)	KLTSCNTSVITQACPKVSF-E?	HIV-1 infection	human	Geretti1994
	Epitope name D2. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.6.				
gp160 (193–218)	gp120 (193–218)	LTSCNSVITQACPKVSFEP-IPIHYC	Vaccine	mouse (H-$2^{d, b}$)	Sjolander1996
	Vaccine *Vector/Type:* protein *HIV component:* gp160 • Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein.				
gp160 (198–212)	Env (1007)	TSVITQACPKVSFEP	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCRs for two clonotypes was Vβ3 and Vβ8.1-2. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (198–215)	Env (1007)	TSVITQACPKVSFEPIPI	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ6. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (199–211)	Env (204–216)	SVITQACSKVSFE	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • A weak or transient proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.				
gp160 (199–211)	Env (204–216)	SVITQACSKVSFE	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.				
gp160 (199–211)	gp120 (204–216)	SVITQACSKVSFE	Vaccine	mouse (H-$2^{bxk, sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response in mice representing four haplotypes.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (200–214)	gp120 (205–219 LAI)	VITQACPKVSFEPIP	Peptide-HLA interaction	human (HLA-DR)	Gaudebout1997

Keywords binding affinity.

- Peptide binds to both HLA-DR*1101 and HLA-DR*0401 with high affinity.
- Because of the distinctive binding pockets of HLA-DR*1101 and HLA-DR*0401, peptides that bound both were considered candidates for promiscuous HLA-DR binding.

gp160 (201–212)	Env (1007)	ITQACPKVSFEP	Vaccine	mouse (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)

Keywords inter-clade comparisons, epitope processing, TCR usage.

- This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was Vβ3.
- The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TSVITQACPKVSFEP and ITQACPKVSFEPIPI)
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.
- Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.
- 80 unique clonotypes were characterized from six mice.
- H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).
- Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.

gp160 (206–220)	Env (1007)	PKVSFEPIPIHYCAP	Vaccine	mouse (H-2 IA^b)	Surman2001

Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)

Keywords inter-clade comparisons, epitope processing.

- This epitope is located in the C2 region of 1007 (US, clade B) and 12 hybridomas recognized the peptide with Vβ usage of Vβ4,6,7,8.1-2,8.3,11,12 and others not determined.
- C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.
- The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.
- Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (206–225)	gp120 (211–230 MN)	PKISFEPIPIHYCAPAGFAI	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, Th1. **Epitope name** 1957. • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 5/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 2/6 vaccinated with plasmid gp120 DNA.				
gp160 (206–230)	gp120 (206–230)	PKVSFEPIPIHYCAPAGFA-ILKCNN	Vaccine	mouse ($H\text{-}2^{d,b}$)	Sjolander1996
	Vaccine *Vector/Type:* protein *HIV component:* gp160 • Study showing that T-cell determinants from glycoproteins can be dependent on the glycosylation of the protein.				
gp160 (208–218)	Env (UG92005)	ITFEPIPIHYC	Vaccine	mouse ($H\text{-}2\ IA^b$)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing. • This epitope is located in the C2 region of UG92005 (UG, clade D) and its was recognized by two hybridomas with Vβ usage Vβ12 and not determined. • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKITFEPIPIHYCAP and ITFEPIPIHYCAPAG) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (208–222)	Env (UG92005)	ITFEPIPIHYCAPAG	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the C2 region of UG92005 (UG, clade D) and it was recognized by five hybridomas with Vβ usage Vβ5, 8.2, 12 and not determined. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (208–227)	gp120 (210–229 89.6)	VSFQPIPIHYCVPAGFAMLK	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 19. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 6/10 BALB/c mice tested, and in 6/10 CBA/J mice.				
gp160 (209–220)	gp120 (MN)	SFEPIPIHYCAP	HIV-1 infection	human (DR)	Malhotra2003
	Keywords HAART, vaccine-specific epitope characteristics, acute infection, cross-presentation by different HLA. **Epitope name** SP12. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy. • This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. The CD4+ clones showed MHC-restricted cytotoxicity and secreted high levels of cytokines when stimulated. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintainted in Env. • Seven out of 12 clones recognized this conserved C3 region of gp120. Clone one was mapped to the optimal epitope and was found to be presented by HLA-DR. The peptide showed promiscuous binding to DRB1*0101, DRB1*0401, DRB1*1302, DRB1*0701, DRB1*0901, DRB4*0101, DRB5*0101.			
gp160 (210–218)	Env (186–194 1035)	FEPIPIHYC	Vaccine	mouse (Class II I Ab)	Zhan2003
	Vaccine *Vector/Type:* vaccinia prime with gp120 boost *Strain:* B clade 1035 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** epitope processing, vaccine-induced epitopes, escape, TCR usage. **Assay type** proliferation, T-cell Elispot. • A very narrow Th response was stimulated in C57BL/6 mice vaccinated with vaccinia expressed HIV-1 env clone 1035. Five of seven different Th hybridomas isolated from five immunized mice immunized reacted with the peptide PKVSFEPIPIHYCAP, located in the C2 region of gp120. TCR Vβ usage indicated each of the clones was unique. Splenic populations from other C57BL/6 mice immunized with 1035 env confirmed that the gp120 specific T-helper response was focused on the PKVSFEPIPIHYCAP peptide. The authors suggest the protein structural context may contribute to the immunodominance of this peptide. • The minimal epitope was mapped for one of the hybridomas, and was FEPIPIHYC. • The natural variant, fDpipihyc, did not stimulate a response in three of the hybridomas.			
gp160 (210–223)	gp120 (215–228)	FEPIPIHYCAFPGF	Vaccine	mouse (H-2^{bxk})	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (212–231)	gp120 (221–240 W6.ID)	PIPIHYCAPAGFAILKCNNK	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21 • An HIV seronegative volunteer was vaccinated with rgp120 and a QS21/MPL adjuvant and HIV-1 specific T-cell lines were isolated. • Two T-cell lines react specifically with this peptide.				
gp160 (212–231)	gp120 (212–231 IIIB)	PIPIHYCAPAGFAILKCNN-K?	HIV-1 infection	human	Geretti1994
	Epitope name D4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 4.2.				
gp160 (214–220)	Env (1007)	PIHYCAP	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Keywords inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined. • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (PKVSFEPIPIHY-CAP and PIHYCAPAGFAILKC) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (215–225)	Env (1007)	IHYCAPAGFAI	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the C2 region of 1007 (US, clade B) and the Vβ usage of the TCR was not determined. • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and IHYCAPAGFAILKCN) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (216–225)	Env (UG92005)	HYCAPAGFAI	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	Keywords inter-clade comparisons, epitope processing, TCR usage.				
	• This epitope is located in the C2 region of UG92005 (UG, clade D) and Vβ usage of its TCR was not determined.				
	• The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (EPIPIHYCAPAGFAI and HYCAPAGFAILKCND)				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.				
	• 80 unique clonotypes were characterized from six mice.				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (220–234)	gp120 (225–240 SF2)	PAGFAILKCNNKTFN	in vitro stimulation or selectio		Manca1993
	• T-cell line derived from unprimed, uninfected individual.				
	• Responds to APC pulsed with either synthetic peptide or gp120.				
	• Human MAbs 448-D and 450-D enhance APC gp120 uptake and presentation.				
gp160 (220–234)	gp120 (IIIB)	PAGFAILKCNNKTFN	Vaccine	human	Pozzi1994
	Vaccine *Vector/Type:* Streptococcus gordonii *HIV component:* gp120				
	Keywords immunodominance.				
	Epitope name pep24.				
	• This previously described immunodominant Th cell epitope was fused to the streptococcal surface protein M6 (emm-6.1), for expression on the surface of the bacterium Streptococcus gordonii.				
	• Recombinant bacteria showed efficient MHC class II mediated presentation of gp120 to T-cells by stimulation of a proliferative response in a human T cell clone specific for pep24.				
gp160 (220–235)	gp120 (IIIB)	PAGFAILKCNNKTFNY	in vitro stimulation or selectio	human (DR2)	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*.				
	• Peptide priming does not always induce T-cells that recognize whole protein.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• gp120 priming induced T-cells that recognize this peptide.				
gp160 (220–235)	gp120 (220–235 HXB2) **Keywords** escape.	PAGFAILKCNNKTFNY	in vitro stimulation or selectio	human (DR2)	Guzman1998
	• Listeria monocytogenes, an intracellular pathogen which is ingested by macrophages and can escape from the phagosome to replicate in the cytoplasm, was used successfully as carrier to deliver this gp120 epitope to CD4+ T-cells.				
gp160 (220–235)	gp120 (191–205 HXB2)	PAGFAILKCNNKTFNY	in vitro stimulation or selectio	human (DR2)	Fenoglio1999
	• gp120 pep24 epitope exhibited antagonistic activity against proliferation of gp120-specific T-cells when flanked by unrelated amino acid sequence. • The glutathione S-transferase (GST)-peptide system can be used to display peptides; antigenicity was maintained when this peptide was expressed at the C-term end, but antagonism resulted when this peptide was expressed at the N-term end.				
gp160 (222–241)	gp120 (222–241 IIIB) **Epitope name** D5.	GFAILKCNNKTFNGTGPCT-N?	HIV-1 infection	human	Geretti1994
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 4.8.				
gp160 (223–231)	gp120 (238–246 HXB2) **Keywords** TCR usage.	FAILKCNNK	in vitro stimulation or selectio	human	Li Pira1998
	• Clonal heterogeneity was broad for a recall response to tetanus toxoid or PPD, but oligoclonal to primary HIV antigens, dominated in this case by TCR Vβ 22 usage. • Donor of PBMC that recognized this epitope had HLA-DR alleles 2 and 6. • The only (detected) immunogenic variant of this epitope was derived from strain NOF (YAILKCNNK)				
gp160 (223–231)	gp120 (194–202 HXB2)	FAILKCNNK	in vitro stimulation or selectio	human (DR2, 6)	Manca1996
	• Epitope was the minimal stimulatory sequence defined for two Th lines stimulated *in vitro*. • One Th line was stimulated by gp120, one by a Glutathione-S-transferase (GST)-peptide fusion. • Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line. • Constructs combining GST and the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells but not at the N-term end.				
gp160 (223–231)	gp120 (194–202 HXB2)	FAILKCNNK	in vitro stimulation or selectio	human (DR2, 6)	Manca1996
	• Epitope was the minimal stimulatory sequence defined for two Th lines stimulated *in vitro*. • One Th line was stimulated by p66, one by a Glutathione-S-transferase (GST)-peptide fusion protein. • Alanine substitutions at position 914, 196, and 202 abrogated activity for the GST-peptide stimulated line, but not for a gp120 stimulated line. • Constructs linking GST to the PAGFAILKCNNKTFNY gp120 peptide at the C-term end of GST stimulated Th cells, constructs linking at the N-term end did not. • The C and N termini of GST are not intrinsically permissive or non-permissive, presentation is epitope specific (see SSTVNDIQKLV for contrast)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (223–231)	gp120 (237–245 SF2, HXB2)	FAILKCNNK		mouse (H-2^{d})	Fenoglio2000
	Keywords inter-clade comparisons, immunodominance. • This peptide is an immunodominant Th epitope in BALB/c mice. • Substitutions in positions 237, 241, 243, 244 with Ala all cause reduced recognition. • Most natural analogs they tested did not cross-react, including peptides based on clade A, B, C, D, E and O sequences. • Position 237 and 244 when substituted with Ala cause an antagonistic response and the natural analogues of this epitope to loose antigenicity. • Some of the naturally occurring variants also cause an antagonistic response.				
gp160 (230–245)	gp120 (IIIB)	NKTFNGKGPCTNVSTY	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (232–251)	gp120 (232–251 IIIB)	TFNGTGPCTNVSTVQCTHG-I?	HIV-1 infection	human	Geretti1994
	Epitope name E1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 3.9.				
gp160 (235–247)	gp120 (240–252)	GTGPCTNVSTVQC	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two.				
gp160 (238–257)	gp120 (240–249 89.6)	PCTNVSTVQCTHGIRPVVST	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 22. **Donor HLA** H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was highly reactive in 6/10 BALB/c mice tested, but not in any (0/10) CBA/J mice.				
gp160 (240–255)	gp120 (IIIB)	TNVSTVQCTHGRPIY	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*.				
gp160 (242–261)	gp120 (242–261 IIIB)	VSTVQCTHGIRPVVSTQLL-L?	HIV-1 infection	human	Geretti1994
	Epitope name E2.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 3.4.				
gp160 (242–261)	gp120 (242–261 IIIB)	VSTVQCTHGIRPVVSTQLLL	SHIV infection	macaque (DRB1*0406)	Lekutis1997a
	• A novel C2 region Th epitope was described in SHIV-89.6 infected Macaca mulatta.				
gp160 (250–265)	gp120 (IIIB)	GIRPIVSTQLLLNGSC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (252–271)	gp120 (252–271 IIIB)	RPVVSTQLLLNGSLAEEEV-V?	HIV-1 infection	human	Geretti1994
	Epitope name E3. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, average SI = 7.4.				
gp160 (262–281)	gp120 (262–281 IIIB)	NGSLAEEEVVIRSVNFTDN-A?	HIV-1 infection	human	Geretti1994
	Epitope name E4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 3.1.				
gp160 (264–287)	gp120 (269–292 NL43)	SLAEEEVVIRSANFTDNAK-TIIVQ	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients. • 50% of vaccinees had a stimulation index of greater than 5 to this peptide.				
gp160 (269–283)	gp120 (269–283 IIIB, B10)	EVVIRSANFTDNAKT	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (270–285)	gp120 (IIIB)	VVIRSDNFTNNAKTIC	in vitro stimulation or selectio	human	Manca1995b
• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.					
gp160 (272–291)	gp120 (272–291 IIIB)	IRSVNFTDNAKTIIVQLNT-S?	HIV-1 infection	human	Geretti1994
Keywords immunodominance. **Epitope name** E5. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 5.0.					
gp160 (274–288)	gp120 (274–288 IIIB, B10)	SANFTDNAKTIIVQL	HIV-1 infection	human	Wahren1989b, Wahren1989a
• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.					
gp160 (276–295)	gp120 (MN)	NFTDNAKTIIVHLNESVQIN	HIV-1 infection	human	Malhotra2003
Keywords acute infection. **Epitope name** NN20. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy. • This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail.These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintainted in Env.					
gp160 (280–296)	gp120 (IIIB)	NAKTIIVQLNESVAIC	in vitro stimulation or selectio	human	Manca1995b
• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.					
gp160 (288–307)	gp120 (290–309 89.6)	LNESVVINCTRPNNNTRRRL	Vaccine	mouse	Dai2001
Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 27. **Donor HLA** H-2k, H-2d.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in only 1/10 BALB/c mice tested, but reacted in 8/10 CBA/J mice.				
gp160 (289–297)	gp120 (292–300 SF2)	NESVAINCT	Vaccine	human	Botarelli1991
	Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* gp120 • A non-glycosylated form of SF2 gp120, env 2-3, was used as an immunogen – 20% of T-cell clones do not recognize the glycosylated form.				
gp160 (290–306)	gp120 (296–312 LAI)	SVVEINCTRPNNNTRKS	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (292–310)	gp120 (292–310 IIIB)	VEINCTRPNNNTRKRIRIQ?	HIV-1 infection	human	Geretti1994
	Epitope name F1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • Only 1/15 responders recognized this peptide, but it had the highest SI in the study of 9.9.				
gp160 (296–307)	gp120 (301–324 RF)	CTRPNNNTRKSI	HIV-1 infection		deLorimier1994
	Keywords epitope processing. • Proton NMR spectroscopy was employed to analyze the solution conformation of a hybrid peptide, T1-SP10RF, in order to better understand the immunogenicity of its' T helper (KQIINMWQEVGKAMYA, CTRPNNNTRKSI), CTL (SITKGPGRVIYATG) and B-cell epitopes (RKSITKGPGRVIYATG). • This epitope embedded in the T1-SP10RF peptide does not form a helical amphipathic conformation. It lacks random-coil conformations, and this may make a peptide less susceptible to complete proteolytic degredation and be favored within epitopes.				
gp160 (296–314)	gp120 (303–321 IIIB)	CTRPNNNTRKSIRIQRGPG-(Y)	Vaccine	goat	Palker1989
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB • Goats were immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1.				
gp160 (297–321)	gp120 (302–324 MN)	TRPNYNKRKRIHIGPGRAF-YTTK	Vaccine	mouse (H-2^d)	Oscherwitz1999b
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 • Epitope presented as a tandem repeat (eight copies) elicits stronger B-cell and T-cell responses than the epitope presented as a single copy. • This study indicates that the increased response was not due to neodeterminants created at the junction of the peptides, but rather due to an epitope density effect, increased immunogenicity through a high ratio of epitope to protein.				
gp160 (297–330)	Env (303–335 BX08)	TRPNNNTRKSIHIGPGRAF-YATGEIIGDIRQAH	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 6/10 reacted to this peptide. • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual – this peptide was particularly immunogenic, eliciting a CTL response in five vaccinees. • None of the 12 tested had an IgG response to gp120 or gp160 and vaccinees could be differentiated from HIV-1 seropositive individuals with a commercial HIV detection kit – no neutralizing antibodies were observed.				
gp160 (298–307)	Env (UG92005)	RPYNNTRKGI	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by a hybridoma with Vβ usage not determined. • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (TINCTRPYNNTRKGI and RPYNNTRKGIHIGPG) • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (298–319)	gp120 (300–319 89.6)	RPNNNTRRRLSIGPGRAFYA	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 28. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 7/10 BALB/c mice tested, and in 5/10 CBA/J mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (301–325)	gp120 (IIIB)	NNTRKSIRIQRGPGRAFVT-IGKIGN	Vaccine	mouse	Sasaki1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Env, Rev *Adjuvant:* QS21 **Keywords** Th1. • The env response is what is being sought, but co-expression of rev is required. • Intramuscular versus nasal vaccination with DNA vaccine with a QS-21 adjuvant was studied. • QS-21 enhanced the IgG2a response mediated via Th1 cytokines IFNγ and IL-2 and delayed type hypersensitivity (DTH) in response to the V3 peptide was measured by a foot pad swelling test [Sasaki1998]				
gp160 (302–315)	gp120 (307–322 IIIB)	NTRKSIRIQRGPGR	Vaccine	mouse	Goodman-Snitkoff1990
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 • Identification of putative Th epitopes that can stimulate an antibody response in peptide-immunized mice.				
gp160 (302–321)	gp120 (302–321 IIIB)	NTRKRIRIQRGPGRAFVTI-G?	HIV-1 infection	human	Geretti1994
	Epitope name F2. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 5.6.				
gp160 (302–327)	gp120 (307–332 MN)	NKRKRIHIGPGRAFYTTKN-IIGTIR	Vaccine	mouse	Anderson2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 *Adjuvant:* Montanide (ISA 51) • Hypervariable epitope constructs (HECs) are degenerative peptide cocktails that are made in a single peptide synthesis reaction. Vaccination with a V3 degenerative peptide cocktail containing 64 distinct peptides, NTRK-[SR]-I-[HR]-IGPG-[RQ]-AFY-[AT]-TG-[DE]-IG-[DN]-IRQ, elicited broader and more durable Th responses than the MN V3 peptide alone in BALB/c mice immunized and boosted with V3 peptides, although the MN peptide elicited a transient MN-specific V3 response.				
gp160 (305–321)	gp120 (312–329)	(CG)KSIRIQRGPGRAFVT-IG	HIV-1 infection	human	Adams1997
	• Used as positive control in study examining T-cell response to four p24 Gag peptides.				
gp160 (308–319)	gp120 (subtype C)	(CKR)KIHIGPGQAFYT	HIV-1 infection	mouse (H-$2^{b, d, k, s}$)	Ahluwalia1997
	Keywords Th1. • A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b Ab response was enhanced by the presentation in the ISCOM suggestive of a Th1 response.				
gp160 (308–321)	gp120 (MN)	RIHIGPGRAFYTTK	Vaccine	mouse (H-2^{d})	Klinman1995
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 **Epitope name** SP10. • Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 10-mer from V3 contributes to this response.				
gp160 (308–322)	gp120 (308–322 IIIB)	RIHIGPGRAFYTTKN		human	Furci1997
	• 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but only 1/11 exposed-uninfected individuals recognized this peptide. • 1/18 unexposed-uninfected controls could recognize this peptide. • Erroneously documented as IIIB sequence - most likely MN peptide.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide **Epitope name** P18. • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • Despite the proliferative response to this peptide in mice and humans, no response was observed in 3 rhesus monkeys.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Wasik1997
	Keywords responses in children, Th1, Th2. **Epitope name** P18. • The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1+ infants. • IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol. • IL-4 production from Th2 cells was inversely correlated with the CTLp frequency. • The HIV-1+ children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to uninfected children. • The children that did not mount a good CTL response had dramatically decreased numbers of Th1 relative to Th2 cells.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Wasik2000
	Keywords responses in children, kinetics, Th1. **Epitope name** P18. • Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease. • The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK		human	Pinto1995
	Epitope name P18. • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.				
gp160 (308–322)	gp120 (315–329 MN)	RIHIGPGRAFYTTKN		human	Pinto1995
	Epitope name P18. • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Clerici1989
	Epitope name P18. • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Clerici1991a
	Epitope name P18. • Peptides stimulate Th cell function and CTL activity in similar patient populations.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	human	Clerici1991b
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** P18. • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK		human	Clerici1992
	Epitope name P18. • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Clerici1997
	Epitope name P18. • used in a study of the influence of pentoxifylline on HIV specific T-cells.				
gp160 (308–322)	gp120 (MN)	RIHIGPGRAFYTTKN		human	Clerici1992
	• Epitope P18 MN: Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.				
gp160 (308–322)	gp160 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection, HIV-1 exposed seronegative	human	Wasik1999
	Keywords immunodominance. **Epitope name** P18. • IL-2 responses associated with beta-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months. • In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide (KQIINMWQEVGKAMYA) were more frequent than responses to P18. • T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human	Kaul1999
	Epitope name P18. • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001a
	Keywords inter-clade comparisons, responses in children, mother-to-infant transmission. **Epitope name** P18. • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4. • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (308–322)	gp120 (315–329 MN)	RIHIGPGRAFYTTKN	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001a
	Keywords inter-clade comparisons, responses in children, mother-to-infant transmission. **Epitope name** P18. • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4. • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (308–322)	Env (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection, HIV-1 exposed seronegative		Clerici1993a
	Keywords mother-to-infant transmission. **Epitope name** P18IIIB. **Assay type** cytokine production. • Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected. • PBL from 10/21 of the mother showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.				
gp160 (308–322)	Env (MN)	RIHIGPGRAFYTTKN	HIV-1 infection, HIV-1 exposed seronegative		Clerici1993a
	Keywords mother-to-infant transmission. **Epitope name** P18MN. **Assay type** cytokine production. • Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected. • PBL from 10/21 of the mother showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.				
gp160 (308–322)	Env (IIIB)	RIQRGPGRAFVTIGK	HIV-1 exposed seronegative		Clerici1994a
	Epitope name P18IIIB. **Assay type** cytokine production. • Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.				
gp160 (308–322)	Env (MN) **Epitope name** P18MN. **Assay type** cytokine production. • Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection. • Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.	RIHIGPGRAFYTTKN	HIV-1 exposed seronegative		Clerici1994a
gp160 (308–322)	HIV-1 (IIIB) **Epitope name** P18IIIB. **Assay type** cytokine production. • IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.	RIQRGPGRAFVTIGK	HIV-1 infection		Clerici1994b
gp160 (308–322)	HIV-1 (MN) **Epitope name** P18MN. **Assay type** cytokine production. • IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.	RIHIGPGRAFYTTKN	HIV-1 infection		Clerici1994b
gp160 (308–322)	Env (315–329) **Keywords** mother-to-infant transmission. **Epitope name** P18 MN. **Assay type** cytokine production. • The proliferative responses in cord blood at delivery to a cocktail of HIV Envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery. • The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).	RIHIGPGRAFYTTKN	HIV-1 infection	human	Kuhn2001b
gp160 (308–322)	Env (315–329 IIIB) **Keywords** responses in children, mother-to-infant transmission. **Epitope name** P18 IIB. **Assay type** proliferation. • T helper proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery.	RIQRGPGRAFVTIGK	HIV-1 infection	human	Kuhn2001b

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human (DR)	Baier1995
	Epitope name P18. • Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and IgD Fab fragments to enhance uptake by antigen presenting cells thus increase immunogenicity.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Vaccine	mouse (H-2 A^d)	Takahashi1990
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** P18. • Induces both class II restricted CD4+ Th cells, and class I restricted CD8+ CTL.				
gp160 (308–322)	gp120 (315–329 IIIB)	RIQRGPGRAFVTIGK	Peptide-HLA interaction	mouse (H-2 I-A^d)	Takeshita1995
	Epitope name P18. • Binds Class II H-2 I-A^d requiring riqrgPgRaFvti, and Class I H-2 D^d, requiring iGPgRaFvtI.				
gp160 (308–322)	Env (IIIB)	RIQRGPRAFVTIGK	Vaccine	mouse (H-2^d)	Lu1999
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* MIP-1alpha **Keywords** Th1. **Epitope name** P18. • MIP-1a expression plasmid co-inoculated with a DNA vaccine consisting of HIV-1 pCMV160IIIB and pcREV enhanced the HIV-specific T-cell immune response as measured by a CTL test against using V3 peptide pulsed targets, and a DTH test to V3 peptide. • The IgG1/IgG2a response was lowered with co-inoculation of MIP-1 alpha, suggesting it preferentially elicits a Th1 response.				
gp160 (308–327)	gp120 (306–325 MN)	RIHIGPGRAFYTTKNIIGIT	HIV-1 infection	human (DRB1*0101)	Hayball1997
	• Tandem repeated presentation of epitope enhances binding to class II molecule and therefore induction of T-cell proliferation. • Tandem peptides are thought to enhance proliferation through improved recruiting of CD4 to the activation complex, which can counter-balance gp120's sequestering of CD4 and consequential inhibition of a proliferative response.				
gp160 (309–323)	gp120 (309–323 IIIB, B10)	EQRGPGRAFVTIGKI	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (309–325)	gp120 (314–330)	IQRGPGRAFVTIGKIGN	HIV-1 infection	human	Caruso1997
	Keywords rate of progression. • As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71. • The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost. • This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.				
gp160 (310–328)	gp120 (310–329 89.6)	SIGPGRAFYARRNIIGDIRQ	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 29.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Donor HLA H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 2/10 BALB/c mice tested, and in 8/10 CBA/J mice.				
gp160 (311–319)		RGPGRAFVT	Vaccine	mouse	Barouch2002
	Vaccine *Vector/Type:* DNA *Strain:* B clade BH10 *HIV component:* gp120 *Adjuvant:* GM-CSF • gp120 encoding DNA co-injected with a plasmid carrying GMCSF gave meager CD4+ T-cell responses in BALB/c mice relative to bicistronic gp120 and GMCSF cloned into the same vector and expressed from the same promoter. • The bicistronic gp120/GM-CSF vaccine induced an approximately 10-fold increase of CD4+ T cell proliferative responses to gp120, as well as a significant increase in IL-2, IL-4, IL-10, IFNγ and GM-CSF production, compared to immunization with the monocistronic pVIJ-gp120 with GMCSF. The enhanced proliferative responses were substantiated by CD4+ T-cell Elispot. • Both mono and bicistronic DNA vaccines induced similar CTL responses directed against the H-2Dd restricted P18 peptide RGPRAFTVTI in murine splenocytes despite the enhanced proliferative responses.				
gp160 (311–320)	gp120 (IIIB)	RGPGPAFVTI	Vaccine	mouse (H-2^d)	Xin1998
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* IL-2 **Keywords** Th1. • Intranasal immunization with IL-2 expression plasmid in addition to DNA vaccine amplifies cellular response to antigen, probably via activation of Th type 1 (Th1) cells.				
gp160 (311–320)	gp120 (IIIB)	RGPGPAFVTI	Vaccine	mouse (H-2^d)	Xin1999
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* IL-15 **Keywords** Th1. • Intranasal immunization with IL-15 expression plasmid in addition to DNA vaccine increases DTH response and CTL activity to the antigen, and decreases the serum IgG1 to IgG2a ratio, enhancing Th type 1 (Th1) cell-mediated immunity. • Expression of IL-2 or IL-15 can enhance Th1 response to the vaccine, but they to do not appear to elicit a synergistic response.				
gp160 (311–320)	gp120 (IIIB)	RGPGPAFVTI	Vaccine	mouse (H-2^d)	Ihata1999
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* CD40 **Keywords** Th1, Th2. • CD40L expression increases DTH, and Th1-dependent responses based on enhanced IgG2a titers, with no lowering of IgG1 titers. • Elispot assay indicated co-injection with hCD40L resulted in greater numbers of IFNγ producing Th1cells, as well as increased IL-4 producing Th2 cells. • Results suggest hCD40L enhance both Th1 and Th2 cells, and such a pattern of induction is unique among adjuvants, as most adjuvants increase either Th1 or Th2.				
gp160 (311–322)	Env (IIIB)	RGPGRAFVTIGK	Vaccine	mouse (H-2^d)	Kusakabe2000
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* GM-CSF **Keywords** Th1, Th2. • The timing of delivery of the pGM-CSF expression plasmid for intramuscular DNA pCMV160IIIB/REV vaccination impacts the Th response, maximizing Th2 responses when administered 3 days prior to the DNA vaccine, and Th1 responses when administered 3 days after the DNA vaccine.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (314–328)	gp120 (314–328 IIIB, B10)	GRAFVTIGKIGNMRQ	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (314–341)	gp120 (319–346 NL43)	GRAFVTIGKIGNMRQAHCN-ISRAKWNAT	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160				
	• There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients.				
	• More than 25% of vaccinees had a stimulation index of greater than 5 to this peptide.				
gp160 (315–328)	Env (UG92005)	RAYYTTNIVGNIRQ	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	Keywords inter-clade comparisons, epitope processing, TCR usage.				
	• This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridomas with Vβ usage not determined, but one used Vα 8.				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.				
	• 80 unique clonotypes were characterized from six mice.				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (317–331)	gp120 (324–338 IIIB)	FVTIGKIGNMRQAHC	Vaccine	mouse (H-$2^{k,d}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160				
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (317–331)	gp160 (324–338 IIIB)	FVTIGKIGNMRQAHC	Vaccine	mouse (H-2^k, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	• B10.BR (H-$2A^k$, E^k) and B10.D2 (H-$2A^d$, E^d) mice immunized with rec gp160 showed a proliferative response to this peptide.				
	• FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including FVTIGKIGNMRQAHC and is referred to as a "multideterminant region" or cluster peptide.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (317–336)	gp120 (321–340 MN)	YTTKNIIGTIRQAHCNSRA	Vaccine	guinea pig	Chattergoon2002

Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA)
Keywords vaccine-specific epitope characteristics, Th1.
Epitope name 1987.

- Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid.
- A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides.
- 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, as did 4/6 vaccinated with plasmid gp120 DNA.

gp160 (317–349)	gp160 (324–356 IIIB)	FVTIGKIGNMRQAHCNISR-AKWNNTLKQIDSKL	HIV-1 infection, Vaccine	human, mouse (H-2^k, H-2^d)	Berzofsky1991b, Berzofsky1991a

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)

- FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide.
- Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people.
- This cluster peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k) and B10.D2 mice (H-$2A^d$, E^d), but shorter peptides from within this region stimulated H-2^k, H-2^d, H-2^b and H-2^s responses.
- IL-2 production in response to this peptide was observed in 58% (21/36) of asymptomatic HIV-infected individuals.

gp160 (319–338)	gp120 (320–339 89.6)	RRNIIGDIRQAHCNISRAKW	Vaccine	mouse	Dai2001

Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Keywords epitope processing, immunodominance.
Epitope name Peptide 30.
Donor HLA H-2k, H-2d.

- Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences.
- This peptide was highly reactive in 7/10 BALB/c mice tested, and in 7/10 CBA/J mice and was considered one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.

gp160 (319–338)	gp120 (320–339 89.6)	RRNIIGDIRQAHCNISRAKW	Vaccine	mouse (H-2^k, H-2^d)	Dai2001

Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)
Keywords immunodominance.

- Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence.
- This peptide was recognized by 7/10 CBA/J and 7/10 BALB/c mice with SI $>$ 4, averaging 6.3 and 4.8, and is considered to be promiscuously immunodominant.
- Uniquely immunodominant sequences tended to be in the inner domain of the protein.

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (321–336)	gp120 (IIIB)	RIIGDIRKAHCNISRY	in vitro stimulation or selectio	human	Manca1995b
• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.					
gp160 (322–336)	Env (1007)	IIGDIRQAHCNISRE	Vaccine	mouse (H-2 IA^b)	Surman2001
Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the V3 region of 1007 (US, clade B) and was recognized by three hybridomas with Vβ usage Vβ 6 and not determined. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.					
gp160 (322–336)	Env (UG92005)	IVGNIRQAHCNVSKA	Vaccine	mouse (H-2 IA^b)	Surman2001
Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (322–336)	Env (UG92005)	IVGNIRQAHCNVSKA	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	Keywords inter-clade comparisons, epitope processing, TCR usage.				
	• This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by three hybridomas with Vβ usage Vβ 6, 8.1, and not determined.				
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.				
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells.				
	• Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined.				
	• Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO.				
	• 80 unique clonotypes were characterized from six mice.				
	• H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41).				
	• Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (322–341)	gp120 (322–341 IIIB)	KIGNMRQAHCNISRAKWNN-T?	HIV-1 infection	human	Geretti1994
	Epitope name F4.				
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.				
	• IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				
	• 1/15 responders recognized this peptide, SI = 7.6.				
gp160 (324–336)	Env (UG92005)	GNIRQAHCNVSKA	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	Keywords inter-clade comparisons, epitope processing, TCR usage.				
	• This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by two hybridoma with Vβ usage Vβ8.2 and not determined.				
	• The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (IVGNIRQAHCN-VSKA and GNIRQAHCNVSKAKW)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (324–338)	Env (UG92005)	GNIRQAHCNVSKAKW	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the V3 region of UG92005 (UG, clade D) and was recognized by eleven hybridomas with Vβ usage Vβ5, 7, 8.1, 8.2, 11 and not determined – a Vβ 8.1's and Vβ 8.2 also were shown to use Vα 8, and one of the ND used Vα 2. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (327–341)	gp120 (327–341 HXB2)	RQAHCNISRAKWNNT	Vaccine	mouse (I-A^d)	Warren1992
	Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* gp120 • Minimum epitope and MHC restriction determined for CTL clone that recognizes the N-terminal flank of the V3 loop.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (327–346)	gp120 (331–350 MN)	RQAHCNISRAKWNDILRQIV	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, Th1. **Epitope name** 1988. • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 4/5 animals vaccinated with rec gp120 responded by DTH to this peptide, and 2/6 responded that were vaccinated with plasmid gp120 DNA.			
gp160 (330–350)	gp120 (330–349 IIIB)	HCNISRAKWNNTLKQIASK-LR?	HIV-1 infection	human	Geretti1994
	Epitope name F5. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 5.5.			
gp160 (331–345)	gp120 (IIIB)	CNISRAQWNNTLEQI	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (332–354)	gp120 (337–359 NL43)	NISRAKWNATLKQIASKLR-EQFG	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients. • More than 30% of vaccinees had a stimulation index of greater than 5 to this peptide.				
gp160 (335–349)	gp120 (342–356 IIIB)	RAKWNNTLKQICSKL	Vaccine	mouse (H-$2^{k, t4, i5}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (335–349)	gp160 (342–356 IIIB)	RAKWNNTLKQIDSKL	Vaccine	mouse (H-2^{k}, H-2^{b}, H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • B10.BR (H-$2A^{k}$, E^{k}), B10.A(5R) (H-$2A^{b}$, E^{b}) and B10.S(9R) (H-$2A^{s}$, E^{s}) mice immunized with rec gp160 showed a proliferative response to this peptide. • FVTIGKIGNMRQAHCNISRAKWNNTLKQIDSKL encompasses several murine Th epitopes including RAKWNNTLKQIDSKL and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (337–356)	gp120 (341–360 MN)	KWNDTLRQIVSKLKEQFKNK	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, Th1.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Epitope name 1989. • Hartley guinea pig were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 3/5 animals vaccinated with rec gp120 responded by DTH to this peptide, and 2/6 responded that were vaccinated with plasmid gp120 DNA.				
gp160 (339–359)	gp120 (340–359 89.6)	NNTLQQIVIKLREKFRNKTI	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 32. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 6/10 BALB/c mice tested, and in 4/10 CBA/J mice and was considered one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.			
gp160 (339–359)	gp120 (340–359 89.6)	NNTLQQIVIKLREKFRNKTI	Vaccine	mouse (H-2^k, H-2^d)	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** immunodominance. • Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI $>$ 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant. • Uniquely immunodominant sequences tended to be in the inner domain of the protein.			
gp160 (341–356)	gp120 (IIIB)	TLEQIVKKLREQFGNC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (342–361)	gp120 (342–361 IIIB)	LKQIASKLREQFGNNKTII-F?	HIV-1 infection	human	Geretti1994
	Epitope name G1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 6.0.				
gp160 (344–357)	gp120 (346–359)	QIVKKLREQFGNNK	HIV-1 infection	human	Krowka1990
	• Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (349–368)	gp120 (350–369 89.6)	LREKFRNKTIAFNQSSGGD	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 33. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 3/10 BALB/c mice tested, and in 5/10 CBA/J mice.			
gp160 (350–370)	gp120 (350–370 IIIB)	REQFGNNKTIIFKQSSGGD-PE?	HIV-1 infection	human	Geretti1994
	Epitope name G2. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, average SI = 3.2.			
gp160 (353–360)	gp120 (355–362 IIIB)	FGNNKTII	SHIV infection	macaque	Lekutis1997a
	• C3 region minimal epitope determined through fine epitope mapping. • Cell line was lost prior to confirmation of MHC requirements.				
gp160 (363–372)	gp120 (368–377 LAI)	QSSGGDPEIV	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (364–378)	gp120 (364–378 IIIB, B10)	SSGGKPEIVTHSFNC	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (369–383)	gp120 (369–383 IIIB, B10)	PEIVTHSFNCGGEFF	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (380–393)	gp120 (380–393 IIIB)	GEFFYCNSTQLFNS?	HIV-1 infection	human	Geretti1994
	Keywords immunodominance. **Epitope name** G4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Five peptides were recognized most frequently: C2 (aa 142-161), C3 (aa 152-171), C5 (aa 172-191), E5 (aa 272-291) and G4 (aa 380-393). The first three were in or near V2, the other two were proximal to the V3 and V4 loops. • 4/15 responders recognized this immunodominant peptide, average SI = 4.4.				
gp160 (381–395)	gp120 (IIIB)	EFFYCNTTQLFNNTW	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (392–411)	gp120 (392–411 IIIB)	NSTWFNSTWSTEGSNNTEG-S?	HIV-1 infection	human	Geretti1994
	Epitope name G5. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 9.3.				
gp160 (394–408)	gp120 (394–408 IIIB, B10)	TWFNSTWSTKGSNNT	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (396–411)	gp120 (IIIB)	FNNTWRLNHTEGTKGC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (399–413)	gp120 (399–413 IIIB, B10)	TWSTKGSNNTEGSDT	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (404–423)	gp120 (400–419 89.6)	GTNGTEGNDIITLQCRIKQI	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 38. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 8/10 BALB/c mice tested, and in 6/10 CBA/J mice, and was considered one of the 3 immunodominant peptides identified that were shared in both mouse strains: RRNIIGDIRQAHCNISRAKW, NNTLQQIVIKLREKFRNKTI, GTNGTEGNDIITLQCRIKQI.				
gp160 (404–423)	gp120 (400–419 89.6)	GTNGTEGNDIITLQCRIKQI	Vaccine	mouse ($H\text{-}2^k$, $H\text{-}2^d$)	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** immunodominance.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Promiscuous immunodominant epitopes in gp120 were mapped by overlapping peptides in CBA/J H-2^k and BALB/c H-2^d mice, and all were found to be in the outer domain, proximal to regions of structural disorder indicated by the crystal structure or by sequence divergence. • This peptide was recognized by 4/10 CBA/J and 6/10 BALB/c mice with SI $>$ 4, averaging 4.9 and 5.5 and is considered to be promiscuously immunodominant. • Uniquely immunodominant sequences tended to be in the inner domain of the protein.				
gp160 (405–420)	Env (1007)	SNNTVGNPIILPCRI	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the V4C4 region of 1007 (US, clade B) and was recognized by 13 hybridomas with Vβ usage Vβ 4, 7, 8.1, 8.2, 10, 12 and not determined – one of the Vβ 8.2 was shown to utilize Vα 2. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (410–429)	gp120 (410–429 PV22)	GSDTITLPCRIKQFINMWQE	HIV-1 infection	human (DR4)	Callahan1990
	• Synthetic peptides representing natural variants were used to test for recognition in the context DR4.				
gp160 (410–429)	gp120 (410–429 PV22)	GSDTITLPCRIKQFINMWQE	HIV-1 infection	human (DR4(Dw10))	Polydefkis1990
	• Human CD4+ T-cell clones lyse recombinant vaccinia virus-infected cells that synthesize envelope gp160.				
gp160 (412–431)	gp120 (412–431 IIIB)	DTITLPCRIKQIINMWQKV-G?	HIV-1 infection	human	Geretti1994
	Epitope name H2. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 5.7.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (416–431)	gp120 (IIIB)	LPCRIKQIINMWQEVY	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (418–436)	Env (417–435)	CRIKQIINMWQGVGKAMYA	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.				
gp160 (421–436)	gp120 (426–441 IIIB)	KQFINMWQEWGKAMYA		human	Furci1997
	• Epitope T1 variant: 9/11 exposed-uninfected individuals in this study had a proliferative response to a C5 peptide, but none reacted with this previously defined epitope. • IIIB position 435 listed as W in this epitope as opposed to V in the sequence.				
gp160 (421–436)	gp120 (428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Wasik2000
	Keywords responses in children, kinetics, Th1. **Epitope name** T1. • Th responses measured by IL-2 responses to P18 and T1 in HIV-1 infected infants were undetectable at less than 1 month of age, and remained low in children with AIDS symptoms, but increased with age in children with slowly progressive disease. • The kinetics and intensity of the CTL activity during the first year of life was related to the child's ability to make Th1 responses.				
gp160 (421–436)	gp120 (428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Wasik1997
	Keywords responses in children, Th1, Th2. **Epitope name** T1. • The breadth and intensity of the CTL response and the type of Th response was studied in seven rapidly progressing HIV-1+ infants. • IL-2 and γ IFN production from Th1 cells correlated with the CTLp frequency against HIV-1 Gag, Env, Nef and Pol. • IL-4 production from Th2 cells was inversely correlated with the CTLp frequency. • The HIV-1+ children with strong CTL responses had levels of anti-CD3 MAb induction of Th1 cells comparable to those of uninfected children.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	human	Berzofsky1988
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T1. • Proliferative response to T1 and T2 peptides in 14 immunized, uninfected humans.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	goat	Palker1989
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Epitope name** T1. • Goats immunized with peptides containing V3 type-specific neutralizing determinants coupled to T1.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Clerici1989
	Epitope name T1. • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Clerici1991a
	Epitope name T1. • Peptides stimulate Th cell function and CTL activity in similar patient populations.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	human	Clerici1991b
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T1. • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA		human	Clerici1992
	Epitope name T1. • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	mouse	diMarzo Veronese1994
	Vaccine *Vector/Type:* bacteriophage coat protein *Strain:* B clade MN *HIV component:* V3 • Epitope T1 was engineered into a filamentous bacteriophage coat protein, and the Th epitope stimulated Ab production to the V3 loop.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	chimpanzee	Haynes1993
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Epitope name** T1. • Hybrid T1-V3 peptide immunogenicity reduced when the fusogenic domain of gp41 was added.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Clerici1997
	Epitope name T1. • Used in a study of the influence of pentoxifylline on HIV specific T-cells.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA		human	Pinto1995
	Epitope name T1. • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers.				
gp160 (421–436)	gp160 (428–433 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection, HIV-1 exposed seronegative	human	Wasik1999
	Keywords immunodominance. **Epitope name** T1. • IL-2 responses associated with beta-chemokine expression were detectable at birth in the majority of uninfected infants born to HIV+ mothers, declining by age 6 months. • T1 peptide: In both uninfected and infected infants of HIV-positive mothers, responses to the T1 peptide were more frequent than responses to P18 (RIQRGPGRAFVTIGK) • T1 is a highly conserved epitope, whereas P18 has a higher mutation rate due to its location in the immunodominant V3 loop region.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Kaul1999
	Epitope name T1. • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]				
gp160 (421–436)	gp120 (MN)	KQIINMWQEVGKAMYA	HIV-1 infection, Vaccine	human	Bartlett1998
	Vaccine *Vector/Type:* peptide *Strain:* B clade MN **Epitope name** T1.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• C4-V3 PV (polyvalent HIV envelope synthetic peptide immunogen) consisted of T1 helper epitope presented in tandem with a V3 loop CTL epitope from one of four different North American strains. • This was a pilot phase I study involving vaccination of ten HIV-infected subjects who were HLA-B7-positive. • Enhanced lymphoproliferative response to peptide was observed in 5/8 vaccinees – increase in neutralizing antibody responses in 4/8 vacinees.				
gp160 (421–436)	gp120	KQIINMWQEVGKAMYA	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001a
	Keywords inter-clade comparisons, responses in children, mother-to-infant transmission. **Epitope name** T1. • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4. • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.				
gp160 (421–436)	gp120 (428–443 RF)	KQIINMWQEVGKAMYA	HIV-1 infection		deLorimier1994
	Keywords epitope processing. **Epitope name** T1. • Proton NMR spectroscopy was employed to analyze the solution conformation of a hybrid peptide, T1-SP10RF, in order to better understand the immunogenicity of its' T helper (KQIINMWQEVGKAMYA, CTRPNNNTRKSI), CTL (SITKGPGRVIYATG) and B-cell epitopes (RKSITKGPGRVIYATG). • As a free peptide, the T1 segment, a T-helper epitope is in an extended conformation with nascent helical conformation. It may form a beta strand in native gp120, and a nonnative conformation may account for the inability of free T1 peptide to elicit antibody responses, in contrast to the T1 segment in native gp120. It lacks random-coil conformations, and it is suggested that this may make the peptide less susceptible to complete proteolytic degredation, and be favored within epitopes.				
gp160 (421–436)	Env (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection, HIV-1 exposed seronegative		Clerici1993a
	Keywords mother-to-infant transmission. **Epitope name** T1. **Assay type** cytokine production. • Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected. • PBL from 10/21 of the mothers showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.				
gp160 (421–436)	Env (IIIB)	KQIINMWQEVGKAMYA	HIV-1 exposed seronegative		Clerici1994a
	Epitope name T1. **Assay type** cytokine production.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection. • Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.				
gp160 (421–436)	HIV-1 (IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection		Clerici1994b
	Epitope name T1. **Assay type** cytokine production. • IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.				
gp160 (421–436)	Env (428–443)	KQIINMWQEVGKAMYA	HIV-1 infection	human	Kuhn2001b
	Keywords responses in children, mother-to-infant transmission. **Epitope name** T1. **Assay type** proliferation. • T helper proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery. • The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	HIV-1 infection	human (DR)	Baier1995
	Epitope name T1. • Linked HIV-1 T1 and P18 peptides to anti-HLA-DR and anti-IgD Fab fragments to enhance uptake by antigen presenting cells and thus increase immunogenicity.				
gp160 (421–436)	Env (421–436 IIIB)	KQIINMWQEVGKAMYA	Vaccine	mouse (Ek)	Ahlers2001
	Vaccine *Vector/Type:* peptide *Strain:* modified B clade IIIB *HIV component:* Env **Keywords** binding affinity, Th1. **Epitope name** T1. **Assay type** cytokine production, Th support of CTL response. • BALB/c and A.AL were immunized with an Env-peptide vaccine construct containing the CTL epitope P18IIIB and a T helper epitope. • Substitution of Glu (wt) to Ala, kqiinmwqAvgkamya, caused increased affinity for MHC class II Ek. This resulted in the upregulation of CD40L in the responding Th cells, and shifted the response towards Th1. Increased Th responses stimulated DCs to produce higher levels of IL-12, and B7-1 and B7-2, thus enhance CTL responses. • The modified epitope, T1A, elicited stronger protection against increasing doses of viral challenge with vaccinia expressing HIV-1 IIIB gp120 compared to the wildtype epitope T1.				
gp160 (421–436)	gp120 (428–443 IIIB)	KQIINMWQEVGKAMYA	Vaccine	mouse (H-2^d)	Klinman1995
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Epitope name** T1.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Hybrid T1-V3 peptide activates IL-4 and IL-6 in a dose dependent manner.				
gp160 (421–436)	gp120 (428–443 IIIB, B10) **Epitope name** T1. • 1 of 2 functional epitopes identified using an amphipathic helix epitope prediction algorithm.	KQIINMWQEVGKAMYA	computer prediction	mouse (H-$2^{k, d, s}$)	Cease1987
gp160 (421–436)	gp120 (428–443 IIIB) **Vaccine** *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** T1. • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.	KQIINMWQEVGKAMYA	Vaccine	mouse (H-$2^{k, d, t4}$)	Hale1989
gp160 (421–436)	gp120 (428–443 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* B clade IIIB **Epitope name** T1. • first identified Th epitope in HIV. • Alanine at position 436 (instead of E in wild-type) enhances MHC binding and antigenicity of peptide by several orders of magnitude. • Vaccines with a CTL epitope linked to a more potent helper epitope yielded greatly enhanced CTL response relative to the wildtype helper epitope. • T1 peptide linked to CTL epitopes in four vaccine constructs used to immunize mice: KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTIGK, KQIINMWQEVGKAMYAPPISGQIRRIQRGPGRAFVTI, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTIGK, KQIINMWQAVGKAMYAPPISGQIRRIQRGPGRAFVTI.	KQIINMWQEVGKAMYA	Vaccine	mouse (H-2^{k})	Ahlers1997b
gp160 (421–436)	gp160 (428–443 IIIB) **Vaccine** *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • B10.BR (H-$2A^{k}$, E^{k}), B10.D2 (H-$2A^{d}$, E^{d}) and B10.S(9R) (H-$2A^{s}$, E^{s}) mice immunized with rec gp160 showed a proliferative response to this peptide. • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including KQIINMWQEVGKAMYA and is referred to as a "multideterminant region" or cluster peptide.	KQIINMWQEVGKAMYA	Vaccine	mouse (H-2^{k}, H-2^{s}, H-2^{d})	Berzofsky1991b, Berzofsky1991a
gp160 (421–436)	gp120 (428–443 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* B clade IIIB **Epitope name** T1. • C3H $H2^{k}$ mice were used for immunization in the study because H-2^{k} mice are particularly good T1 responders – T1 can be presented by $E\alpha E\beta^{k}$ but not $E\alpha E\beta^{b}$ – the nature of the T1 class II molecular interaction was thoroughly explored. • Alanine substitutions across peptide did not negatively affect MHC binding or effective presentation of epitope, except at three critical residues (432N, 435Q, 439K), however substitutions with larger side chains often diminished activity – only a few amino acids were found to be critical for class II interaction and for maintaining T-cell receptor specificity. • A gain in potency was observed when 436E was replaced with A, suggesting that substitutions in positions that interfere with binding might allow the design of a more potent vaccine.	KQIINMWQEVGKAMYA	Vaccine	mouse (H-2Eα Eβ^{k})	Boehncke1993
gp160 (421–444)	Env (gp160) (HIV-1 IIIB) **Vaccine** *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* Env *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), Montanide (ISA 51) **Keywords** mucosal immunity.	KQIINMWQEVGKAMYAPPI-SGQIR	Vaccine	macaque	Belyakov2001

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type proliferation. • Intrarectal vaccination with a Th and CTL peptide vaccine provided better protection against intrarectal challenge with pathogenic SHIV-Ku1 than subcutaneous administered vaccine. In some animals after the initial viremia, viral loads were diminished to undetectable levels in the blood and intestine, and CD4+ T cells were better preserved. • The CD4 T-cell proliferative response correlated with the level of the CTL response.				
gp160 (421–444)	gp160 (428–451 IIIB)	KQIINMWQEVGKAMYAPPI-SGQIR	HIV-1 infection, Vaccine	human, mouse (H-2^{k}, H-2^{b}, H-2^{s}, H-2^{d})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide. • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people. • This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-2A^{k}, E^{k}), B10.D2 mice (H-2A^{d}, E^{d}), B10.A(5R) mice (H-2A^{b}, E^{b}), and B10.S(9R) mice (H-2A^{s}, E^{s}) • IL-2 production in response to this peptide was observed in 73% (8/11) of asymptomatic HIV-infected individuals.				
gp160 (421–444)	gp120 (428–451 IIIB)	KQIIMNWQEVGKAMYAPPI-SGQIR	Vaccine	mouse (H2^{d})	Shirai1996a
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Epitope name** T1. • Linked to a CTL epitope from hepatitis C virus, induced CD4+ helper cells producing IL-2.				
gp160 (423–440)	gp120 (428–445)	FINMWQEVGKAMYAPPIS	HIV-1 infection	human	Caruso1997
	Keywords rate of progression. • As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71. • The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost. • This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.				
gp160 (424–438)	gp120 (424–438 IIIB, B10)	INMWQEVGKAMYAPP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (425–439)	gp160 (432–446 IIIB)	NMWQEVGKAMYAPPI	Vaccine	mouse (H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • B10.S(9R) (H-2A^{s}, E^{s}) mice immunized with rec gp160 showed a proliferative response to this peptide. • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including NMWQEVGKAMYAPPI and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (425–439)	gp120 (432–446 IIIB)	NMWQEVGKAMYAPPI	Vaccine	mouse (H-2^{t4})	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (426–441)	gp120 (IIIB)	MWQEVGKAMYAPPIGC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (430–444)	gp120 (437–451 IIIB)	VGKAMYAPPISGQIR	Vaccine	mouse (H-$2^{k, d, i5, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (430–444)	gp160 (437–451 IIIB)	VGKAMYAPPISGQIR	Vaccine	mouse (H-2^{k}, H-2^{b}, H-2^{s}, H-2^{d})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^{k}$, E^{k}), B10.D2 mice (H-$2A^{d}$, E^{d}), B10.A(5R) mice (H-$2A^{b}$, E^{b}), and B10.S(9R) mice (H-$2A^{s}$, E^{s}) • KQIINMWQEVGKAMYAPPISGQIR encompasses several murine Th epitopes including VGKAMYAPPISGQIR and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (430–453)	gp120 (430–453)	VGKAMYAPPISGQIRCSSN-ITGLL	Vaccine	mouse (H-2^{b})	Sjolander1996
	Vaccine *Vector/Type:* protein *HIV component:* gp160 **Keywords** epitope processing. • Study demonstrates that T-cell determinants from glycoproteins can depend on the glycosylation of the protein. • Peptide stimulation of an *in vitro* proliferative response required *in vivo* priming with glycosylated protein. • Local glycosylation sites thought not to be part of the epitope, but may be important for epitope processing.				
gp160 (432–451)	gp120 (432–451 IIIB)	KAMYAPPISGQIRCSSNIT-G?	HIV-1 infection	human	Geretti1994
	Epitope name H4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 1/15 responders recognized this peptide, SI = 6.3.				
gp160 (433–447)	Env (UG92005)	AMYAPPIAGLIQCSS	Vaccine	mouse (H-2 IA^{b})	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This epitope is located in the C4 region of UG92005 (UG, clade D) and was recognized by ten hybridomas with Vβ usage Vβ 6, 8.1, 8.2, 13, 14 and not determined – among the ND Vβ set, three Vαs were identified, Vα 2, 8, and 11. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (436–451)	gp120 (IIIB)	APPIGGQISCSSNITY	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (438–460)	gp120 (443–465 NL43)	PISGQIRCSSNITGLLLTR-DGGN	Vaccine	human	Sitz1999
	Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp120, gp160 • There was a great breadth of proliferative response to env peptides in 19 HIV-1 infected rgp160 and 17 HIV-1 infected rgp120 vaccine recipients. • Close to 40% of vaccinees had a stimulation index of greater than 5 to this peptide.				
gp160 (439–448)	gp120 (151–160 W6.ID)	IGGQIRCSSN	Vaccine	human	Jones1999
	Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120 *Adjuvant:* MPL-SE adjuvant, QS21 • HIV-1 specific T-cell lines isolated from an HIV seronegative volunteer vaccinated with rgp120 and a QS21/MPL adjuvant. • One T-cell line responds to two overlapping peptides, and the region of overlap is IGGQIRCSSN. • The IIIB version of the first reactive peptide, EVGKAMYAPPIGGQIRCSSN, has a single substitution and induces proliferation as well as the original W61D peptide: evgkamyappiSgqircssn.				
gp160 (446–461)	gp120 (IIIB)	SSNITGLLLTRDGGTC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (452–471)	gp120 (452–471 IIIB)	LLLTRDGGNSNNESEIFRP-G?	HIV-1 infection	human	Geretti1994
	Epitope name I1. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 3.5.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (456–470)	gp120 (IIIB)	RDGGTNVTNDTEVFRC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (459–473)	gp120 (459–473 IIIB, B10)	GNSNNESEIFRPGGG	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (468–483)	gp120 (466–481)	FRPGGGDMRDNWRSEL	HIV-1 infection	human	Krowka1990
	• Conjugation of HIV peptides to liposomes and rIL-2 stimulation may enhance cell-mediated responses.				
gp160 (472–491)	gp120 (472–491 IIIB)	GGDMRDNWRSELYKYKVVK-I?	HIV-1 infection	human	Geretti1994
	Epitope name I3. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 2/15 responders recognized this peptide, average SI = 7.2.				
gp160 (474–488)	gp120 (474–488 IIIB, B10)	DMRDNWRSELYKYKV	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (476–490)	gp120 (483–497 IIIB)	RDNWRSELYKYKVVK	Vaccine	mouse (H-$2^{d, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (476–490)	gp160 (483–497 IIIB)	RDNWRSELYKYKVVK	Vaccine	mouse (H-2^{k}, H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in B10.BR mice (H-$2A^{k}$ and B10.S(9R) mice (H-$2A^{s}$, E^{s}) • RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including RDNWRSELYKYKVVK and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (476–499)	gp160 (483–506 IIIB)	RDNWRSELYKYKVVKIEPL-GVAPT	HIV-1 infection, Vaccine	human, mouse (H-2^{k}, H-2^{b}, H-2^{s}, H-2^{d})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide. • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people. • This cluster peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^{k}$, E^{k}), B10.D2 mice (H-$2A^{d}$, E^{d}), B10.A(5R) mice (H-$2A^{b}$, E^{b}), and B10.S(9R) mice (H-$2A^{s}$, E^{s})				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• IL-2 production in response to this peptide was observed in 52% (14/27) of asymptomatic HIV-infected individuals.				
gp160 (479–498)	gp120 (481–500 MN)	WRSELYKYKVVTIEPLGVAP	Vaccine	guinea pig	Chattergoon2002
	Vaccine *Vector/Type:* DNA, protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** vaccine-specific epitope characteristics, Th1. **Epitope name** 2013. • Hartley guinea pigs were intradermally injected with either recombinant protein or plasmid expressed gp120 and monitored for delayed type hypersensivity (DTH) responses after vaccination, which are related to Th1 T-cell responses. CFA did not augment responses in animals vaccinated with plasmid. • A total of 7 gp120 peptides elicited a delayed type hypersensivity (DTH) response after vaccination, out of a set of 60 overlapping peptides that spanned gp120. The vaccine delivery system, DNA versus rec protein, resulted in the recognition of distinct peptides. • 0/5 animals vaccinated with rec gp120 responded by DTH to this peptide, while 6/6 vaccinated with plasmid gp120 DNA responded.				
gp160 (482–501)	gp120 (482–501 IIIB)	ELYKYKVVKIEPLGVAPTKA	Vaccine	macaque	Lekutis1997b
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Env • HIV-1 env DNA vaccine induced Th cell response to this epitope in a rhesus monkey. • Epitope was recognized by both monkeys used in this study.				
gp160 (482–501)	gp120 (482–501 IIIB)	ELYKYKVVKIEPLGVAPTK-A?	HIV-1 infection	human	Geretti1994
	Epitope name I4. • Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 3/15 responders recognized this peptide, average SI = 6.0.				
gp160 (483–502)	gp120 (480–499 89.6)	LYKYKVVRIEPIGVAPTRAK	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** epitope processing, immunodominance. **Epitope name** Peptide 46. **Donor HLA** H-2k, H-2d. • Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in 7/10 BALB/c mice tested, and in only 1/10 CBA/J mice.				
gp160 (484–496)	gp120 (484–496 HXB2)	YKYKVVKIEPLGV	Vaccine	macaque (DR*W201)	Lekutis1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB2 *HIV component:* Env • Variants of this epitope with substitutions at position 490(K) retained ability to bind to MHC class II, but failed to induce proliferation/cytokine secretion in HIV-1 env-specific CD4+ Th cells. • The modified peptide antagonized the wildtype peptide-induced proliferative response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (484–498)	gp120 (484–498 IIIB, B10)	YKYKVVKIEPLGVAP	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (484–499)	gp120 (492–506 IIIB)	CKYKVVKIEPLGVAPT	Vaccine	mouse (H-$2^{d, k, t4, i5}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160				
	• Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (485–499)	gp160 (492–506 IIIB)	KYKVVKIEPLGVAPT	Vaccine	mouse (H-2^{k}, H-2^{b}, H-2^{s}, H-2^{d})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA)				
	• This peptide elicited proliferative responses in cells from all H-2 haplotypes tested: B10.BR mice (H-$2A^{k}$, E^{k}), B10.D2 mice (H-$2A^{d}$, E^{d}), B10.A(5R) mice (H-$2A^{b}$, E^{b}), and B10.S(9R) mice (H-$2A^{s}$, E^{s})				
	• RDNWRSELYKYKVVKIEPLGVAPT encompasses several murine Th epitopes including KYKVVKIEPLGVAPT and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (485–500)	gp120 (IIIB)	KYKVIKIEPLGIAPTC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*.				
	• Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (486–494)	gp120 (486–494 IIIB)	YKVVKIEPL	SHIV infection	macaque (DRB*W201)	Lekutis1997a
	• C5 region minimal epitope determined through fine epitope mapping.				
gp160 (487–512)	gp120 (494–518 IIIB)	KVVKIEPLGVAPTKAKRRV-VQREKRC	Vaccine	mouse	Goodman-Snitkoff1990
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB				
	• Identification of putative Th epitopes that stimulate an antibody response in peptide immunized mice.				
gp160 (492–512)	gp120 (492–512 IIIB)	EPLGVAPTKAKRRVVQREK-RA?	HIV-1 infection	human	Geretti1994
	Epitope name I5.				
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools.				
	• After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders.				
	• IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation.				
	• 1/15 responders recognized this peptide, SI = 4.9.				
gp160 (493–511)	gp120 (490–508 89.6)	PIGVAPTRAKRRTVQREKR	Vaccine	mouse	Dai2001
	Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)				
	Keywords epitope processing, immunodominance.				
	Epitope name Peptide 47.				
	Donor HLA H-2k, H-2d.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Helper T-cell proliferative responses to gp120 vaccines in 2 mouse strains, CBA/J and BALB/c, were mapped using 47 overlapping peptides that span gp120. Promiscuously immunodominant peptides were identified in both mice strains that were located in the outer domain of gp120 and were associated with regions of local structural disorder in proximal N-terminal segments, suggesting 3-D protein structure influences Th antigen processing and the frequency of immunogenic sequences. • This peptide was reactive in only 2/10 BALB/c mice tested, and in 8/10 CBA/J mice.				
gp160 (499–511)	gp120 (IIIB)	TKAKRRVVEREKR	in vitro stimulation or selectio	human (DR)	Wilson1997b
	• Thought to be a mimic of a HLA class II DR β chain variable region. • Response to this epitope may cause a breakdown of self-tolerance. • Presentation of epitope induced autoreactive T-cell lines in PBMC from uninfected donors. • Suppression of proliferation to soluble antigens by the CD8+ fraction of TKAKRRVVEREKR stimulated T-cells was observed.				
gp160 (499–519)	gp41 (MN)	TKAKRRVVQREKRAAIGALF	HIV-1 infection	human	Malhotra2003
	Keywords HAART, acute infection. **Epitope name** TF20. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy. • This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintainted in Env.				
gp160 (519–543)	Env (519–543)	FLGFLGAAGSTMGAASLTL-TVQARC	Vaccine	macaque	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice, and in rhesus monkeys. • Proliferative response to this peptide was observed in 3/3 immunized rhesus monkeys.				
gp160 (519–543)	Env (519–543)	FLGFLGAAGSTMGAASLTL-TVQARQ	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.				
gp160 (519–543)	gp41 (519–543)	FLGFLGAAGSTMGAASLTL-TVQARC	Vaccine	mouse (H-$2^{bxk, sxd}$)	Sastry1991
	Vaccine *Vector/Type:* peptide • Peptides induced T-cell proliferative response to immunizing peptide and to gp160.				
gp160 (547–561)	gp41 (547–561 IIIB, B10)	GIVQQQNNLLRAIEA	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (562–576)	gp41 (562–576 IIIB, B10)	QQHLLQLTVWGIKQL	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (570–589)	gp41 (MN)	VWGIKQLQARVLAVERYLKD	HIV-1 infection	human (DR)	Malhotra2003
	Epitope name VD20. **Assay type** cytokine production, proliferation, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining. • 92 acutely or early HIV infected subjects were tested for Env- and Gag-specific Th responses. There was an overall low probability of detecting HIV-1-specific Th responses, Env responses were rare and (5%) and only detected very early in infection, probably reflecting a low frequency of response and impaired lymophoproliferative capacity, not viral escape. Gag-specific Th responses were observed more frequently (16%), were found throughout the acute and early infection phases, and predominated after ARV therapy. • This epitope is one of six Env-specific Th responses detected in one patient 11 days post-infection that were studied in detail. The CD4+ clones showed MHC-restricted cytotoxicity and secreted high levels of cytokines when stimulated. These Th reponses were not detected at subsequent time points, despite the Env specific Th cells being maintained as detected by TCR clonal transcripts, and the epitope sequence being maintainted in Env. • This peptide showed promiscuous binding to DRB1*0101, DRB1*1101, DRB1*1302, DRB1*0701, DRB1*0801 DRB4*0101 DRB5*01.				
gp160 (572–591)	gp41 (572–591)	GIKQLQARILAVERYLKDQQ	Vaccine	mouse (H-$2^{d, b}$)	Brown1995
	Vaccine *Vector/Type:* peptide • This peptide was a good immunogen in BALB/c and CBA mice, producing a strong proliferative response. • At least one of the four residues GIKQ enhances stimulation, and in CBA mice these residues influence the ability to prime T-cells *in vivo*. • QLQARILAVERY stimulated the greatest *in vitro* T-cell response. • VERYLKDQQ was the minimal reactive sequence recognized by a T-cell line.				
gp160 (576–591)	gp41 (576–591)	LQARILAVERYLKDQQ	Vaccine	mouse (H-$2^{d, b}$)	Brown1995
	Vaccine *Vector/Type:* peptide • This peptide was a poor immunogen in BALB/c and CBA mice used in this experiment, producing a weak proliferative response.				
gp160 (578–608)	gp41 (585–615 IIIB)	ARILAVERYLKDQQLLGIW-GCSGKLICTTAV	Vaccine	mouse	Goodman-Snitkoff1990
	Vaccine *Vector/Type:* peptide • Identification of putative Th epitopes that can stimulate an antibody response in peptide immunized mice.				
gp160 (579–601)	gp41 (579–601)	RILAVERYLKDQQLLGGIW-GCSGK	Vaccine	mouse (H-$2^{d, b}$)	Brown1995
	Vaccine *Vector/Type:* peptide • This peptide was a good immunogen in BALB/c and CBA. • This peptide produced a strong Th response in both mice strains which was more responsive towards GIKQLQARILAVERYLKDQQ and LQARILAV-ERYLKDQQ than to immunizing peptide.				
gp160 (579–604)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWG-CSGKLIC	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (586–597)	Env (586–598)	YLRDQQLLGIWG	HIV-1 infection	human, chimpanzee	Nehete1998b
	• HIV-infected chimpanzees and HIV-positive patients show positive proliferative responses to multiple peptides from five conserved regions of the HIV-1 Env.				
gp160 (586–598)	Env (586–598)	YLRDQQLLGIWGC	Vaccine	macaque, mouse	Nehete1993
	Vaccine *Vector/Type:* peptide • Synthetic peptide derived from conserved region of the HIV-1 envelope that stimulates a proliferative response in mice. • Proliferative response to this peptide was observed in 1/3 immunized rhesus monkeys, with a weak transient response in the other two.				
gp160 (593–604)	gp41 (593–604 IIIB)	LGIWGCSGKLIC	HIV-1 infection	human	Bell1992
	• Elicits T-cell proliferation and B cell responses, but only during the asymptomatic phase of HIV infection.				
gp160 (593–604)	gp41 (598–609 LAV-1)	LGLWGCSGKLIC	Vaccine	mouse ($H2^d$)	Schrier1988
	• Murine T-dependent B-cell response – 7/29 had a proliferative response to this peptide.				
gp160 (594–603)	gp41 (594–603 IIIB)	GIWGCSGKLI	HIV-1 infection	human	Kelleher1998b
	• Epitope documented as a "previously described' epitope [Bell1992], but in Bell *et al.* it was described as gp41(594-603 IIIB), LGIWGCSGKLIC. • Immunization with a p24-VLP virus-like particle did not significantly impact CD4+ lymphocyte count, viral load, or p24 antibody titre. • Immunization with p24-VLP did not increase the proliferative response to this gp41 epitope, however, there was a modest, short-lived increased proliferative response to p24.				
gp160 (594–604)	gp41 (consensus)	GIWGCSGKLIC	HIV-1 infection	human	Mutch1994
	• Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people.				
gp160 (598–609)	gp41 (603–614 LAI)	CSGKLICTTAVP	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (604–615)	gp41 (609–620 LAI)	CTTAVPWNASWS	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (606–620)	gp41 (1035)	TNVPWNASWSNKSLE	Vaccine	mouse (Class II I Ab)	Zhan2003
	Vaccine *Vector/Type:* vaccinia prime with gp120 boost *Strain:* B clade 1035 *HIV component:* Env *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** epitope processing, vaccine-induced epitopes, escape, TCR usage. **Assay type** T-cell Elispot. • A very narrow Th response was stimulated in C57BL/6 mice vaccinated with vaccinia expressed HIV-1 env clone 1035, to the peptide PKVSFEPIPIHYCAP, located in the C2 region of gp120. The only other peptide recognized using Elispot on Env overlapping peptides to test vaccine responses in the mice was this one: TNVPWNASWSNKSLE, located in gp41.				
gp160 (606–620)	gp41 (UG92005)	TNVPWNASWSNKSLE	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This gp140 epitope of UG92005 (UG, clade D) was recognized by five hybridomas with Vβ usage Vβ 8.1, 14 and not determined – one of the Vβ 8.1 was shown to utilize Vα 8. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				
gp160 (609–616)	gp41 (consensus)	PWNASWSN	HIV-1 infection	human	Mutch1994
	• Core region of peptides that can stimulate proliferative responses from seronegative and seropositive people.				
gp160 (611–620)	gp41 (1007, UG92005)	NASWSNKSLE	Vaccine	mouse (H-2 IA^b)	Surman2001
	Vaccine *Vector/Type:* DNA, protein, vaccinia *Strain:* B clade 1007, D clade UG92005 *HIV component:* gp140 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** inter-clade comparisons, epitope processing, TCR usage. • This gp41 epitope is conserved in 1007 (US, clade B) and UG92005 (UG, clade D) and was recognized by two hybridomas from two different mice that were vaccinated with different clades – the Vβ usage was Vβ 4 and 14. • The epitope described here is the region of overlap of two 15 mers that were both able to stimulate IL-2 production from the hybridoma (T[TN]VPWNASWSNKSLE and NASWSNKSLEQIWNN) – the only difference between 1007 and UG92005 for these two proteins is that 1007 has a T and UG92005 has an N in the second position of the first peptide. • C57BL/6 mice were immunized with a prime-boost strategy involving three HIV-1 Env antigens: Mice were primed with DNA given i.m., 3-4 weeks later boosted with VV, and 3-4 weeks later boosted again with purified protein in Freund's adjuvant. • The vaccinia construct is a pSC11-based VV vector with the first 38 amino acids contributed by BH10 and the rest of gp120 and gp41 by the vaccine strain, the DNA construct is in the pJW4303 vector with a CMV promotor, and the purified protein is expressed from the pJW4303 vector transfected into CHO-K1 cells. • Ten days after the final boost, hybridomas were made and tested for IL-2 production using either B6 spleen cells or H-2 IA^b transfected L cells as targets and Vβ usage was determined. • Mice were immunized with an Env from either one of two clades: HIV-1 1007, a clade B strain isolated from an individual from Memphis Tennesee, and HIV-1 92UG005, a clade D vaccine isolated from Uganda in 1992 through the WHO. • 80 unique clonotypes were characterized from six mice. • H-2 IA^b restricted T-helper epitopes were concentrated in 5 distinct regions within the Env sequence (2 clonotype responses in V2, 26 in C2, 22 in V3, 23 in V4C4, and 7 in gp41). • Epitope hotspots tended to be proximal to heavily glycosylated regions of the Env sequence, in exposed, non-helical strands of the protein. The non-uniform localization may be influenced by differential antigen processing and the glycosylation site proximity may allow binding to lectins and promote trafficking through processing pathways.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (614–629)	gp41 (IIIB)	WSNKSLEDIWDNMTWC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (634–649)	gp41 (IIIB)	EIDNYTNTIYTLLEEC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (647–661)	gp41 (647–661 IIIB, B10)	EESQNQQEKNEQELL	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (650–662)	gp41 (655–667 LAI)	QNQQEKNEQELLE	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (667–681)	gp41 (667–681 IIIB, B10)	ASLWNWFNITNWLWY	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (682–696)	gp41 (682–696 IIIB, B10)	IKLFIMIVGGLVGLR	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				
gp160 (724–745)	gp41 (731–752)	PRGPDRPEGIEEEGGERDR-DRS	Vaccine	mouse (H-2^{k})	McInerney1999
	Vaccine *Vector/Type:* peptide in cowpea mosaic virus (CPMV) *HIV component:* gp41 *Adjuvant:* Quillaja saponin (Quil-A) **Keywords** Th1. • A gp41 peptide was expressed in a cowpea mosaic virus (CPMV) and mice were vaccinated with a purified chimeric particle – out of five adjuvants tested, only Quil A could stimulate anti-gp41 antibodies and an *in vitro* proliferative response. • The antibodies were predominantly IgG2a, suggesting a Th1 response.				
gp160 (732–744)	gp41 (737–749 LAI)	GIEEEGGERDRDR	HIV-1 infection	human	Schrier1989
	• Stimulates T-cell proliferation in HIV-infected donors.				
gp160 (780–794)	gp41 (787–801 IIIB)	RIVELLGRRGWEALK	Vaccine	mouse (H-$2^{d, k, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (780–794)	gp160 (787–801 IIIB)	RIVELLGRRGWEALK	Vaccine	mouse (H-2^{k}, H-2^{d}, H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^{k}$, E^{k}), B10.D2 mice (H-$2A^{d}$, E^{d}), and B10.S(9R) mice (H-$2A^{s}$, E^{s}) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including RIVELLGRRGWEALK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^{k} mice.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (780–813)	gp160 (787–820 IIIB)	RIVELLGRRGWEALKYWWN-LLQYWSQELKNSAVS	HIV-1 infection, Vaccine	mouse (H-2^{k})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide. • Six multideterminant region cluster peptides were evaluated Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people. • This cluster peptide elicited proliferative responses in cells from only B10.BR mice (H-2A^{k}, E^{k}), and not from B10.D2 mice (H-2A^{d}, E^{d}), B10.A(5R) mice (H-2A^{b}, E^{b}), or B10.S(9R) mice (H-2A^{s}, E^{s}) • IL-2 production in response to this peptide was observed in 59% (17/29) of asymptomatic HIV-infected individuals.			
gp160 (794–808)	gp41 (801–815 IIIB)	KYWWNLLQYWSQELK	Vaccine	mouse (H-2^{k})	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (794–808)	gp160 (801–815 IIIB)	KYWWNLLQYWSQELK	Vaccine	mouse (H-2^{k}, H-2^{d}, H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^{k}, E^{k}), B10.D2 mice (H-2A^{d}, E^{d}), and B10.S(9R) mice (H-2A^{s}, E^{s}) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including KYWWNLLQYWSQELK and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^{k} mice.				
gp160 (799–813)	gp41 (806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	mouse (H-2$^{k, d, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (799–813)	gp41 (806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	mouse (H-2$^{k, d, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (799–813)	gp160 (806–820 IIIB)	LLQYWSQELKNSAVS	Vaccine	mouse (H-2^{k}, H-2^{d}, H-2^{s})	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^{k}, E^{k}), B10.D2 mice (H-2A^{d}, E^{d}), and B10.S(9R) mice (H-2A^{s}, E^{s}) • RIVELLGRRGWEALKYWWNLLQYWSQELKNSAVS encompasses several murine Th epitopes including LLQYWSQELKNSAVS and is referred to as a "multideterminant region" or cluster peptide, but the longer peptide only stimulates cells from H-2^{k} mice.				
gp160 (814–829)	gp41 (IIIB)	WLNATAIAVTEGTDRC	in vitro stimulation or selectio	human	Manca1995b
	• Peptide stimulation of PBMC from non-infected individuals *in vitro*. • Peptide priming does not always induce T-cells that recognize whole protein.				
gp160 (821–835)	gp41 (828–842 IIIB)	AVAEGTDRVIEVVQG	Vaccine	mouse (H-2^{k})	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (821–835)	gp160 (828–842 IIIB)	AVAEGTDRVIEVVQG	Vaccine	mouse (H-2^k, H-2^b, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-2A^k, E^k), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s) • AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes including AVAEGTDRVIEVVQG and is referred to as a "multideterminant region" or cluster peptide.				
gp160 (821–838)	gp41 (827–843)	YVAEGTDRVIEVVQGACR	HIV-1 infection	human	Caruso1997
	Keywords rate of progression. • As HIV-1-infected individuals progress to disease, T-cells show reduced ability to proliferate in response to HIV antigen, but retain the ability to express the activation antigens CD25 and CD71. • The ability to express activation markers in response to HIV is retained, but the response to tetanus toxoid recall antigen is lost. • This study investigated CD25 and CD71 expression in PBMC from patients at various stages of progression, measuring the response to *in vitro* stimulation by peptide cocktail containing four antigenic Env peptides, or p17 and p24.				
gp160 (821–853)	gp160 (828–860 IIIB)	AVAEGTDRVIEVVQGAYRA-IRHIPRRIRQGLER	HIV-1 infection, Vaccine	human, mouse (H-2^k, H-2^b, H-2^s, H-2^d)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • AVAEGTDRVIEVVQGAYRAIRHIPRRIRQGLER encompasses several murine Th epitopes and is referred to as a "multideterminant region" or cluster peptide. • Six multideterminant region cluster peptides were evaluated for Th responses in different MHC/HLA backgrounds after vaccination of mice with gp160, or in infected people. • This cluster peptide elicited proliferative responses in cells from all four MHC types tested: B10.BR mice (H-2A^k, E^k), B10.D2 mice (H-2A^d, E^d), B10.A(5R) mice (H-2A^b, E^b), and B10.S(9R) mice (H-2A^s, E^s) • IL-2 production in response to this peptide was observed in only 8% (1/12) of asymptomatic HIV-infected individuals.				
gp160 (827–835)	gp41 (834–842 IIIB)	DRVIEVVQG	Vaccine	mouse (H-2^k)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Suggested H-2^k epitope based on region of overlap.				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	macaque	Hosmalin1991
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** TH4. • Peptide priming to induce T-cell help enhances antibody response to gp160 immunization. • Called Th4.1 and TH4.				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	HIV-1 infection	human	Clerici1997
	Epitope name TH4. • used in a study of the influence of pentoxifylline on HIV specific T-cells.				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR		human	Pinto1995
	Epitope name TH4. • CTL activity analyzed in parallel with Th reactivity in exposed but uninfected health care workers. • Called Th4.1 and TH4.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (827–841)	gp41 (834–848 IIIB) **Epitope name** TH4. • Peptides stimulate Th cell function and CTL activity in similar patient populations. • Called Th4.1 and TH4.	DRVIEVVQGAYRAIR	HIV-1 infection	human	Clerici1991a
gp160 (827–841)	gp41 (834–848 IIIB) **Vaccine** *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** TH4. • Immunizing uninfected individuals with rgp160 results in stronger Th response than does natural infection. • Called Th4.1 and TH4.	DRVIEVVQGAYRAIR	Vaccine	human	Clerici1991b
gp160 (827–841)	gp41 (834–848 IIIB) **Epitope name** TH4. • Cell-mediated immune response to HIV-1 peptides in HIV-1 exposed seronegative men. • Called Th4.1 and TH4.	DRVIEVVQGAYRAIR		human	Clerici1992
gp160 (827–841)	gp41 (834–848 IIIB) **Epitope name** TH4. • IL-2 production detection of Th lymphocytes from asymptomatic HIV-positive individuals. • Called Th4.1 and TH4.	DRVIEVVQGAYRAIR	HIV-1 infection	human	Clerici1989
gp160 (827–841)	gp41 (834–848 IIIB) **Epitope name** TH4. • Kenyan sex workers that remained seronegative were found to frequently have HIV-env peptide specific Th responses detected by an IL-2 assay (11/20 cases) and mucosal genital tract anti-HIV IgA (16/21 cases) • Helper epitopes used in this study were noted to be previously described [Clerici1989], and were not explicitly described in [Kaul1999]	DRVIEVVQGAYRAIR	HIV-1 infection	human	Kaul1999
gp160 (827–841)	gp41 **Keywords** inter-clade comparisons, responses in children, mother-to-infant transmission. **Epitope name** TH4, Th4.1. • In a S. African perinatal transmission study, 33% (33/86) of cord blood samples from infants with seropositive mothers produced T-helper responses (measured by a bioassay measuring IL2 production in a murine cell line and confirmed with a proliferation assay) against a peptide cocktail containing Th epitopes P18 MN, P18 IIIB, T1, T2, and TH4. • The mothers were predominantly infected with subtype C, but the T help response was detectable in a number of cord blood samples despite using peptides based on B subtype reagents. • 3/33 infants with cord blood T help responses to Env were infected *in utero*, 2/33 were lost to follow up, and 28/33 were not infected. 6/53 of the infants with cord blood that was unresponsive to Env peptide stimulation were infected before delivery, and 8/47 contracted HIV intrapartum or via breast-feeding. • Measurable HIV specific T help responses elicited in the immunologically immature newborn, possibly in response to *in utero* exposure, are associated with a protective natural immunity that helps block mother-infant transmission of HIV-1.	DRVIEVVQGAYRAIR	HIV-1 infection, HIV-1 exposed seronegative	human	Kuhn2001a
gp160 (827–841)	Env (834–848 IIIB) **Keywords** mother-to-infant transmission. **Epitope name** TH4.1.	DRVIEVVQGAYRAIR	HIV-1 infection, HIV-1 exposed seronegative		Clerici1993a

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type cytokine production. • Cord blood samples in 8/23 infants with HIV+ mothers showed IL-2 production in response to peptides from HIV-1 gp1260, demonstrating that Th cell priming to HIV env determinants can occur in utero. HIV-specific Th immunity in utero may be protective, as none of the 8 with HIV-1 specific Th activity became infected, while 3/15 infants with no detectable Th activited were infected. • PBL from 10/21 of the mother showed HIV-1 specific Th activity through IL-2 production in response to Env peptides.				
gp160 (827–841)	Env (IIIB)	DRVIEVVQGAYRAIR	HIV-1 exposed seronegative		Clerici1994a
	Epitope name TH4.1. **Assay type** cytokine production. • Six of eight HIV-exposed health care workers had transient HIV-specific T-helper responses after percutaneous exposure to HIV, responding to two or more Env peptides among the set T1, T2, Th4.1, P18IIIB and P18MN. Responses were lost after 12-56 weeks. The HIV-specific Th responses occurred without seroconversion or PCR evidence for infection. • Six of the eight HIV-exposed individuals responded to two or more peptides, whereas, only one individual exposed to HIV-negative blood responded to one peptide.				
gp160 (827–841)	HIV-1 (IIIB)	DRVIEVVQGAYRAIR	HIV-1 infection		Clerici1994b
	Epitope name TH4.1. **Assay type** cytokine production. • IL-10-specific mRNA was upregulated in PBMC from asymptomatic, HIV-infected (HIV+) patients, and was particularly high in those with severely compromised Th cells function. Th response to HIV peptides *in vitro* could be restored by IL-10 Ab.				
gp160 (827–841)	Env (834–848)	DRVIEVVQGAYRAIR	HIV-1 infection	human	Kuhn2001b
	Keywords responses in children, mother-to-infant transmission. **Epitope name** TH4-1. **Assay type** proliferation. • Th proliferative responses in cord blood at delivery to a cocktail of HIV envelope peptides were infrequent (1/41) among infants whose HIV-positive mothers received antiretroviral prophylaxis at delivery to prevent transmission. Responses were 10 times more frequent among infants of HIV-seropositive women who had no antiretroviral treatment (7/29). Reductions of HIV-specific responses occurred despite persistance of detectable HIV RNA in the mothers at delivery. • The reduction of Th responses in newborns raises the possibility that anti-retrovial exposure during pregnancy may block subsequent immune protection. The authors point two relevant citations that showed ARV exposed infants had a more rapid course of progression (Kuhn *et al.*, JID 182:104 (2000)), but were at no greater risk of infection due to subsequent breast feeding (Ditrame *et al.*, Lancet 354:2050 (1999)).				
gp160 (827–841)	gp41 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	mouse (H-$2^{k, i5}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 **Epitope name** TH4. • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types. • Called Th4.1 and TH4.				
gp160 (827–841)	gp160 (834–848 IIIB)	DRVIEVVQGAYRAIR	Vaccine	mouse (H-2^k, H-2^b)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k) and B10.A(5R) mice (H-$2A^b$, E^b)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (827–853)	Env (HIV-1 IIIB)	DRVIEVVQGAYRAIRHIPR-RIRQGLER	Vaccine	macaque	Belyakov2001
	Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB, SIV *HIV component:* Env, Gag, Pol *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72), Montanide (ISA 51) **Keywords** mucosal immunity. **Assay type** proliferation. • Different HIV strains were used for different regions: env HIV-1 IIIB, gag SIV, pol SIV • Intrarectal vaccination with a Th and CTL peptide vaccine provided better protection against intrarectal challenge with pathogenic SHIV-Ku1 than subcutaneous administered vaccine. In some animals after the initial viremia, viral loads were diminished to undetectable levels in the blood and intestine, and CD4+ T cells were better preserved. • The CD4 T-cell proliferative response correlated with the level of the CTL response.				
gp160 (829–843)	gp160 (836–850 IIIB)	VIEVVQGAYRAIRHI	Vaccine	mouse (H-2^k, H-2^b)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k) and B10.A(5R) mice (H-$2A^b$, E^b)				
gp160 (834–841)	gp41 (841–848 IIIB)	QGAYRAIR	Vaccine	mouse (H-2^{i5})	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Suggested H-2^k epitope based on region of overlap.				
gp160 (834–848)	gp41 (841–855 IIIB)	QGAYRAIRHIPRRIR	Vaccine	mouse (H-$2^{d, t4, i5}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (834–848)	gp160 (841–855 IIIB)	QGAYRAIRHIPRRIR	Vaccine	mouse (H-2^k, H-2^b, H-2^d, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.A(5R) mice (H-$2A^b$, E^b), B10.D2(H-$2A^d$, E^d), and B10.S(9R) mice (H-$2A^s$, E^s)				
gp160 (839–848)	gp41 (846–855 IIIB)	AIRHIPRRIR	Vaccine	mouse (H-$2^{d, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Suggested H-$2^{d,t4}$ epitope based on region of overlap.				
gp160 (839–853)	gp41 (846–860 IIIB)	AIRHIPRRIRQGLER	Vaccine	mouse (H-$2^{d, t4}$)	Hale1989
	Vaccine *Strain:* B clade IIIB *HIV component:* gp160 • Six multideterminant helper T-cell regions are recognized by mice of three or four MHC types.				
gp160 (839–853)	gp160 (828–842 IIIB)	AIRHIPRRIRQGLER	Vaccine	human, mouse (H-2^k, H-2^b, H-2^s)	Berzofsky1991b, Berzofsky1991a
	Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* Complete Freund's Adjuvant (CFA) • This peptide elicited proliferative responses in cells from B10.BR mice (H-$2A^k$, E^k), B10.A(5R) mice (H-$2A^b$, E^b), and B10.S(9R) mice (H-$2A^s$, E^s)				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
gp160 (842–856)	gp41 (842–856 IIIB, B10)	HIPRRIRQGLERILL	HIV-1 infection	human	Wahren1989b, Wahren1989a
	• 12 gag and 18 env peptides were identified that could commonly evoke T-cell responses.				

III-B-15 Env Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	gp120 (IIIB)		Vaccine	mouse	Shiver1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* gp120, gp160 **Keywords** Th1. • DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T-cell proliferative response with Th1-like secretion of γ interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs. • An intramuscular route of inoculation gave a stronger proliferative response than intradermal. • A proliferative response could be detected in all lymph tissues tested: spleen, PBMC, and mesenteric, iliac, and inguinal lymph nodes.			
Env	gp120		Vaccine	mouse	Kim1997d
	Vaccine *Vector/Type:* DNA *HIV component:* Gag, gp160, Pol *Adjuvant:* CD86 • A gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86, gives an increase in the proliferative responses to gp120 in mice.				
Env	gp120			human	De Berardinis1997
	• Sequences flanking helper T-cell immunogenic domains can be important for immunogenicity.				
Env	gp120		HIV-1 infection	human	Rosenberg1997
	• A strong proliferative response to p24 and gp160 was found in a healthy long term survivor.				
Env	gp120		HIV-1 infection	macaque	Kent1997b
	Keywords Th1, Th2. • Macaca nemestrina can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response. • A strong proliferative response against gp160 with IL-4 production, indicating a Th2 response, was found with 4 weeks of infection. • The gp160 proliferative response by 8 weeks produces both IL-4 and γ interferon, indicating both Th1 and Th2 responses.				
Env	gp120 (HXBc2)		Vaccine	macaque	Letvin1997
	Vaccine *Vector/Type:* DNA prime with gp160 boost *Strain:* B clade HXBc2 *HIV component:* gp160 • Vaccination of Macaca mulatta (rhesus monkeys) with a HXBc2 env DNA prime and a protein boost elicited a T-cell proliferative response, a CTL response, and type-specific neutralizing antibodies. • Vaccinated animals challenged with SHIV-HXB2 were protected from infection.				
Env	gp120 (MN)		HIV-1 infection, Vaccine	human	MacGregor1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* Env, Rev • An HIV DNA env and rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30, 100 or 300 μg, was safe. • All three groups showed an increased proliferative response after vaccination.				
Env	Env			human	Mazzoli1997
	• Study of HIV-specific immunity in seronegative partners of HIV-positive individuals – Env peptides could stimulate IL-2 production in 9/16 HIV-exposed seronegative individuals, and only 1/50 low-risk controls. • Exposed-uninfected produced more IL-2 and less IL-10 then HIV-infected individuals. • 8/9 of those whose PBMC produce IL-2 in response to Env peptides had concomitantly detected urinary or vaginal tract anti-HIV IgA.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Env	Env		HIV-1 infection	human	Plana1998
	Keywords HAART.				
	• Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses.				
Env	Env		HIV-1 infection	human	Kelleher1998a
	Keywords HAART.				
	• Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses.				
Env	gp160		HIV-1 infection, Vaccine	human	Ratto-Kim1999
	Vaccine *Vector/Type:* protein *HIV component:* gp160				
	• Vaccinations with rgp160 did not enhance Th immunoproliferative responses in individuals who were immunized every 2 months for 5 years starting early in infection.				
Env	gp160		HIV-1 infection, Vaccine	human	Leandersson2000
	Vaccine *Vector/Type:* protein *HIV component:* gp160				
	Keywords inter-clade comparisons.				
	• 27 HIV subtype B, 4 subtype C, 2 D and one of each subtype E, F, G infected individuals were either given rgp160 B clade immunizations or placebo. All rgp160 immunized individuals showed increased proliferation responses to the B clade immunizing antigen rgp160.				
	• gp120 was prepared from A, B, C, D, and E subtype virions and used as antigenic stimulus – 7 of 10 tested individuals responded to native gp120 from at least one additional subtype in addition to B subtype, while a placebo recipient did not respond to any gp120.				
	• This study shows that cross-subtype HIV-specific T-cell proliferative responses can be stimulated in patients already infected with another HIV-1 subtype – all immunized subjects could respond to the subtype B immunogen, but many developed responses to at least one more subtype.				
Env	gp160 (MN)		Vaccine	human	Gorse1999a
	Vaccine *Vector/Type:* gp160 prime with gp120 boost *Strain:* B clade MN *HIV component:* gp120, gp160				
	Keywords Th1, Th2.				
	• Helper T-cell memory responses were induced by MN rgp160 as measured by proliferation and Th1 and Th2 cytokine release – this response could be boosted by MN rgp120.				
Env	gp120		Vaccine	macaque	Heeney1998b
	Vaccine *Vector/Type:* fowlpoxvirus, ISCOM *Strain:* B clade SF2 *HIV component:* gp120				
	Keywords Th1, Th2.				
	• Vaccinated monkeys with the highest level of Th1 and Th2 responses and the highest levels of NAbs were protected against a SHIV SF13 challenge – the ISCOM strategy gave more potent anti -gp120 responses than the Fowl pox strategy.				
	• When animals were challenged 4 months after boost, those that maintained high levels of HIV-1 specific IFNγ responses, indicative of a Th 1 response, were still protected.				
Env	(IIIB)		HIV-1 infection, Vaccine	human	Boyer1999
	Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Env, Rev				
	• A DNA vaccine containing env and rev was tested for safety and immune response in 15 HIV+ asymptomatic individuals.				
	• Enhanced proliferative activity and higher levels of MIP-1 alpha were detected in multiple study subjects.				
Env	Env		Vaccine	mouse	Rodríguez1999
	Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 *Adjuvant:* GM-CSF/ENV chimera				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• A chimeric GM-CSF-env antigen expressed in a vaccinia vector elicits a higher HIV-specific env cellular immune response than when native env is used.				
Env	Env (LAI)		Vaccine	macaque	Kent1998
	Vaccine *Vector/Type:* DNA prime with vaccinia boost *Strain:* B clade LAI *HIV component:* Env, Gag **Keywords** Th1, Th2. • Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T-cell immunity than either vaccine alone. • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5-4, but after boosting with rHIV-fowlpox virus, there was a 6-17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced.				
Env	gp120		Vaccine	macaque	Heeney1999
	Vaccine *Vector/Type:* DNA, protein, virus-like particle (VLP), ISCOM **Keywords** Th1, Th2. • Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge. Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response. DNA, protein+adjuvant, VLP and ISCOM vaccines were tested. • HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production.				
Env	gp160 (MN)		HIV-1 infection, Vaccine	human	Kundu1998a
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp160 • This study followed 10 HLA-A2 asymptomatic HIV+ individuals as they received MN gp160 vaccinations over a two year period. • There was an increased lymphoproliferative response but this did not impact viral load or CTL response.				
Env	gp120 (SF2)		Vaccine	macaque	Verschoor1999
	Vaccine *Vector/Type:* DNA, protein, ISCOM *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* MF59 • 16 rhesus Macaques were vaccinated with either an epidermal SF2 gp120 DNA vaccine, rgp120 with a MF59 adjuvant, or rgp120 incorporated into ISCOMs. • DNA vaccination elicited a weak Th type 1 response and low antibody response, rgp120/MF59 triggered a strong antibody response, and rgp120/ISCOM induced both kinds of Th cells, and a strong humoral response. • Animals were challenged with SF13 SHIV. Early induction of Th type 1 and type 2 responses with the rgp120/ISCOM vaccine provided the most effective immunity, protecting from infection.				
Env	Env (MN)		Vaccine	mouse	Kim1998
	Vaccine *Vector/Type:* DNA *Strain:* B clade MN *HIV component:* Env, Gag, Pol *Adjuvant:* CD80, CD86 • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses.				
Env	Env (LAI, MN)		Vaccine	human	Salmon-Ceron1999
	Vaccine *Vector/Type:* canarypox *Strain:* B clade LAI, B clade MN *HIV component:* Gag, gp120, gp41, Protease • A live attenuated canarypox vector expressing MN gp120 and LAI gp41/gag/protease could induce CTL and a lymphoproliferative response in healthy uninfected volunteers.				
Env	Env		Vaccine	macaque	Akahata2000
	Vaccine *Vector/Type:* DNA *Strain:* ZF1 *HIV component:* complete genome • Rhesus macaques were vaccinated by i.m. injection with naked plasmid DNA carrying an HIV-1 complete genome vaccine, strain ZF1, with a mutated zinc finger in the nucleocapsid to prevent packaging.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Env and Gag specific CTL but no antibody responses were induced in 2/4 vaccinated monkeys (MM145 and MM153) • 2/4 monkeys (MM146 and MM143) produced antibodies against p24 and/or gp160, but no CTL response was detected. • PBMC from all vaccinated monkeys produced IFNγ, in response to HIV-1 gp160, indicating a Th response – this response was 5 times higher in MM145, the animal with the strongest CTL response. • 4 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM145 and MM153 (with a homologous Env) decreased to near or below the detection limit. • 6-8 weeks post-challenge with SHIV NM-3rN plasma viral loads of both MM146 and MM143 decreased near or below the detection limit.				
Env	gp120 (W6.ID)		HIV-1 infection	human	Zhang2001b
	• T-helper cell proliferative responses to HIV p24, p55 and gp120 were tested in 27 patients with HIV infection – vigorous responses directed at Gag were detected in ten patients, but an Env specific response was detected in only one patient.				
Env	gp160		HIV-1 infection	human	Blazevic2000
	Keywords HAART. • Prolonged viral suppression resulting from potent anti-retroviral therapy did not allow an HIV T helper response to p24 or gp160, but Th proliferative responses to influenza, alloantigen, and PHA did develop in many HIV+ patients, and asymptomatic patients had stronger and more frequent Th response recovery than AIDS patients.				
Env	gp120		HIV-1 infection	human	Oxenius2000
	Keywords HAART. • Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.				
Env	gp120		Vaccine	human	Sabbaj2000
	Vaccine *Vector/Type:* canarypox prime with gp120 boost *HIV component:* gp120 **Keywords** Th1, Th2. • Proliferative responses in PBMC of uninfected individuals that were vaccinated with canarypox vector expressing HIV-1 antigens (ALVAC-HIV) and boosted with a recombinant gp120 subunit vaccine gave a Th1 and Th2 proliferative response upon stimulation with HIV-1 Env. • All vaccinees produced IFNγ and IL10, most also produced IL-2, IL-6, IL-4 and IL-5.				
Env	gp120		HIV-1 infection, Vaccine	human	Hladik2001
	Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp120 **Keywords** Th1. • 16/29 HIV-1 infected and 24/30 vaccinated individuals had DTH reactions within 48 hours after an intradermal rec gp120 injection. Of nine DTH positive individuals, none had detectable proliferative responses. Thus skin testing may be a sensitive way to identify people with Th recall responses to vaccines, or in the absence of lymphoproliferaion. • No 48 hour DTH responses were detected among uninfected volunteers, although 10/35 (40%) of the high risk and 11/32 (34%) of the low risk individuals developed an induration resembling DTH after 7-12 days, that may be indicative of primary induction of HIV-1 specific Th1-immunity.				
Env	gp120		HIV-1 infection	human	Wilson2000b
	Keywords rate of progression, Th1, Th2. • Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses. • None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction. • Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1+ LTNP, progressors, and HIV-1 controls.				
Env	gp160		HIV-1 infection	human	Kalams1999a
	Keywords rate of progression, Th1. • The strength of p24 specific Gag proliferative responses (SIs) were inversely correlated with viral load in 21 ARV naive patients. The responses were Th1, IFNgamma producing. • Proliferative responses against gp160 were rarely observed (only 4 cases).				
Env	Env		Vaccine	human	MacGregor2002
	Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade MN *HIV component:* Env, Rev *Adjuvant:* Bupivacaine **Keywords** early-expressed proteins. • A phase I clinical trial of a HIV-1 Env and Rev DNA vaccine with a CMV promoter was conducted and Th proliferative, CTL and Elispot responses monitored. The construct was modified for safety and included no LTRs or packaging signals. The vaccine strategy was safe, and elicited strong CD4-T cell responses, but not CD8 T-cell responses. Rev elicited strong Th responses, and is a early produced protein so may confer advantages. • With a 300 ug dose, 4/6 individuals had a lymphocyte proliferation (LP) responses to gp120, 3/6 to Rev. • With a 1000 ug dose, 4/6 individuals had a LP and 2/6 had IFNgamma Elispot responses to gp160; 3/6 had LP, and 4/6 had IFNgamma Elispot responses to Rev. • No responses to three specific CTL epitopes were observed by Elispot in individuals with appropriate HLA. Some cytoxic activity against whole protein was observed that was CD4+ T-cell mediated.				
Env			HIV-1 infection	human	Clerici2002b
	Keywords HAART. • Specific immunity was compared in a two-year study of chronically HIV-1 infected i) HAART-naive patients who were not progressing and had strong immune responses, ii) newly treated patients followed for 24 months after initiation of HAART, iii) and long-term HAART patients who had been on HAART at least 12 months prior to the study. • HAART naïve patients had strongest proliferative responses at time zero, but long-term HAART patients the most significant increase in specific responses over the two year study period against HIV-1 gp160, influenza, and Candida. Similarly, IL-2 and IFNγ production in responses to gp160 was highest in the naïve group at time zero, but increased the most in the long-term HAART treated patients. • Short-term HAART patients showed a significant improvement in their CD4+ T cell count and a reduction of plasma viremia, and had augmented IL-7 production, which was slightly reduced in long-term HAART patients.				
Env	gp160		HIV-1 infection	human	Palmer2002
	Keywords HAART. • CD4+ T cell proliferative responses from 33 HIV-1 infected patients with HAART suppression were compared to 19 patients with active viral replication (HAART failures and HAART naive). Patients with HAART suppression showed stronger p24- and p66-specific proliferative responses compared to patient groups with active HIV-1 replication, suggesting active viral replication *in vivo* specifically reduces proliferation responses. • gp160 proliferation responses were apparent in 7/32 donors tested, but weaker overall, with a median value for the suppressed group not above that found for HIV seronegative controls.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• No differences in the frequency of HIV-specific CD4+ T-cells that were positive for cytokine secretion in a flow cytometry assay were found in the HAART suppressed group versus the group with active viral replication.				
Env	gp120 (IIIB)		HIV-1 infection	human	Geretti1994
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 4/15 responders recognized this peptide, average SI = 4.4.				
Env	gp120 (IIIB)		HIV-1 infection	human	Geretti1994
	• Th proliferative responses were studied in 36 asymptomatic HIV-1+ patients. PBMC from 15/36 patients responded to stimulation with gp120 synthetic overlapping peptide pools. 10 of the responding patients recognized three or more peptide pools. • After 12 months, most responses were lost or diminished, and specific responses fluctuated. 4/10 of the responders at baseline had new responses at 12 months, as did 5/15 non-responders. • IL-2 production was a more sensitive and well-preserved measure of Th function than proliferation. • 4/15 responders recognized this peptide, average SI = 4.4.				
Env	gp120 (SF2)		HIV-1 infection	human	Imami2002b
	Keywords inter-clade comparisons, rate of progression. • 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. • In a comparison of responses to HIV-1 proteins based on 10 non-progressors, 3 immunologically discordant, and 70 progressors, SIs were always much higher for non-progressors and immunologically discordant than progressors. Among the non-progressors, the responses to different antigens were greater using p24 peptides than native p24. Native p24, Nef, gp120 proteins, and Remune (gp120 depleted HIV-1, p24 is subtype G), had roughly comparable distributions of SI values from the non-progressors, Nef and gp120 responses were somewhat diminished in immunologically discordant patients.				
Env	(BRU)		Vaccine	mouse	Haas1991
	Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade BRU *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA) • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				
Env	gp120 (HIV-1,IIIB)		HIV-1 exposed seronegative	human	Fowke2000
	Keywords HIV exposed persistently seronegative (HEPS). **Assay type** cytokine production. • A cohort of Nairobi sex-worders were defined to be resistant to infection by virtue of remaining seronegative despite repeated high risk exposure. 24 were tested for HIV specific T-helper responses detemined by IL-2 production *in vitro* in response to gp120 peptides or soluble gp120 protein. • In 7/17 resistant women showed IL-2 stimulation >= 2.0, and specific CTL responses were detected in 15/22 resistant women. 0/12 of the control low-risk subjects had detecatble T-cell responses.				
Env	gp160		HIV-1 infection, Vaccine	human	Hejdeman2003
	Vaccine *Vector/Type:* protein *HIV component:* gp160 *Adjuvant:* aluminum phosphate **Keywords** HAART, immunotherapy.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type proliferation.				
	• Groups of ten asymptomatic HAART-treated HIV-1+ patients with undetected viral loads were monitored for two years after i) no immunization, ii) immunization with rgp160, or iii) immunization with tetanus. Ten NIV-1 negative volunteers were immunized with tetanus as a control. Results were compared with an rgp160 group tested before HAART was available. The HAART-treated group had increased magnitude and duration of proliferative response to rgp160, maintaining the response for the two year study period. CD4 T-cell responses to tetenus were also improved in the HAART group.				
	• The recall response to tetanus toxoid and tuberculin were boosted by the rgp160 immunization, particularly in the HAART-treated group.				
Env			HIV-1 exposed seronegative		Puro2000
	Keywords HIV exposed persistently seronegative (HEPS), acute infection, early treatment.				
	Assay type cytokine production.				
	• This was a case report of a health care worker who had an percutaneous injury and exposure to HIV, and was immediatedly given combination therapy. The individual remained HIV Ab negative, but had tranisiently detectable viral RNA 2-3 weeks after the exposure. 58 weeks after exposure a Th response was detected by IL-2 production in response to HIV Env peptides.				
Env			Vaccine	rabbit	Radaelli2003
	Vaccine *Vector/Type:* fowlpoxvirus, DNA prime with virus-like particle (VLP) boost *Strain:* B clade 89.6 *HIV component:* Env, Gag-Pol				
	Keywords Th1, Th2.				
	Assay type cytokine production.				
	• Rabbits were immunized with fowlpox recombinant vectors or expression plasmids, which express either SIVmac239 gag/pol or HIV-1 env 89.6P genes, and then boosted with virus-like particles (VLPs)(gag/pol SIV with HIV env 89.6).				
	• A lymphoproliferative Th0 profile response and homologous neutralizing Ab were seen in all three groups. The pcDNA3gag/pol SIV construct was more efficient at producing Abs than the fowlpox construct, although the fowlpox env89.6 construct elicited good humoral and cellular responses. VLP boosting was shown to be efficacious; the pseudoviral structure of the VLP providing a more natural protein conformational was considered helpful for eliciting long term memory cells.				
Env	gp160		HIV-1 infection, Vaccine	human	Ratto-Kim2003
	Vaccine *Vector/Type:* canarypox prime with gp160 boost *Strain:* B clade MN/LAI-2 *HIV component:* gp160				
	Keywords vaccine-specific epitope characteristics, vaccine-induced epitopes.				
	Assay type proliferation.				
	• The CD4+ T-helper response to vaccinees given ALVAC-HIV(vCP205) alone, rgp160 MN/LAI-2 alone, or the two combined in a prime-boost was investigated by establishing T cell lines and comparing proliferative responses to a series of peptides (15 mers overlapping by 10) spanning autologous gp160 MN/LAI-2. Th responses against Env during natural HIV-1 infection were also studied.				
	• Broad, strong T-helper responses scattered across the Env were obtained from volunteers who received a prime boost vCP205 + rgp160MN/LAI-2, while those receiving rgp160 responded to fewer peptides, and vCP205 to very few peptides.				
	• HIV-1+ volunteers had less breadth and amplitude of Th responses than vaccinees that got the prime-boost vaccine, although T-cell lines were readily generated from HIV+ individuals. Some vaccinees targeted C1 and C5, while infected individuals did not, and some infected individuals targeted V3, while vaccinees did not.				
	• The authors note that the differences in response may be contributed to by the fact the peptides used to screen the responses were the same as the vaccine strain, and different than the strains in the natural infection, but that there also may be real immunological differences in the two scenarios of vaccine verses natural infection.				
Env	gp120		HIV-1 infection		Sullivan2003
	Keywords HAART.				
	Assay type proliferation.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Lymphoproliferative responses to HIV antigens p24, gp120 and Nef were enhanced in eight patients who were switched from protease inhibitors to non-nucleoside reverse transcriptase inhibitors.				
Env	gp120 **Keywords** HAART. **Assay type** cytokine production, proliferation. • Upon initiating HAART, CD4+ T cell proliferative responses in 36 patients were restored to specific antigens, mitogens, and IL-2. Restored recall responses were largely to persistent antigens, and not to HIV-1 or new antigens, and recall responses were associated with IL-2, not IL-4 production.		HIV-1 infection	human	Hardy2003
Env	gp120 **Vaccine** *Vector/Type:* DNA *HIV component:* Env, Gag, Pol *Adjuvant:* IFN-gamma, IL-2, IL-4 **Keywords** Th1. • Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFNγ drove Th1 immune responses and enhanced CTL responses.		Vaccine	mouse (H-2^d)	Kim2000
Env	gp120 (IIIB) **Vaccine** *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Keywords** Th1, Th2. • Helicobacter pylori induces Th1 responses early, but predominantly Th2 responses later in infection (at 6 weeks) – differentiation of HIV-1 gp160 CD4+ help and CD8+ CTL effector cells in response to HIV gp160-vaccinia vaccination is impaired in BALB/c mice infected with H. pylori.		Vaccine	mouse (H-2^d)	Shirai2001
Env	gp120 (V3) and p24 (IIIB, MN, BH10) **Vaccine** *Vector/Type:* virus-like particle (VLP) *Strain:* A clade UG5.94UG018, B clade IIIB *HIV component:* Gag, gp120 **Keywords** inter-clade comparisons. • Different HIV strains were used for different regions: gp120 A clade UG5.94UG018, HIV-1 IIIB • BALB/c mice were given intraperitoneal immunization in the absence of adjuvants with virus-like particles (VLPs) expressing recombinant subtype A gp120 and Pr55gag. • High dose-independent humoral responses were elicited against both gp120 and p24 peptides, and CTL responses were observed against target cells carrying vaccinia expressed gp120 and Gag. • Recombinant rgp120 (clade B, MN) induced T cell proliferative responses *in vitro* from vaccinated animals.		Vaccine	mouse (H-2^d)	Buonaguro2002
Env	gp160 (IIIB) **Vaccine** *Vector/Type:* peptide, protein *Strain:* B clade IIIB *HIV component:* gp160, V3 *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72) **Keywords** Th1, Th2. • Mice were intranasally immunized with 20 ug of HIV-gp160 and 5 ug of peptide E7 (RIHIGPGRAFYAARK) with the adjuvant LT(R192G), a heat-labile enterotoxin produced by E. coli. • Adjuvant LT(R192G) was required for stimulation of antigen-specific IgG1, IgG2 antibodies, and Th1 and Th2 cytokines responses to gp160, and peptide-specific CTL responses. • Increased IFNγ, IL-10 and IL-6 cytokine production specific to gp160 was measured with co-immunization of gp160 with LT(R192G)		Vaccine	mouse (H2^d)	Morris2000
Env	gp160 (IIIB) **Vaccine** *Vector/Type:* DNA with CMV promotor *Strain:* B clade IIIB *HIV component:* gp160, Rev *Adjuvant:* Br-cAMP **Keywords** Th1.		Vaccine	mouse (H2^d)	Arai2000

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• The CMV promotor responds to the intracellular level of cAMP, and 8 Br-cAMP can increase transgene expression so it was co-administered with a CMV-based DNA vaccine both intranasally and intramuscularly. • 8 Br-cAMP increased serum IgG responses, HIV-specific CTL, DTH and Th1 responses, and IgA in the intranasal vaccination. • A CAT assay study showed adjuvant effect was due to CMV promotor activation.				

III-B-16 Nef Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (1–20)	Nef (1–20 LAI)	MGGKWSKSSVVGWPTVRERM	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (1–20)	Nef (1–20 HXB2)	MGGKWSKSSVIGWPTVRERM	HIV-1 infection	(H-2^d)	Peng2001
	Keywords class I down-regulation by Nef. • Deletion of the 19 N-terminal amino acids from Nef including the myristolation signal eliminates Nef-induced down-regulation of MHC class I and CD4 molecules. Such a construct has the potential to serve as a more potent immunogen. The known T-cell epitopes that that would be disputed by this deletion are minimal, a murine H-2d Th epitope in the peptide MGGKWSKSSVIGWPTVRERM, and a HLA-B8 CTL epitope, WPTVRERM.				
Nef (14–22)	Nef (14–22 SF2)	SAIRERMRR	in vitro stimulation or selectio	human (DRw6)	Wentworth1994
	Keywords epitope processing. **Epitope name** 95.12, 33.6. **Assay type** proliferation. **Donor HLA** DRw52, DRw6, DRw15(2), DQw1, DQw6, DP4. • Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity. • These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided. • The two clones that recognized the epitope SAIRERMRR could also auto-present Nef protein, suggesting that they recognized this epitope in the context of the intact, unprocessed protein.				
Nef (16–35)	Nef (16–35 LAI)	VRERMRRAEPAADGVGAASR	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (31–50)	Nef (31–50 LAI)	GAASRDLEKHGAITSSNTAA	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (43–49)	Nef (47–53 SF2)	ITSSNTA	in vitro stimulation or selectio	human (DQw7)	Wentworth1994
	Keywords epitope processing. **Epitope name** 1.13. **Assay type** proliferation. **Donor HLA** DR1, DR8, DRw52, DQw1, DQw7, DP4. • Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity. • These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (45–69)	Nef (45–69 BRU)	SSNTAATNAACAWLEAQEE-EEVGFP	Vaccine	chimpanzee, rat	Estaquier1992
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* B clade BRU *HIV component:* Nef • Antigenic domain: ATNAACAWL, priming with peptide enhanced subsequent Ab response to Nef protein immunization.				
Nef (45–69)	Nef (45–69)	SSNTAATNAACAWLEAQEE-EEVGFP	Vaccine	rat	Rouaix1994
	Vaccine *Vector/Type:* peptide *Adjuvant:* aluminum hydroxide **Keywords** vaccine-specific epitope characteristics. • Covalently linking the potent Th epitope Nef 45-69, which can induce Th proliferative responses at low doses with no adjuvant in Lou/M rats, to a weaker epitope from Schistosoma mansoni allows the induction of detectable Th responses to the Schistosoma epitope.				
Nef (46–65)	Nef (46–65 LAI)	SNTAATNAACAWLEAQEEEE	Vaccine	mouse (H-2^{d})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (56–68)	Nef (56–68 HXB2)	AWLEAQEEEEVGF	Vaccine	mouse (DQ2, DQ3, DQ5, DQ6, DQ7, DQ8,)	Pancré2002
	Vaccine *Vector/Type:* peptide *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **Keywords** binding affinity, cross-presentation by different HLA, Th1, TCR usage. • This highly conserved Nef epitope has promiscuous HLA-DQ class II binding potential. It has a can bind to 6 different HLA-DQ alleles, but did not bind to any HLA-DR alleles tested. It bound to DQ2 and DQ8 with particularly high affinity, and with DQ7 with low affinity. • DQ transgenic mice (in particular DQ8) mounted strong cellular and humoral responses after immunization with this peptide. • Ex vivo stimulation of CD4+ T-cells from 14 healthy donors (with diverse HLAs) with this peptide presented on autologous DCs resulted in Th1-associated cytokine production. IFNgamma production was stimulated in 7/14 cases, both IFNgamma and IL-2 in 6/14, and just IL-2 in 1/14. No IL-4 or IL-5 production was observed. • Peptide-specific CD4+ T-cell clones with different HLA presenting molecules demonstrated a preference for TCR Vβ6.1.				
Nef (61–80)	Nef (61–80 LAI)	QEEEEVGFPVTPQVPLRPMT	Vaccine	mouse (H-2^{b})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (64–73)	Nef (68–77 SF2)	EEVGFPVRPQ	in vitro stimulation or selectio	human (DRw15(2))	Wentworth1994
	Keywords epitope processing. **Epitope name** 59.25. **Assay type** proliferation. **Donor HLA** DR1, DRw15(2), DQw1, DP4. • Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity. • These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef (66–73)	Nef (70–77 SF2)	VGFPVRPQ	in vitro stimulation or selectio	human (DR1, DRw15(2))	Wentworth1994
	Keywords epitope processing. **Epitope name** 29.16. **Assay type** proliferation. **Donor HLA** DR1, DRw15(2), DQw1, DP4. • Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity. • These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.				
Nef (66–97)	Nef (66–97 LAI)	VGFPVTPQVPLRPMTYKAA-VDLSHFLKEKGGL	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide. • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual. • 5/12 tested had an IgG response to this peptide.				
Nef (76–95)	Nef (76–95 LAI)	LRPMTYKAAVDLSHFLKEKG	Vaccine	mouse (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (91–110)	Nef (91–110 LAI)	LKEKGGLEGLIHSQRRQDIL	Vaccine	mouse (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (98–112)	Nef (98–112 BRU)	EGLIHSQRRQDILDL	Vaccine	chimpanzee	Estaquier1992
	Vaccine *Vector/Type:* peptide prime with protein boost *Strain:* B clade BRU *HIV component:* Nef • Peptide alone could stimulate monkey T-cells in the absence of carrier protein – required carrier protein in rat.				
Nef (104–123)	Nef (106–125 HXB3)	QRRQDILDLWIYHTQGYFP-D?	Vaccine	mouse (H-2^b)	Sandberg2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB3 *HIV component:* Nef • A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization. • Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun. • Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes.				
Nef (106–125)	Nef (106–125 LAI)	RQDILDLWIYHTQGYFPDWQ	Vaccine	mouse (H-2^b)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (117–147)	Nef (117–147 LAI)	TQGYFPDWQNYTPGPGVRY-PLTFGWCYKLVP	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide. • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual. • 10/12 tested had an IgG response to this peptide.				
Nef (121–140)	Nef (121–140 LAI)	FPDWQNYTPGPGVRYPLTFG	Vaccine	mouse (H-2^{b})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (136–155)	Nef (136–155 LAI)	PLTFGWCYKLVPVEPDKVEE	Vaccine	mouse (H-2^{d})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (151–170)	Nef (151–170 LAI)	DKVEEANKGENTSLLHPVSL	Vaccine	mouse (H-2^{d})	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (164–183)	Nef (166–185 HXB3)	LLHPVSLHGMDDPEREVLE-W?	Vaccine	mouse (H-2^{b})	Sandberg2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB3 *HIV component:* Nef • A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization. • Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun. • Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes.				
Nef (166–185)	Nef (166–185 LAI)	HPVSLHGMDDPEREVLEWRF	Vaccine	mouse (H-$2^{b, d}$)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (179–198)	Nef (181–205 HXB3)	EVLEWRFDSRLAFHHVARE-L?	Vaccine	mouse (H-2^{b})	Sandberg2000
	Vaccine *Vector/Type:* DNA *Strain:* B clade HXB3 *HIV component:* Nef • A strong T helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization. • Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes.				
Nef (181–188)	Nef (185–192 SF2)	LVWRFDSK	in vitro stimulation or selectio	human (DP5)	Wentworth1994
	Keywords epitope processing. **Epitope name** 6.38. **Assay type** proliferation. **Donor HLA** DRw11, DRw52, DQw7, DP5. • Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity. • These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.				
Nef (181–205)	Nef (181–205 LAI)	LEWRFDSRLAFHHVARELH-PEYFKN	Vaccine	mouse (H-2^d)	Hinkula1997
	Vaccine *Vector/Type:* DNA *Strain:* B clade LAI *HIV component:* Nef, Rev, Tat • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein. • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev.				
Nef (182–205)	Nef (182–205 LAI)	EWRFDSRLAFHHVARELHP-EYFKN	Vaccine	human	Gahery-Segard2000
	Vaccine *Vector/Type:* lipopeptide • Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial. • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide. • 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual. • None of the 12 tested had an IgG response to this peptide.				
Nef (185–200)	Nef (183–198)	FDSRLAFHHVARELHP	HIV-1 infection	human	Ranki1997
	• T-cell response to this epitope persisted after seroreversion.				
Nef (186–206)	Nef(p27) (185–205 BRU)	DSRLAFHHVARELHPEYFK-NC	Vaccine	chimpanzee	Bahraoui1990
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* gp160, Nef, p17/p24 Gag, p25 Gag *Adjuvant:* muramyl-dipeptide base adjuvant (Syntex) **Keywords** immunodominance. **Epitope name** PF63. • Six chimpanzees were immunized with rec vaccinia viruses (VV) expressing HIV-1 gp160, Gag, and Nef. • 2/6 chimpanzees showed persistent T-helper proliferative responses against a putative immunodominant epitope located at the C-term end of Nef.				
Nef (191–199)	Nef (195–203 SF2)	FHHMARELH	in vitro stimulation or selectio	human (DR1)	Wentworth1994
	Keywords epitope processing. **Epitope name** 3.2. **Assay type** proliferation. **Donor HLA** DR1, DR8, DRw52, DQw1, DQw7, DP4. • Seven CD4+ T-cell clones that proliferated in responses to SF2 Nef were generated *in vitro* by stimulation of PBMC from uninfected donors. These CD4+ clones also had cytotoxic activity.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• These seven clones were capable as of presenting their epitopes to themselves, if Nef peptides were provided.				
Nef	Nef (LAI)		HIV-1 infection	human	daSilva1998
	• This study compares the level of variation in Nef CTL epitopes to helper and MAb epitopes from the same region. • CTL epitopes tend to be more conserved than either helper or MAb epitopes and there are stronger functional constraints in the regions where CTL epitopes cluster.				
Nef	Nef		Vaccine	human	Calarota1999
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat **Keywords** HAART. • 9/9 HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated. • The nef DNA immunization induced the highest and most consistent CTLp activity, IFNγ production, and IL-6 and IgG responses. • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination.				
Nef	Nef		HIV-1 infection, Vaccine	human	Calarota2001
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Rev, Tat *Adjuvant:* CpG immunostimulatory sequence (ISS) **Keywords** review, Th1. • This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals.				
Nef	Nef		HIV-1 infection	human	Oxenius2000
	Keywords HAART. • Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable.				
Nef	Nef		HIV-1 infection	human	Wilson2000b
	Keywords rate of progression, Th1, Th2. • Dysfunction of HIV-1 specific proliferative responses, but not responses to other antigens, is evident in HIV-1 progressive disease. • Vigorous HIV-1 specific responses to p24, Nef and gp120 with SI between 8-99 were seen in 6/7 long term non-progressors (LTNP), the seventh had a borderline responses. IL-2 production was seen in all cases, and IL-4 production was also evident many responses. • None of the progressors (0/5) had HIV-1 specific proliferative responses, or IL-2 or IL-4 induction. • Non-HIV antigens (cytomegalovirus, PPD, Staphylococcus enterotoxin B, tetanus toxoid) gave similar responses in HIV-1+ LTNP, progressors, and HIV-1 controls.				
Nef	Nef (BRU)		Vaccine	mouse	Moureau2002
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG **Keywords** Th2. • BALB/c mice were immunized with Nef alone, Nef with Freund's adjuvant, or Nef encapsulated in poly(DL-lactide-co-glycolide) PLG microparticles. • High Ab titers (predominantly IgG1) against Nef were retained for seven months in the mice infected with Nef-PLG, 3-fold higher than Nef in Freund's, 5-fold higher than Nef alone. • CD4+ T-cell lymphoproliferative were observed, and cytokine profiles indicated this was primarily a Th2 response.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
Nef	Nef (SF2)		HIV-1 infection	human	Imami2002b
	Keywords inter-clade comparisons, rate of progression. • 70 patients with chronic disease progression, 10 clinical non-progressors, and 3 immunologically discordant progressors (individuals who controlled viremia but had progressive CD4+ T-cell decline) were analyzed for their T-helper cell responses to p24 and cytokine profile. • In a comparison of responses to HIV-1 proteins based on 10 non-progressors, 3 immunologically discordant, and 70 progressors, SIs were always much higher for non-progressors and immunologically discordant than progressors. Among the non-progressors, the responses to different antigens were greater using p24 peptides than native p24. Native p24, Nef, gp120 proteins, and Remune (gp120 depleted HIV-1, p24 is subtype G), had roughly comparable distributions of SI values from the non-progressors, Nef and gp120 responses were somewhat diminished in immunologically discordant patients.				
Nef	(BRU)		Vaccine	mouse	Haas1991
	Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade BRU *HIV component:* RT, virus *Adjuvant:* Complete Freund's Adjuvant (CFA) • Of 5 mouse inbred lines tested: DBA/2 (H-2d, Ad, Ed), B10.A(4R) (H-2h4, Ak) and B10.A(5R) (H-2i5) showed particularly good CD4+ T cell proliferative responses to HIV proteins (gp160, gp120, p17, p24, Nef and RT), after vaccination with inactivated virus. • B10.BR (H-2k, Ak, Ek) and C57BL/6 (H-2b and Ab) had weaker responses.				
Nef	Nef				
Nef	Nef		HIV-1 infection		Sullivan2003
	Keywords HAART. **Assay type** proliferation. • Lymphoproliferative responses to HIV antigens p24, gp120 and Nef were enhanced in eight patients who were switched from protease inhibitors to non-nucleoside reverse transcriptase inhibitors.				
Nef	Nef		HIV-1 infection	human	Hardy2003
	Keywords HAART. **Assay type** cytokine production, proliferation. • Upon initiating HAART, CD4+ T cell proliferative responses in 36 patients were restored to specific antigens, mitogens, and IL-2. Restored recall responses were largely to persistent antigens, and not to HIV-1 or new antigens, and recall responses were associated with IL-2, not IL-4 production.				
Nef	Nef		Vaccine	mouse ($H\text{-}2^d$)	Ayyavoo2000
	Vaccine *Vector/Type:* DNA *HIV component:* Nef, Vif, Vpu **Keywords** inter-clade comparisons, Th1. • Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFNγ levels. • Antigen stimulation increased IFNγ production in pVVN-P immunized mice, indicating a Th1 response. • IL-4 production was not significantly changed after antigen stimulation compared to control levels. • Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell.				

III-B-17 HIV-1 Helper T-cell epitopes

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1			HIV-1 infection	human	Kuhn2002
Keywords review, HIV exposed persistently seronegative (HEPS), mother-to-infant transmission. • Intrauterine exposure of infants to HIV from their mothers results in HIV-1 specific T-helper cell proliferative responses in 1/3 of exposed uninfected babies, and HIV-1 specific CTL in some. It is unknown whether these responses are associated with lack of infection, but there is some evidence that HIV-1 T-cell responses may reduce transmission in breastfeeding mothers. Summary tables are provided of CD4 and CD8 T-cell responses detected in earlier studies.					
HIV-1			HIV-1 infection, Vaccine	human	Kahn2000
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** HAART, rate of progression. • No benefit was observed in terms of progression free survival for HIV-1 patients on ART given vaccinations with HIV-1 antigen (N=1,262) versus those vaccinated with placebo (N=1,265). There was no statistically different outcome in HIV RNA, CD4 percentage, or body weight. HIV-1 ART patients that were vaccinated did have higher absolute CD4 counts.					
HIV-1			HIV-1 infection, Vaccine	human	Moss1999
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** HAART. • 15 HIV-1+ patients on ARV given vaccinations with HIV-1 antigen versus vaccinated with placebo. Lymphocyte proliferation of CD4+, CD8+ memory cells and NK cells to p24 and Remune HIV-1 antigen increased in HAART treated patients after vaccination.					
HIV-1			HIV-1 infection, Vaccine	human	Moss1997
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Keywords** Th1. • HIV-1 specific stimulation of T-cell proliferation, and beta-chemokines (RANTES) and Th1-type cytokine (IFNgamma) production are found after immunization of HIV-1+ individuals with HIV-1 immunogen.					
HIV-1			HIV-1 infection, Vaccine	human	Levine1996
Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *HIV component:* gp120 depleted virus *Adjuvant:* Incomplete Freund's Adjuvant (IFA) • Long-term follow up of HIV-1+ individuals given HIV-1 immunogen, suggesting those patients who became HIV-DTH-responsive in response to the HIV-1 immunogen had a better clinical outcome. Of twelve who developed DTH-responsiveness, one got an opportunistic infection and died, and one developed KS. Of the 13 patients who remained HIV-DTH-nonresponsive, 9 (69%) progressed to AIDS and 7 of these had died.					
HIV-1			Vaccine	human	Turner1994
Vaccine *Vector/Type:* HIV-1 immunogen *Adjuvant:* Incomplete Freund's Adjuvant (IFA) • A dose response study of HIV immunogen in IFA was conducted. Doses of 50, 100, 200, or 400 micrograms (total protein) were tested by DTH skin testing to the inactivated HIV-1 antigen. The HIV-1 immunogen was well tolerated, and the minimum dose required to induce HIV-1 DTH was 100 micrograms.					
HIV-1			HIV-1 infection	human, macaque	Wodarz2002
Keywords dynamics, HAART.					

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• Mathematical modeling is used to support the idea that T-helper cell dysfunction results in a compromised ability to maintain an anti-HIV CTL memory response. Models suggest strategies to restore CTL memory through therapy and improve long-term immunological control of the virus.				
HIV-1			HIV-1 infection, Vaccine	human	Imami2002a
	Vaccine *Vector/Type:* DNA, canarypox, gp120 depleted virus HZ321 (REMUNE(TM)), protein, virus-like particle (VLP), adenovirus *Adjuvant:* GM-CSF, Growth Hormone, IL-12, IL-2, IL-7, CpG immunostimulatory sequence (ISS), Thymosin alpha-1 **Keywords** HAART, review, rate of progression, immunotherapy. • This review addresses the use of immunotherapy and therapeutic immunization to help chronically infected patients maintain a strong anti-HIV-1 T-cell response. The loss of anti HIV-1 proliferative responses early after infection is reviewed, as are therapeutic vaccinations, with or without HAART, and strategies for immunomodulation that can be given with or without vaccination.				
HIV-1			HIV-1 infection	human	Heeney2002
	Keywords review, rate of progression, Th1, Th2. • Review of the importance of balanced Th1 and Th2 HIV-specific CD4 T-cell responses in control of infection and for vaccination strategies.				
HIV-1			HIV-1 infection		Bernaschi2002
	Keywords dynamics, rate of progression, escape. • A cellular automata model was used to model the dynamics of HIV-1 infection and progression to disease. The model suggests the long aymptomatic period is due to immune escape mutants with lower viral fitness, and with AIDS resulting from a drastic reduction of the T-helper cell reservoire.				
HIV-1			Vaccine		Altes2002
	Keywords dynamics, kinetics. • This study employs a mathematical model to study the consequences of increasing the T-helper response through a vaccine, which would have counter-balancing effects in a new infection: a more intense response provides more help but also more target cells. The model indicates that if the infecting virus had a low replication rate, then CTLp and CD4 helper cells could control an infection. Only a vaccine that could increase CTL responsiveness could reduce viral set point with observed replication rates. • A CD4+ T-cell response without maintained CTL response was deleterious in this model.				
HIV-1			HIV-1 infection		Bajaria2002
	Keywords dynamics, HAART, rate of progression. • This paper presents a dynamical model of HIV infection and progression that includes CD4 T-cell naive and memory populations distributed between the peripheral blood and the lymph nodes, as well as the effects of HAART. Increasing viral replication and infectivity and decreasing T-cell immunity had impact on the rate of disease progression in this model.				
HIV-1	(HZ321)		Vaccine	mouse	Ayash-Rashkovsky2002
	Vaccine *Vector/Type:* gp120 depleted virus HZ321 (REMUNE(TM)) *Strain:* AG recombinant HZ321 *Adjuvant:* Incomplete Freund's Adjuvant (IFA), CpG immunostimulatory sequence (ISS) **Keywords** Th1, Th2. • Parasitic helminthic infections in humans, common in parts of Africa and Asia, can shift immune responses to Th2 responses. To model this, BALB/c mice were infected with the parasite Schistosoma mansoni, and the infected mice showed a dominant Th2 immune response. Vaccination with gp120-depleted HIV-1 viral particles and incomplete Freund's adjuvant induced Th2 responses in these mice, but this could be shifted towards a Th1 profile when CpG oligodeoxynucleotide was added to the vaccine as an immunostimulatory agent.				
HIV-1	HIV-1 except gp120		HIV-1 infection	human	Ghanekar2001
	Keywords HAART, rate of progression.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	• 12 long term non-progressors (>10 years) went on HAART, while 14 elected not to go on HAART. After a year on HAART, higher frequencies and absolute numbers of HIV-specific memory CD4+ T-cells were observed in untreated patients than patients receiving HAART therapy, tested by stimulation an proliferation responses to HIV Remune antigen (gp120 depleted vaccine). • These results indicate a control of viral replication in therapy-naive patients may be mediated by their ability to respond to recall viral antigen, and that the diminished response in treated patients may contribute to viral rebound.				
HIV-1			HIV-1 infection	human	Pido-Lopez2002
	Keywords HAART, Th2. • The thymic output in HAART-treated HIV-1 infected patients with progressive disease was studied. One patient also receiving steroid treatment therapy had a weak response in a sjTREC assay indicating a dysfunctional thymus, while four patients not on steroids had clear positive sjTREC readings after HAART. Stimulation of PBMC with multiple recall antigens including gp120, p24 and Nef and mitogens, and revealed that in the patient treated with steroids there was and induction of a Th2 type response indicated by increased levels of IL-4 secretion in response to antigen.				
HIV-1			Vaccine		Berzofsky2001
	Vaccine *Vector/Type:* peptide *Adjuvant:* GM-CSF, IL-12, IL-2, IL-4, Tumor Necrosis Factor α (TNFα) **Keywords** binding affinity, review, Th1, Th2, mucosal immunity. **Assay type** Th support of CTL response. • Vaccine clusters were constructed containing T helper, CTL aand neutralizing antibody epitopes, and used to immunize mice. Four things were found to enhance the vaccine immune response: i) increasing the affinity of the peptide for the presenting MHC molecule, called epitope enhancement; ii) increasing the avidity of MHC/peptide complex for the T-cell receptor; iii) incorporating cytokines IL-2, GM-CSF, TFN-α, or IL-12 and IL-4 which steer responses towards Th1 or Th2 responses; iv) inducing mucosal immunity specifically, with intrarectal being most effective.				
HIV-1			Vaccine	human	Boyer2002
	Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag *Adjuvant:* B7, GM-CSF, IL-12, IL-15 **Keywords** review, Th1, Th2. • The first generation of HIV-1 plasmid vaccines in 167 individuals induced T-helper responses in most vaccine recipients, however CTL responses were below a 20% response rate. REV-independent RNA optimized constructs (pGag and pEnv) as well as B7 costimulatory molecules could significantly enhance CD8 effector cell responses. Co-administered GM-CSF enhanced antibody repsonses, IL-12 CTL production. IL-15 increased T cell expansion without increasing T cell help.				
HIV-1	HIV-1		HIV-1 infection		Breen2002
	Keywords review. **Assay type** cytokine production. • HIV-1 triggers immunological dysfunction in multiple ways, including the loss of CD4-positive T helper cells in quantity and function and hyperactivity and changes in the production and activity of cytokines. The role of pro- and anti-inflamatory cytokines are discussed, including IL-10, which can suppress HIV-1, and IL-1, IL-6, TNFα which up-regulate HIV-1.				
HIV-1			HIV-1 infection	human	Clerici1993b
	Assay type cytokine production, proliferation. • rCD4-IgG treatment was associated with improved Th cell function measured by IL-2 production in response to alloantigen or PHA, but not to influenza (a recall antigen response), in 9/10 patients. No clinical benefit was evident. rCD40IgG was also shown to block gp120 induced suppression of Th cells *in vitro*. Proposed mechanisms include: inhibiting HIV-cell fusion by blocking the binding of gp120 to CD4, competing with free gp120 for binding to the CD4 receptor and reducing gp120 induced immunosupression, and gp120-induced direct killing of Th cells.				

HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
HIV-1	Nef		HIV-1 infection	human	Draenert2003

Keywords assay standardization.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining.

- Six different HIV-1 Nef peptide sets ranging in length from 15-20 amino acids with overlap from 10-11 amino acids derived from either the B clade consensus sequences or the B clade sequence B.AU.AF064676 were used to study the impact of using different peptide design strategies to detect CD4 and CD8 T-cell responses. 20 individuals were tested using the six sets of peptides. 17/20 had CD8 T-cell responses to all peptides sets, and 15 of these 17 had CD4 T-cell responses.

HIV-1	Nef		HIV-1 infection	human	Draenert2003

Keywords assay standardization.
Assay type CD8 T-cell Elispot - IFNγ, CD4 T-cell Elispot - IFNγ, Intracellular cytokine staining.

- Six different HIV-1 Nef peptide sets ranging in length from 15-20 amino acids with overlap from 10-11 amino acids derived from either the B clade consensus sequences or the B clade sequence B.AU.AF064676 were used to study the impact of using different peptide design strategies to detect CD4 and CD8 T-cell responses. 20 individuals were tested using the six sets of peptides. 17/20 had CD8 T-cell responses to all peptides sets, and 15 of these 17 had CD4 T-cell responses.
- Although there was a trend in detecting more CD8 T cell responses using the shorter 15-mer peptides, longer 20-mers were best for detecting more CD4 T-cell responses, but neither result was statistically significant. Similar results were seen in the 15 to 20 amino acid range for both IFN gamma Elispot and ICS assays.
- Use of the consensus versus the natural strain identified slightly increased numbers of reactive peptides. Seven reactive peptides were observed with the B consensus peptides but not the B.AU.AF064676 peptides, but on the other hand four reactivites were observed using the B.AU.AF064676 peptides but not the consensus.
- Using an overlap of 10 or 11 amino acids did not make a difference.

HIV-1			HIV-1 infection		Galli2003

Keywords HAART.
Assay type cytokine production.

- HIV-1-infected women who developed Adepose tissue alterations (ATA) while recieving antiretroviral treatment (ART) had a favorable immunological profile with efficient IL-2 production and T-helper function. The authors suggest that ATA may be related to the ART-driven restoration of immune function.
- The most prominant feature of women with ATA that were recieving ART was increased IL-12 production with a lower TNF alpha and IL-10 synthesis.

HIV-1			HIV-1 infection		Norris2002

Keywords review.

- This paper reviews the role of Th cells in controlling HIV-1 infection, and in other viral infections. It describes CD4+ T-cell support of Ab production, CTL responses, as well as antiviral cytokine production and infected-cell killing. HIV+ patients with a low viral load and rare virgorous HIV-specific CD4+ proliferative responses, and the benefit of early treatment in preserving Th HIV-specific responses allowing immune control when therapy is subsequently stopped, are described.

HIV-1			HIV-1 infection	human	Norris2001a

Keywords review, rate of progression, acute infection.

- This review goes over the evidence for HIV-1 specific T-helper cell and CTL responses being critical inhibiting viral replication. LTNPs and those treated during acute HIV-1 infection generate specific T-helper responses, but most chronically infected individuals do not.

HIV-1			HIV-1 and GBV-C co-infection	human	Nunnari2003

Keywords HAART, rate of progression, Th1, Th2.

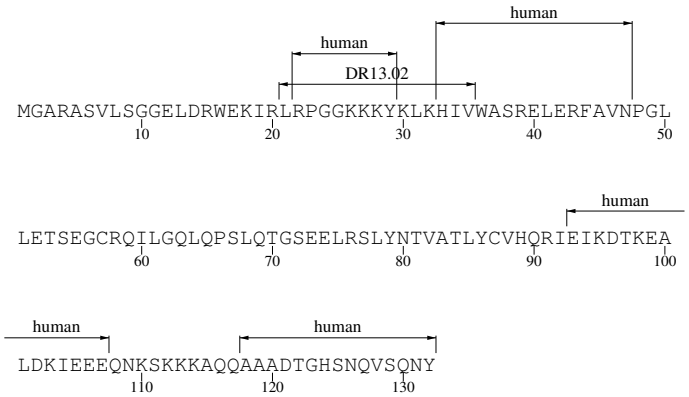
HXB2 Location	Author's Location	Sequence	Immunogen	Species (HLA)	References
	Assay type cytokine production. • HIV-1 positive patients co-infected the GBV-C, the hepatitis G virus, have a longer survival time to AIDs and higher CD4+ T cell counts than patients that were not infected with GBV-C. GBV-C co-infected patients showed an intact Th-1 profile over time, with high serum levels of IL-2 and IL-12, and diminishing Th-2 responses reflected by lower levels of IL-4 and IL-10. The opposite was true for HIV-1+ patients that were not co-infected with GBV-C. • AIDs progression is slower in patients infected with both HIV-1 and hepatitis G virus. It is unclear whether Th-2 and Th-1 cytokines in co-infected patients show cause or consequence of slower AIDs progression. CD4+ cells may support hepatitis G replication.				
HIV-1	HIV-1		HIV-1 infection	human	Korthals Altes2003
	Keywords dynamics, acute infection. • A model of progression was developed that explicitly assumes CD4+ T-cells are both targets of infection and mediators of the immune response. In this model, high vial inoculum with few initial CD4 T-cells resulted in target-cell-limited infection and high viral load, but with large CD4 clones and low initial inoculum, infection was controlled by CD4+ clones.				

III-C

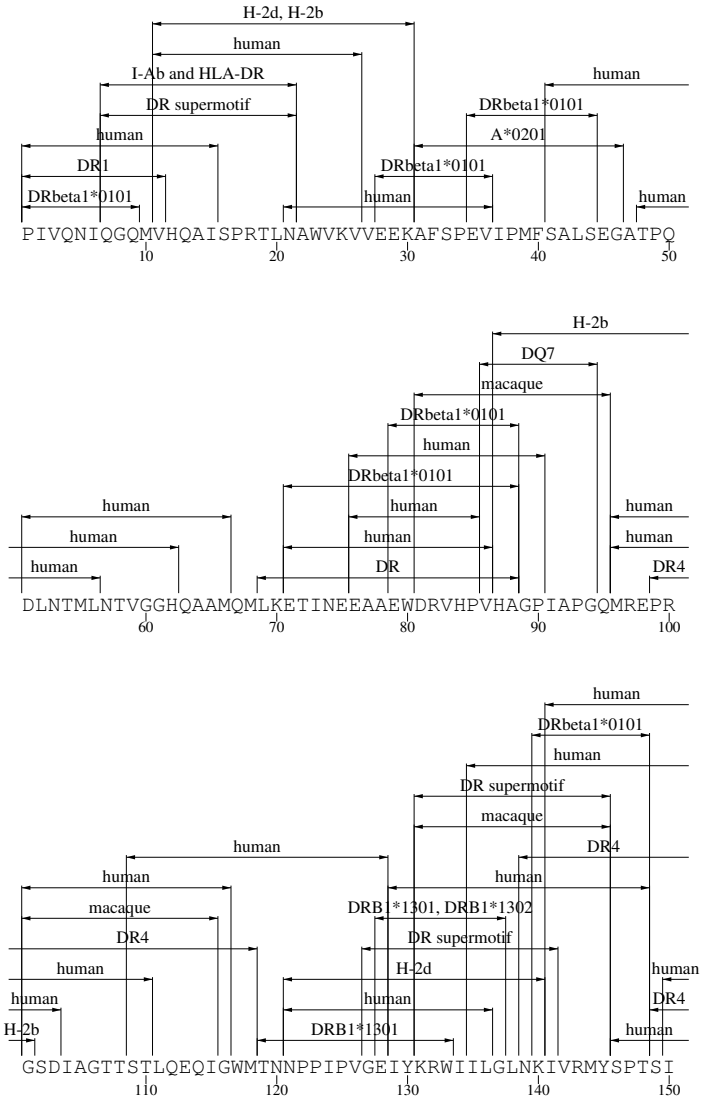
Maps of T-Helper Epitope Locations Plotted by Protein

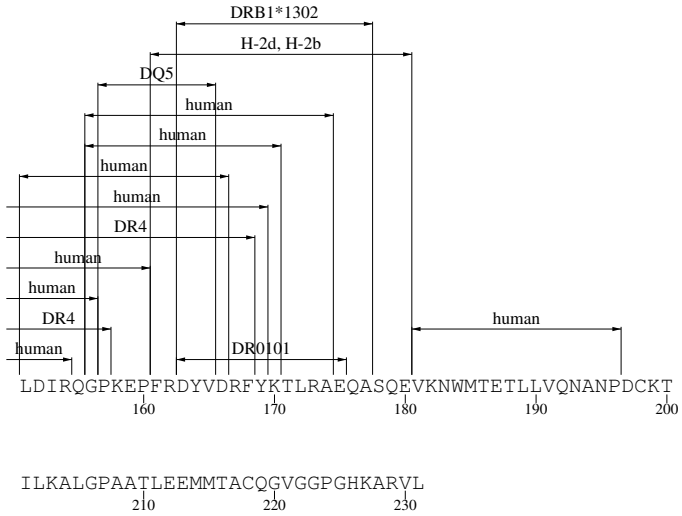
Linear helper T cell epitopes less than twenty-two amino acids long are shown.

III-C-1 p17 T-Helper epitope map

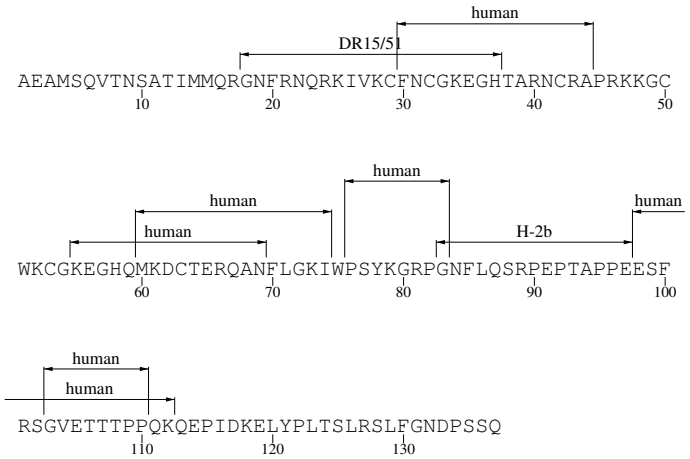


III-C-2 p24 T-Helper epitope map





III-C-3 p2p7p1p6 T-Helper epitope map



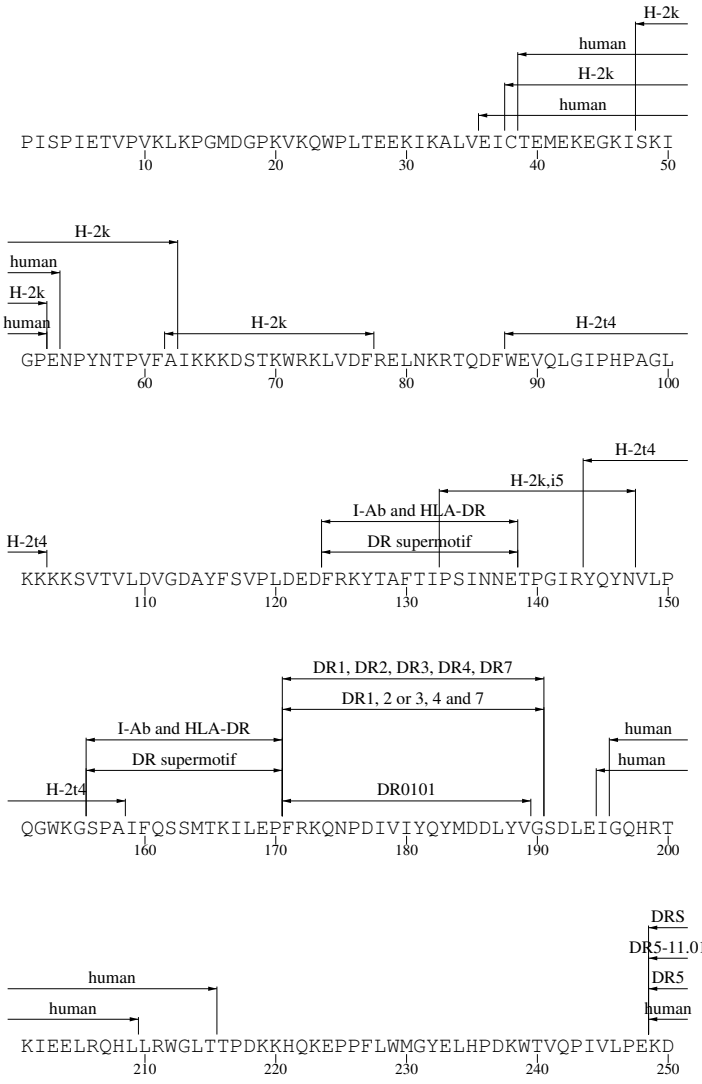
III-C-4 Protease T-Helper epitope map

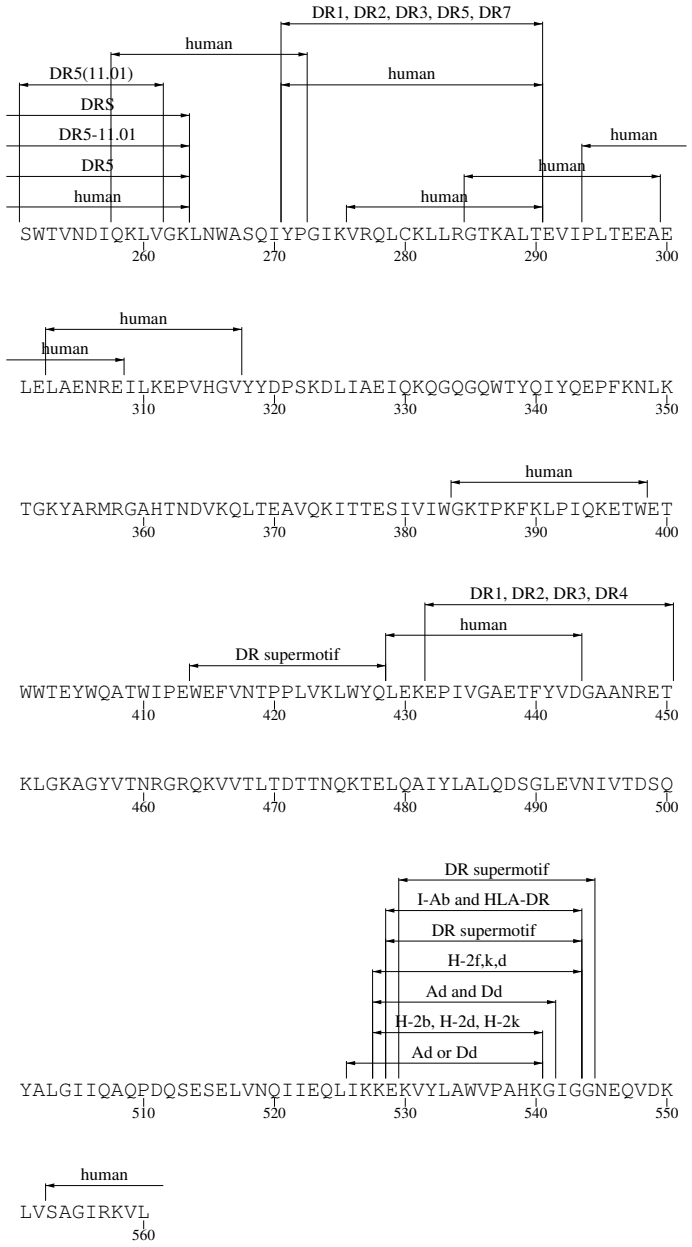
PQVTLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI
10 20 30 40 50

GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF
60 70 80 90

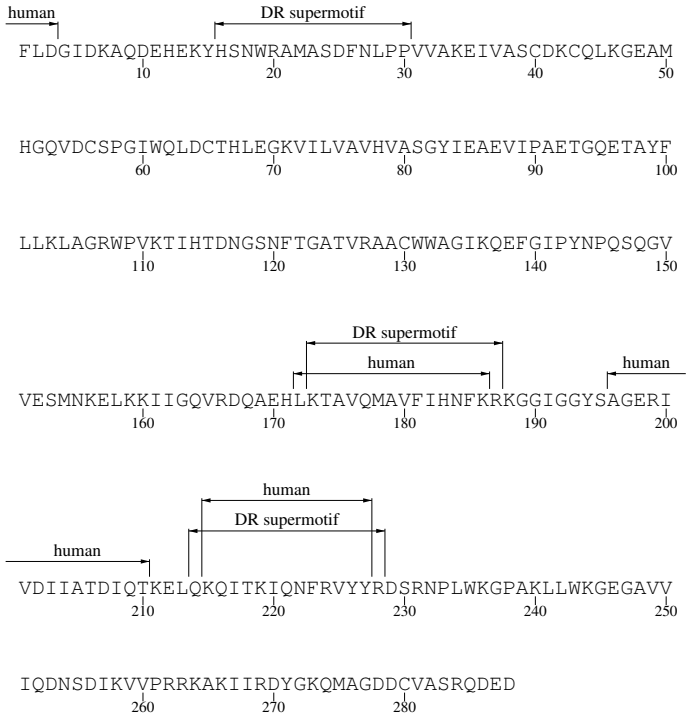
T-Helper

III-C-5 RT T-Helper epitope map

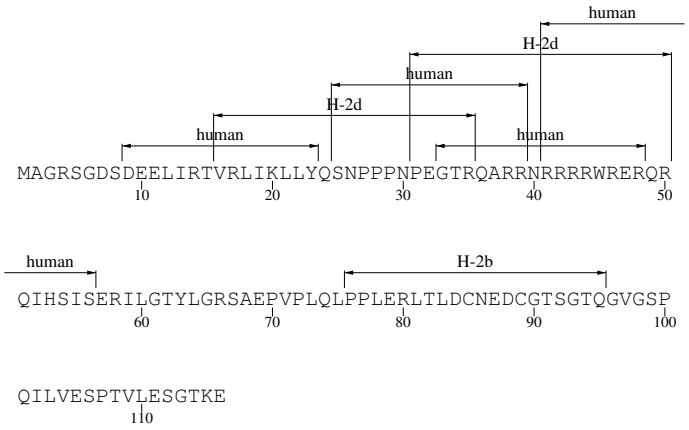




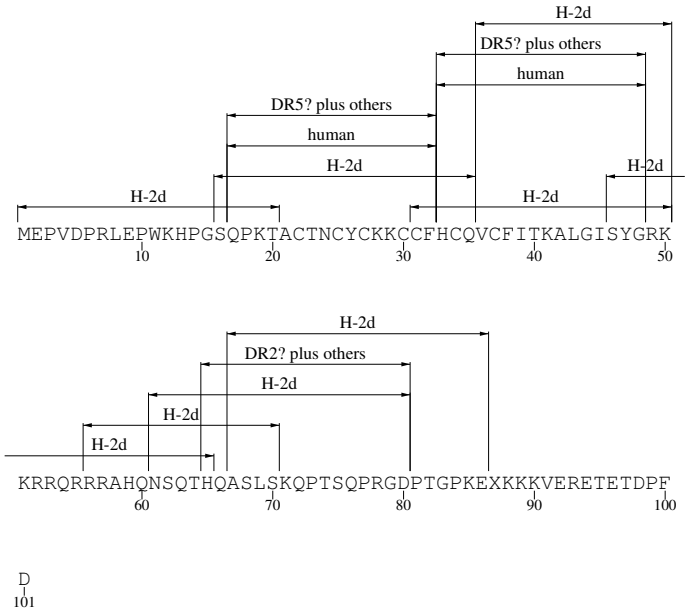
III-C-6 Integrase T-Helper epitope map



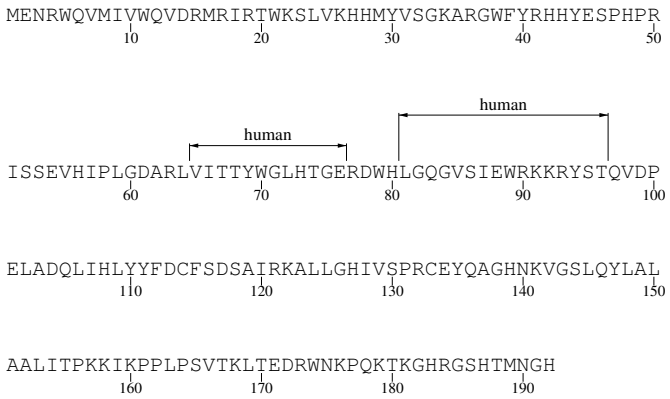
III-C-7 Rev T-Helper epitope map



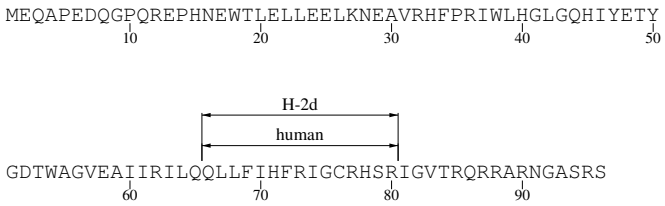
III-C-8 Tat T-Helper epitope map



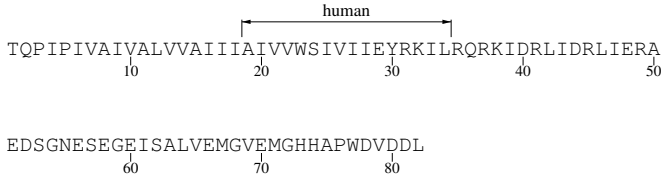
III-C-9 Vif T-Helper epitope map



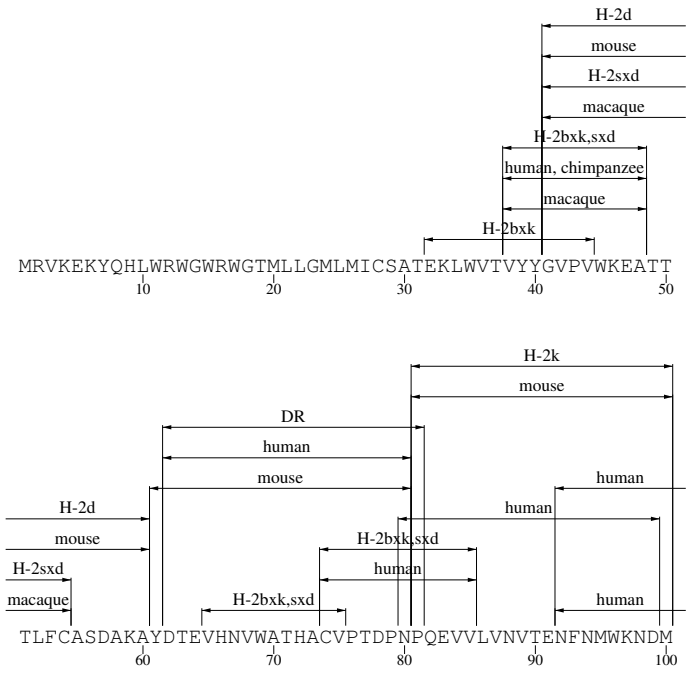
III-C-10 Vpr T-Helper epitope map

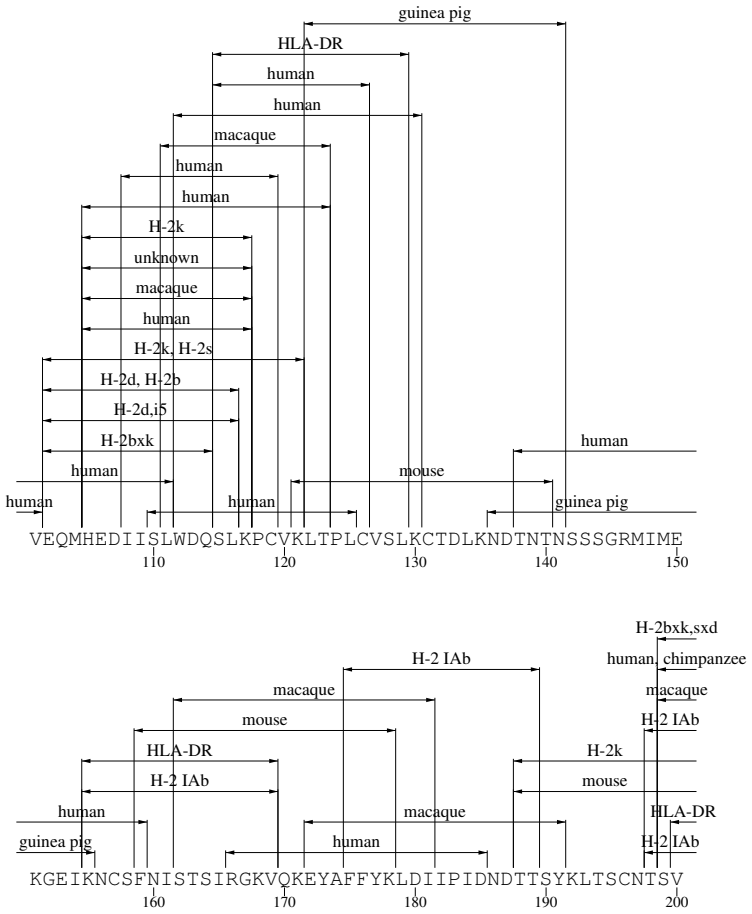


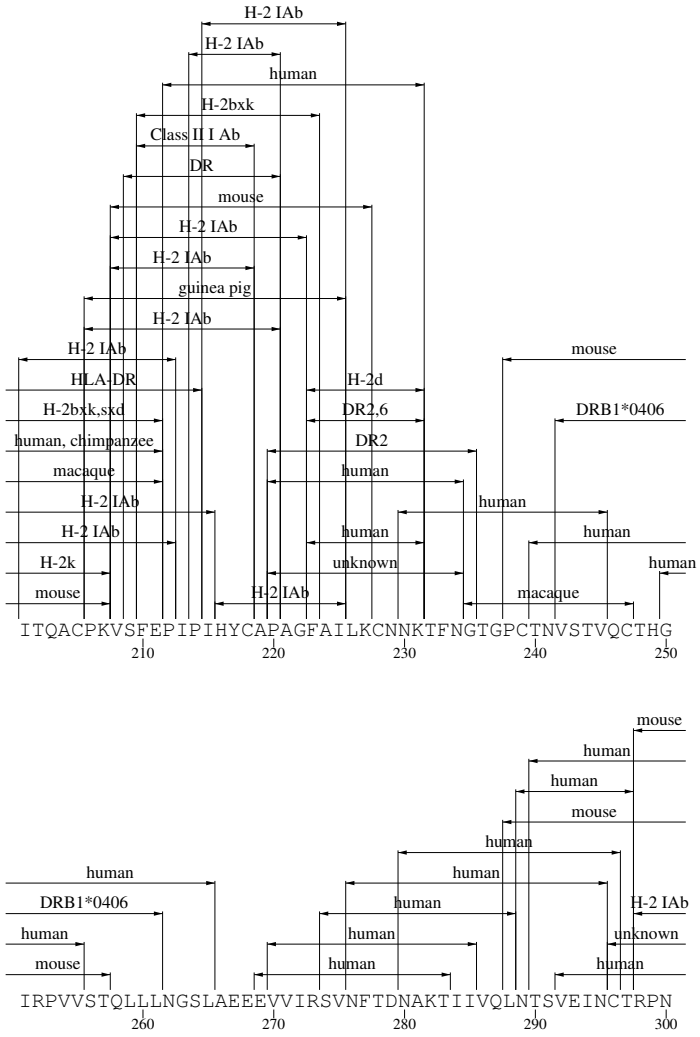
III-C-11 Vpu T-Helper epitope map

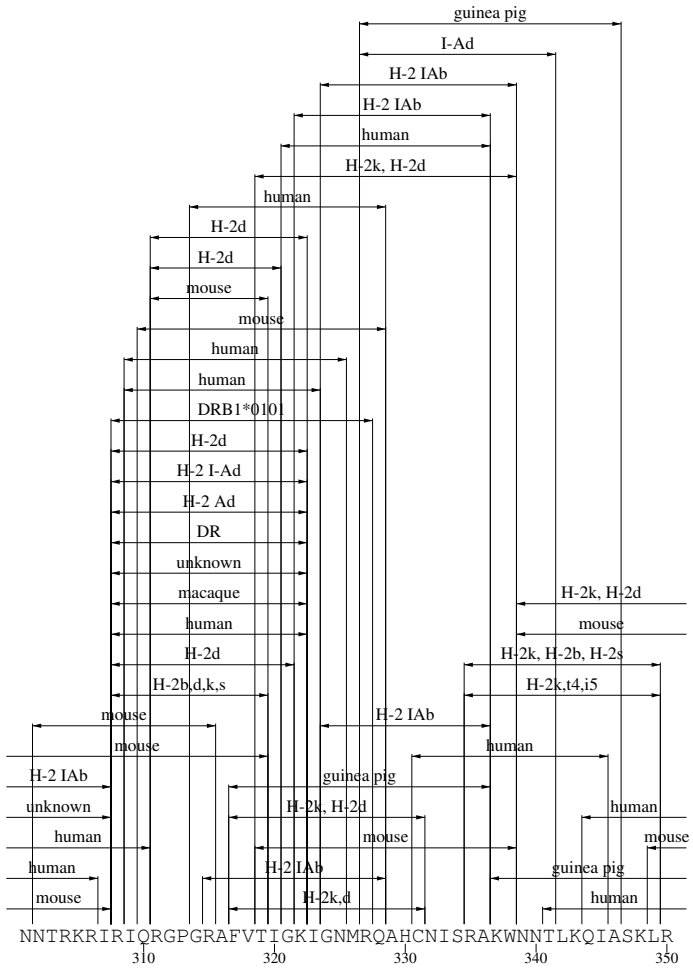


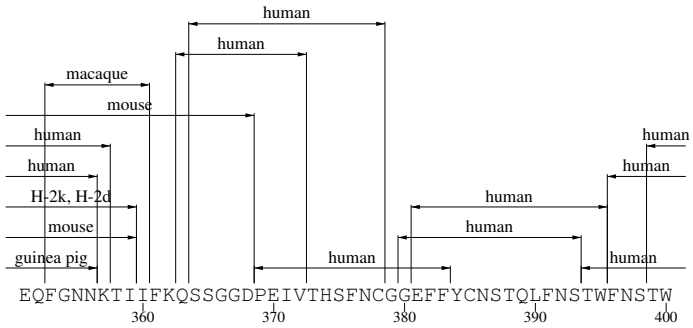
III-C-12 gp160 T-Helper epitope map

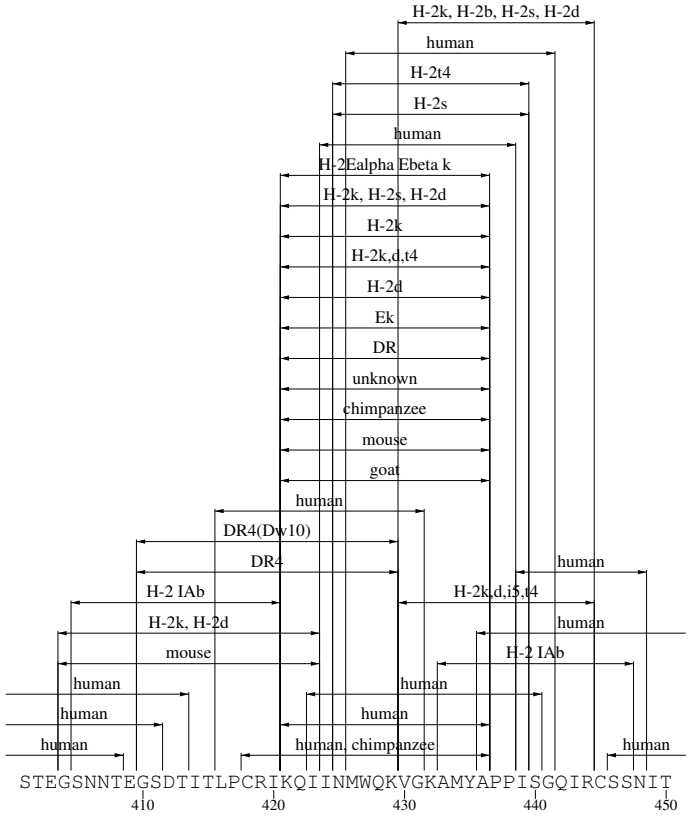


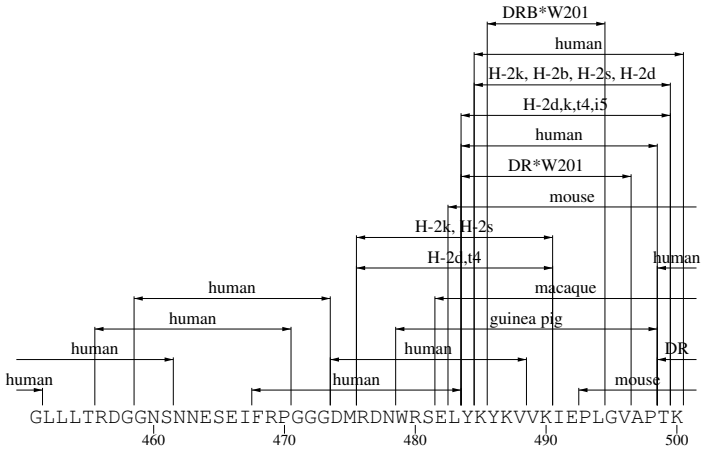


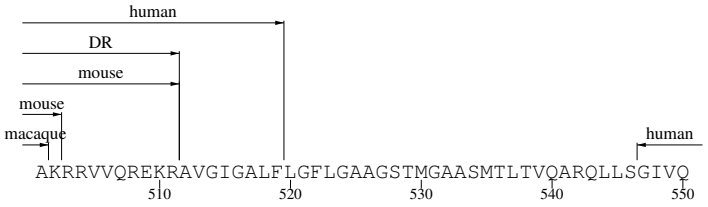

H-2 IAb
H-2 IAb
human
H-2bxk
Class II I Ab
DR
mouse
H-2 IAb
H-2 IAb
guinea pig
H-2 IAb
H-2 IAb
HLA-DR
H-2bxk,sxd
human, chimpanzee
macaque
H-2 IAb
H-2 IAb
H-2k
mouse
H-2d
DR2,6
DR2
human
human
human
unknown
H-2 IAb
mouse
DRB1*0406
human
human
human
human
human
ITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHG
210
220
230
240
250
mouse
human
human
mouse
human
human
DRB1*0406
human
human
H-2 IAb
human
human
unknown
mouse
human
human
IRPVVSTQLLLNGSLAEEEVVIRSVNFTDNAKTIIVQLNTSVEINCTRPN
260
270
280
290
300

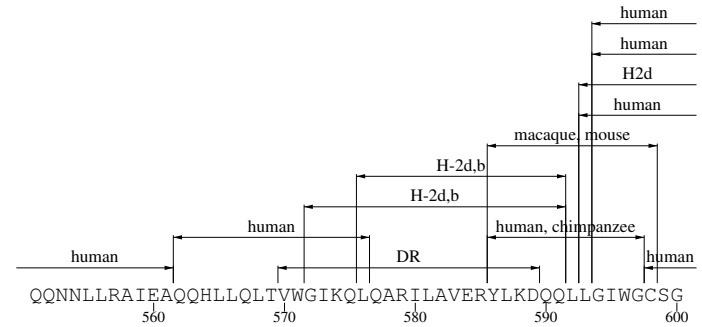

guinea pig
I-Ad
H-2 IAb
H-2 IAb
human
H-2k, H-2d
human
H-2d
H-2d
mouse
mouse
human
human
DRB1*0101
H-2d
H-2 I-Ad
H-2 Ad
DR
unknown
macaque
human
H-2d
H-2b,d,k,s
mouse
mouse
H-2 IAb
guinea pig
unknown
human
human
mouse
H-2 IAb
mouse
H-2k, H-2d
mouse
H-2 IAb
human
H-2k, H-2b, H-2s
H-2k,t4,i5
human
human
mouse
guinea pig
H-2k,d
human
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350

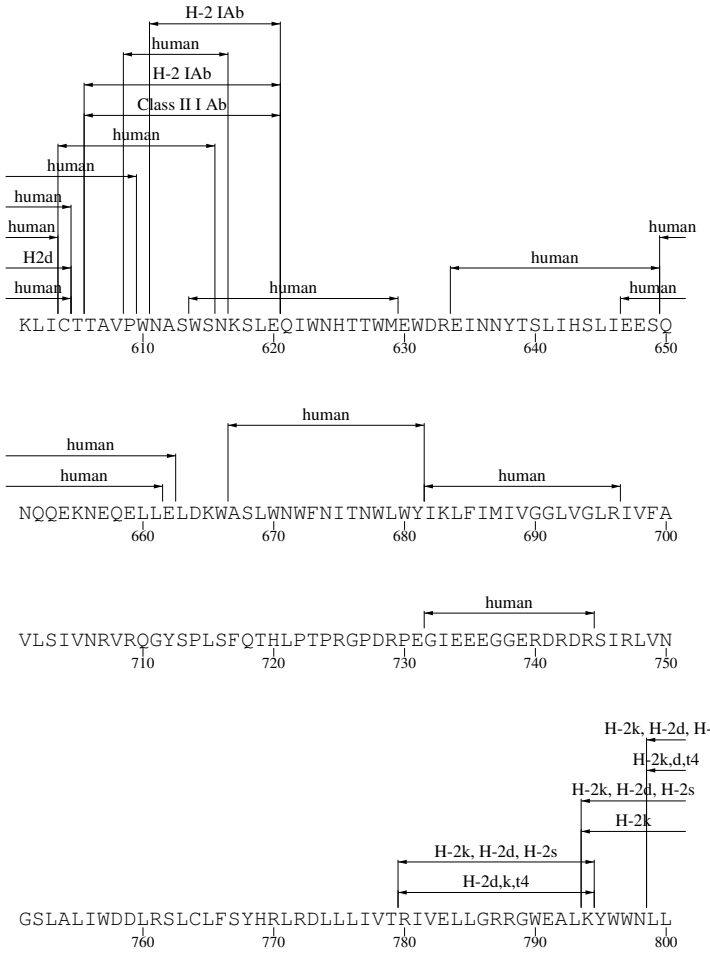

human
human
macaque
mouse
human
human
H-2k, H-2d
mouse
guinea pig
human
human
human
human
human
human
human
EQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
360
370
380
390
400

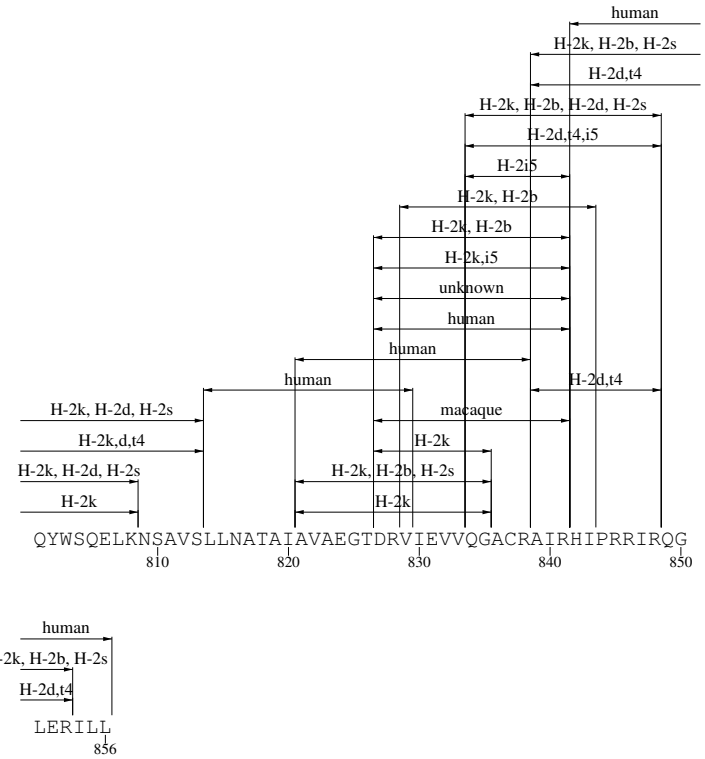

H-2k, H-2b, H-2s, H-2d
human
H-2t4
H-2s
human
H-2Ealpha Ebeta k
H-2k, H-2s, H-2d
H-2k
H-2k,d,t4
H-2d
Ek
DR
unknown
chimpanzee
mouse
goat
human
DR4(Dw10)
DR4
human
H-2 IAb
H-2k,d,i5,t4
H-2k, H-2d
human
mouse
H-2 IAb
human
human
human
human
human
human, chimpanzee
human
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNIT
410
420
430
440
450


DRB*W201
human
H-2k, H-2b, H-2s, H-2d
H-2d,k,t4,i5
human
DR*W201
mouse
H-2k, H-2s
H-2d,t4
human
human
macaque
human
guinea pig
human
human
DR
human
human
mouse
GLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
460
470
480
490
500


human
DR
mouse
mouse
macaque
human
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQ
510
520
530
540
550

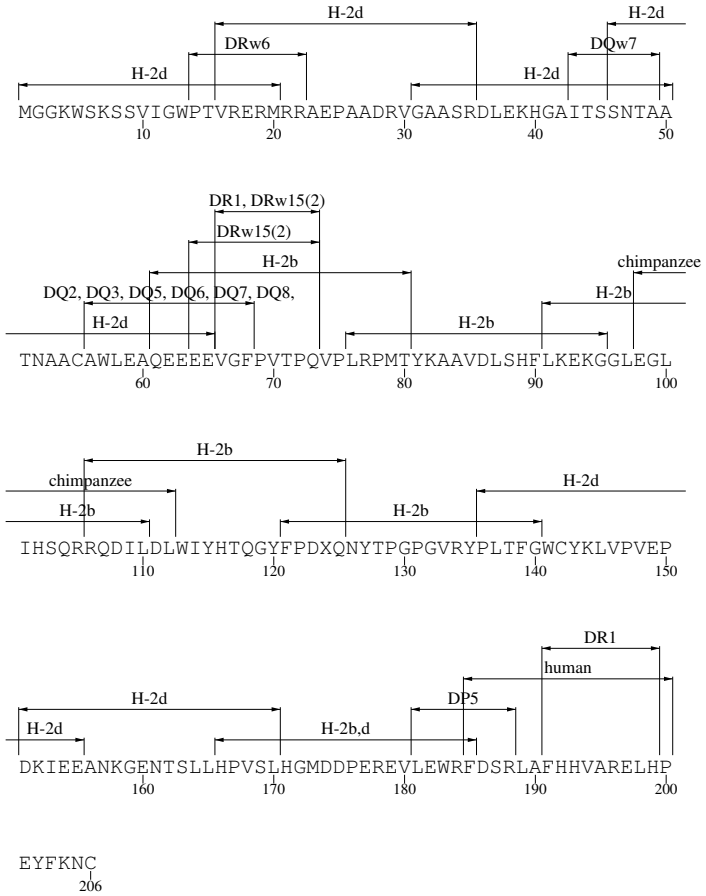

human
human
H2d
human
macaque, mouse
H-2d,b
H-2d,b
human
human, chimpanzee
human
DR
human
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560
570
580
590
600


H-2 IAb
human
H-2 IAb
Class II I Ab
human
human
human
human
H2d
human
human
human
human
human
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610
620
630
640
650
human
human
human
human
NQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
660
670
680
690
700
human
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710
720
730
740
750
H-2k, H-2d, H-2s
H-2k,d,t4
H-2k, H-2d, H-2s
H-2k
H-2k, H-2d, H-2s
H-2d,k,t4
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760
770
780
790
800


human
H-2k, H-2b, H-2s
H-2d,t4
H-2k, H-2b, H-2d, H-2s
H-2d,t4,i5
H-2i5
H-2k, H-2b
H-2k, H-2b
H-2k,i5
unknown
human
human
human
H-2d,t4
H-2k, H-2d, H-2s
macaque
H-2k,d,t4
H-2k
H-2k, H-2d, H-2s
H-2k, H-2b, H-2s
H-2k
H-2k
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQG
810
820
830
840
850
human
H-2k, H-2b, H-2s
H-2d,t4
LERILL
856

T-Helper

III-C-13 Nef T-Helper epitope map



Part IV

HIV Antibody Binding Sites

IV-A

Summary

Part IV summarizes HIV-specific antibodies (Abs) arranged sequentially according to the location of their binding domain, organized by protein. We attempted to make this part as comprehensive as possible. For the monoclonal antibodies (MAbs) capable of binding to linear peptides, we require that the binding site be contained within a region of 30 or so amino acids to define the epitope, but not that the precise boundaries be defined. MAbs that do not bind to defined linear peptides are grouped by category at the end of each protein. Antibody categories, for example CD4 binding site (CD4BS) antibodies, are also noted in the index at the beginning of this part. Studies of polyclonal Ab responses are also included. Responses that are just characterized by binding to a protein, with no known specific binding site, are listed at the end of each protein. For more recent updates, epitope sequence alignments, and search capabilities, please see our web site: `http://www.hiv.lanl.gov/content/immunology`.

IV-A-1 Indices

Three indices are provided. The first provides a concise list of anti-HIV-1 MAbs by cross-competition category, with both discontinuous epitopes (for example, CD4BS) and some well known linear epitopes (for example, cluster I) summarized. The second lists the MAbs' IDs in alphabetical order so one can find their location in the table. The third is a listing by order of appearance in the tables.

IV-A-2 Tables

Each MAb has a twelve-part basic entry:

Number: Order of appearance in this table.

MAb ID: The name of the monoclonal antibody with synonyms in parentheses. MAbs often have several names. For example, punctuation can be lost and names are often shortened (M-70 in one paper can be M70 in another). Polyclonal responses are listed as "polyclonal" in this field.

HXB2 Location: Position of the antibody binding site relative to the viral strain HXB2 (GenBank Accession Number K03455), which is used as a reference strain throughout this publication. The numbering in this table corresponds to the protein maps. Because of HIV-1 variation the epitope may not actually be present in HXB2, rather the position in HXB2 indicates the position aligned to the epitope. HXB2 was selected as the reference strain because so many studies use HXB2, and because crystal structures for HXB2-related proteins are often available. The precise positions of an epitope on the HXB2 reference strain can be readily obtained using the interactive position locator at our web site: `http://www.hiv.lanl.gov/content/hiv-db/LOCATE/locate.html`.

Author Location: The amino acid positions of the epitope boundaries and the reference sequence used to define the epitope are listed as given in the primary publication. Frequently, these positions as published are imprecise, and do not truly correspond to the numbering of the sequence, but they provide a reasonable guide to the peptide's approximate location in the protein. Also, in many cases, position numbers were provided but the reference sequence identification was not. Because of HIV-1's variability, position numbers require a reference strain to be meaningful. Binding sites that cannot be defined through peptide binding or interference studies are labeled as discontinuous. The approximate location on the protein, sequence number, and reference sequence are listed.

Sequence: The amino acid sequence of the binding region of interest, based on the reference strain used in the study defining the binding site. On occasions when only the position numbers and not the actual peptide sequence were specified in the original publication, we tried to fill in the peptide sequence based on the position numbers and reference strain. If the sequences were numbered inaccurately by the primary authors, or if we made a mistake in this process, we may have misrepresented the binding site's amino acid sequence. Because of this uncertainty, epitopes that were not explicitly written in the primary publication, that we determined by looking up the reference strain and the numbered location, are followed

by a question mark in the table.

Neutralizing: **L**: neutralizes lab strains. **P**: neutralizes at least some primary isolates. **no**: does not neutralize. No information in this field means that neutralization was either not discussed or unresolved in the primary publications referring to the MAb.

Immunogen: The antigenic stimulus of the original B cell response. Often this is an HIV-1 infection. If a vaccine was used as the original antigenic stimulation, not a natural infection, this is noted on a separate line, and additional information about the vaccine antigen is provided as available.

Species(Isotype): The host that the antibody was generated in, and the isotype of the antibody.

Research Contact: Information about an antibody or how to obtain it, as well as to provide credit.

References: All publications that we could find that refer to the use of a specific monoclonal antibody. First is a list of all references. Additional details for some of the older references can be found in Part V, although we have tried to keep the entries self-contained since 1997. The "donor" field is meant to serve as a potential guide to a source of information about an antibody or how to obtain it, as well as to provide credit.

Keywords: Keywords for antibody entries were initiated in 2004. The set of keywords includes acute infection; ADCC; adjuvant comparison; anti-idiotype; antibody binding site definition and exposure; antibody generation; antibody interactions; antibody sequence, variable domain; assay development; assay standardization; autologous responses; binding affinity; brain/CSF; co-receptor; complement; enhancing activity; escape; genital and mucosal immunity; HAART; HIV exposed persistently seronegative (HEPS); immunodominance; immunoprophylaxis; immunotherapy; immunotoxin; inter-clade comparisons; isotype switch; kinetics; mimotopes; mother-to-infant transmission; mucosal immunity; rate of progression; responses in children; review; structure; Th1; Th2; vaccine antigen design; vaccine-induced epitopes; vaccine-specific epitope characteristics; and variant cross-recognition or cross-neutralization. The keywords are list when available as part of the main entry, and also follow the note in bold type so references pertaining to particular types of studies can be found quickly.

Notes: Describe the context of each study, and what was learned about the antibody in the study.

IV-A-3 HIV protein binding site maps

The names of MAbs and the location of well characterized linear binding sites of 21 amino acids or less are indicated relative to the protein sequences of the HXB2 clone. This map is meant to provide the relative location of epitopes on a given protein, but the HXB2 sequence may not actually bind to the MAb of interest, as it may vary relative to the sequence for which the epitope was defined. Above each linear binding site, the MAb name is given followed by the species in parentheses. Human is represented by 'h', non-human primate by 'p', mouse by 'm', and others by 'o'. More precise species designations for any given MAb can be found using the web search interface or in the tables in this part.

IV-A-4 Alignments

To conserve space, no epitope alignments are provided in this book, but they can be generated using the MAb search tool at `http://www.hiv.lanl.gov/content/immunology`. All epitopes are aligned to the HXB2 sequence, with the sequence used to define the epitope indicated directly above it. Sequences are sorted by their subtype and country of origin.

The master alignment files from which the epitope alignments were created are available at our web site (`http://www.hiv.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html`). The alignments were modified in some cases to optimize the alignment relative to the defined epitope and minimize insertions and deletions; epitope alignments are generated by anchoring on the C-terminal residue. A dash indicates identity to the consensus sequence, and a period indicates an insertion made to maintain the alignment. Stop codons are indicated with a `$`, and frameshifts by a `#`, or ambiguous codons (nucleotide was `r`, `y`, or `n`) by an `x`; they are inserted to maintain the alignments. In consensus sequences an upper case letter indicates the amino acid was present in all sequences, a lower case letter indicates the amino acid was present in most sequences in a given position, and a question mark indicates two or more amino acids were represented with equal frequency.

IV-B

Cross Reference Listing of MAbs

IV-B-1 MAbs by binding type

Cross reference by protein and binding type of MAb names and their order of appearance in the tables.

Binding type	MAb ID (No.)
p17	
C-term	sc-FV p17 (33)
p24	
C-term	13B5 (115)
Protease	
N-term	1696 (173)
flap region	F11.2.32 (175)
RT	
C2	polyclonal (181)
palm domain	6B9 (201)
thumb domain	5F (202), 5G (203), 7C4 (204)
Integrase	
Integrase DNA binding domain	5D9 (221), 2-19 (224), 8-22 (225), 4-20 (226), 6-19 (227)
Integrase catalytic core	7-16 (218), 4F6 (219)
N-term	1C4 (205), 2C11 (206), 2E3 (207), 3E11 (208), 3F9 (209), 5F8 (210), 6G5 (211), 7B6 (212), 7C6 (213), 6C5 (214), 4D6 (217)
Pol	
C-term	F-6 (245), 33 (253)
Vif	
C-term	TG001 (255)
Tat	
C-term	polyclonal (259), polyclonal (270), polyclonal (271), 1D2F11 (273), 2D9E7 (274), 4B4C4 (275), 5G7D8 (276), NT2/4D5.24 (278), polyclonal (279), polyclonal (290), polyclonal (291), polyclonal (292), 2D9D5 (295)
N-term	polyclonal (259), TA9 (260), TD84 (261), TE135 (262), polyclonal (264), NT3/2D1.1 (265), 1D9D5 (267), polyclonal (270), polyclonal (271), polyclonal (279), TC15 (282), polyclonal (284), polyclonal (285), polyclonal (290), polyclonal (291), polyclonal (292)

Binding type	MAb ID (No.)
Tat basic region	polyclonal (259), TB12 (268), polyclonal (270), polyclonal (271), polyclonal (272), polyclonal (279), polyclonal (290), polyclonal (291), polyclonal (292)
Env (gp160)	
C-HR	polyclonal (1055)
C-domain	polyclonal (640), 5B2 (711), 9G11 (712), TH-Ab1 (713), polyclonal (714), polyclonal (715), polyclonal (716), polyclonal (717)
C-term	105-306 (612), 750-D (614), 722-D (618), polyclonal (619), 1131-A (620), 858-D (621), 989-D (622), 2F5 (707), 14D9 (709), 4E10 (718), Z13 (719), 1575 (740), polyclonal (744), polyclonal (745), 1577 (747), polyclonal (748), T26 (843), 101-342 (935), 101-451 (936), 120-1 (937), D33 (1046)
C1	M85 (308), 7E2/4 (309), 4D4#85 (310), M92 (311), M86 (312), polyclonal (313), 133/237 (314), 133/290 (315), 133/11 (316), D/3G5 (317), D/6A11 (318), D/5E12 (319), L5.1 (320), 4A7C6 (321), 1D10 (322), B242 (323), 133/192 (324), 489.1(961) (325), 5B3 (326), B10 (327), B2 (328), C6 (329), MF49.1 (330), T1.1 (331), T7.1 (332), T9 (333), GV4D3 (334), B27 (335), B9 (336), B35 (337), D/4B5 (338), D/5A11 (339), D/6B2 (340), B18 (341), B20 (342), MF39.1 (343), 187.2.1 (344), 37.1.1(ARP 327) (345), 6D8 (346), M96 (347), MF119.1 (348), MF4.1 (349), MF53.1 (350), MF58.1 (351), MF77.1 (352), T2.1 (353), 11/65 (354), W1 (355), T11 (356), GV1A8 (357), 11 (358), 12G10 (359), 135/9 (360), 7C10 (361), C4 (362), MF46.1 (363), P35 (838), 212A (938), 522-149 (939), L19 (940), M90 (941), MAG 104 (942), MAG 45 (943), MAG 95 (944), MAG 97 (945), T9 (946), p7 (947)
C1-C2	L100 (948)
C1-C4	2/11c (949), A32 (950)
C1-C5	C11 (951), L81 (952)
C2	1006-30-D (404), 847-D (405), 213.1 (409), B12 (410), B13 (411), C13 (412), M89 (413), B21 (414), B23 (415), B24 (416), B25 (417), B3 (418), B26 (419), B29 (420), B36 (421), 110.E (422), 110.C (423)
C3	2H1B (377), 110.D (560), B32 (561), ICR38.1a (572), 2F19C (953), B2C (954), polyclonal (955)
C4	5C2E5 (567), G3-211 (568), G3-537 (569), ICR38.1a (572), G3-299 (573), G3-42 (574), G3-508 (575), G3-519 (576), G3-536 (577), ICR38.8f (578), MO86/C3 (579), 13H8 (580), G45-60 (581), polyclonal (582), 1662 (583), 1663 (584), 1664 (585), 1697 (586), 1794 (587), 1804 (588), 1807 (589), 1808 (590), 4KG5 (775), 1024 (956)
C5	9201 (595), 1C1 (596), 3F5 (597), 5F4/1 (598), 660-178 (599), 9301 (600), B221 (601), H11 (603), W2 (604), M38 (605), 110.1 (608), 42F (609), 43F (610), RV110026 (611), GV1G2 (613), 450-D (615), 670-D (616), 1331A (623), 23A (957), D7324 (958)

Binding type	MAb ID (No.)
CD4BS	polyclonal (570), 1795 (571), 1008-D (755), 1125H (760), FG39 (811), Fbb14 (815), Ia3 (825), Ia7 (826), 10/46c (959), 1027-30-D (960), 1125H (961), 120-1B1 (962), 1202-D (963), 1331E (964), 1570 (965), 1595 (966), 1599 (967), 15e (968), 21h (969), 28A11/B1 (970), 2G6 (971), 35F3/E2 (972), 38G3/A9 (973), 428 (974), 448-D (975), 46D2/D5 (976), 48-16 (977), 50-61A (978), 5145A (979), 558-D (980), 559/64-D (981), 55D5/F9 (982), 588-D (983), 654-D (984), 67G6/C4 (985), 729-D (986), 830D (987), 9CL (988), BM12 (989), D20 (990), D21 (991), D24 (992), D25 (993), D28 (994), D35 (995), D39 (996), D42 (997), D52 (998), D53 (999), D60 (1000), DA48 (1001), DO8i (1002), F105 (1003), F91 (1004), GP13 (1005), GP44 (1006), GP68 (1007), HF1.7 (1008), HT5 (1009), HT6 (1010), HT7 (1011), ICR 39.13g (1012), ICR 39.3b (1013), IgG1b12 (1014), IgGCD4 (1015), L28 (1016), L33 (1017), L41 (1018), L42 (1019), L52 (1020), L72 (1021), M12 (1022), M13 (1023), M6 (1024), MAG 116 (1025), MAG 12B (1026), MAG 29B (1027), MAG 3B (1028), MAG 55 (1029), MAG 72 (1030), MAG 86 (1031), MAG 96 (1032), MTW61D (1033), S1-1 (1034), T13 (1035), T49 (1036), T56 (1037), TH9 (1038), anti-CD4BS summary (1039), b11 (1040), b13 (1041), b14 (1042), b3 (1043), b6 (1044), polyclonal (1045), D33 (1046), (1047)
CD4i	E51 (566), Fbb21 (816), Fbb21 (817), A32 (950), (1047), 17b (1048), 21c (1049), 23e (1050), 48d (1051), 49e (1052), X5 (1053)
Env oligomer	T22 (1054)
Leucine zipper motif	(632), (633)
N-HR	polyclonal (1055)
N-term	polyclonal (641), D33 (1046), 2A2 (1056), AC4 (1057), AD3 (1058), AD3 (1059), ID6 (1060), ID6 (1061)
V1	35D10/D2 (367), 40H2/C7 (368), 43A3/E4 (369), 43C7/B9 (370), 45D1/B7 (371), 46E3/E6 (372), 58E1/B3 (373), 64B9/A6 (374), 69D2/A1 (375), 82D3/C3 (376), polyclonal (591)
V1-V2	4KG5 (775), 11/68b (1062), 62c (1063), CRA-6 (1064), L15 (1065), T52 (1066), T54 (1067)
V1-V2 and V3-V5	polyclonal (1068)
V2	6D5 (364), B33 (365), 697-D (378), C108G (380), 11/4c (385), 8.22.2 (386), 12b (387), G3-136 (388), G3-4 (389), polyclonal (591), (1047), 1088 (1069), 110-B (1070), 1357 (1071), 1361 (1072), 1393A (1073), 66a (1074), 66c (1075), 684-238 (1076), 830A (1077), CRA-3 (1078), CRA-4 (1079), L17 (1080), SC258 (1081)
V2-CD4BS	L25 (1082), L39 (1083), L40 (1084), L78 (1085)

Binding type	MAb ID (No.)
V3	IIIB-V3-26 (424), IIIB-V3-21 (425), polyclonal (426), polyclonal (427), MO97/V3 (428), polyclonal (429), 55/1l (430), 8/38c (431), 8/64b (432), polyclonal (433), polyclonal (434), polyclonal (435), polyclonal (436), 9284 (437), polyclonal (438), polyclonal (439), polyclonal (440), polyclonal (441), MAG 109 (442), MAG 49 (443), MAG 53 (444), MAG 56 (445), 1324-E (446), polyclonal (447), MO99/V3 (448), C311E (449), 924 (451), polyclonal (452), polyclonal (453), 10F10 (454), 2C4 (455), 412-D (456), polyclonal (457), CGP 47 439 (458), polyclonal (459), 178.1 (460), 257-D (461), 311-11-D (462), 41148D (463), 391/95-D (464), Aw (465), Bw (466), DO142-10 (467), Dv (468), Fv (469), Gv (470), Hv (471), polyclonal (472), 50.1 (473), polyclonal (474), BAT123 (475), 838-D (476), 1006-15D (477), 782-D (478), 908-D (479), 1027-15D (480), F19.26-4 (481), F19.48-3 (482), F19.57-11 (483), M77 (484), polyclonal (485), SP.BAL114 (486), SP.SF2:104 (487), polyclonal (488), 19b (489), 4G10 (490), 5F7 (491), G3-523 (492), MN215 (493), Nea 9301 (494), 4117C (495), 419-D (496), 453-D (497), 504-D (498), 83.1 (499), 5023B (500), F58/D1 (501), P1/D12 (502), P4/D10 (503), IIIB-13 V3 (504), IIIB-34 V3 (505), A47/B1 (506), D59/A2 (507), G44/H7 (508), MO96/V3 (509), μ5.5 (510), loop 2 (511), 268-D (512), 386-D (513), 5042A (514), 5042B (515), 418-D (516), 5021 (517), 5025B (518), 5042 (519), 110.3 (520), 110.4 (521), 110.5 (522), 58.2 (523), 537-D (525), 5020 (526), RC25 (527), 5023A (528), 110.6 (529), polyclonal (530), 10/36e (531), 10/54 (532), 11/85b (533), polyclonal (534), 0.5β (535), Cβ1, 0.5β (536), NM-01 (537), 1026 (538), 1034 (539), 59.1 (540), polyclonal (541), 10E3 (542), polyclonal (543), N11-20 (544), 5025A (545), N70-1.9b (546), 902 (547), 694/98-D (548), 9205 (552), 110.I (553), anti-HIV-2 polyclonal (554), IIIB-V3-01 (555), polyclonal (591), 447-52D (723), 4KG5 (775), A1g8 (789), Ag1211 (793), B4a1 (795), B4e8 (796), polyclonal (917), (1047), (1086), 110.J (1087), 1334-D (1088), 2182 (1089), 2191 (1090), 2219 (1091), 2412 (1092), 2442 (1093), 2456 (1094), 39F (1095), 55/68b (1096), 5G11 (1097), 6.1 (1098), 6.7 (1099), 8.27.3 (1100), 8E11/A8 (1101), 9305 (1102), AG1121 (1103), D47 (1104), F5.5 (1105), G3-1472 (1106), K24 (1107), TH1 (1108), anti-gp120/V3 (1109), polyclonal (1110), polyclonal (1111), polyclonal (1112), polyclonal (1113), polyclonal (1114), polyclonal (1115), polyclonal (1116), polyclonal (1121), D27 (1123), D56 (1124)
V3 discontinuous	11/75a/21/41 (1117), 41.1 (1118), 55/45a/1l (1119)
V3 mimotope	1108 (1120)
V3-C4	MO101/V3,C4 (549), polyclonal (1122)
V3-C5	MO101/V3,C4 (550), MO101/V3,C4 (551)
V4	D/6D1 (556), 4D7/4 (557), 36.1(ARP 329) (558), C12 (559), polyclonal (562), B15 (563), B34 (564), polyclonal (591), polyclonal (1121)
V5	polyclonal (591), polyclonal (592)
V5-C5	CRA1(ARP 323) (593), M91 (594), 8C6/1 (602)
adjacent to cluster II	2F5 (707), 14D9 (709)
alpha-helical hairpin intermediate	98-6 (703), polyclonal (931)
carbohydrates at glycosylation residues in C2, C3, C4, and V4	2G12 (1125)
cluster I	50-69 (644), 246-D (662), 181-D (665), 240-D (666), F240 (667), D49 (668), D61 (669), T32 (670), T34 (671), 3D6 (698), 7B2 (785), 1367 (1126)

Binding type	MAb ID (No.)
cluster II	D50 (700), 98-6 (703), 167-7 (704), ND-15G1 (705), 167-D (706), 2.2B (766), 126-6 (1127), 1342 (1128), 1379 (1129), Fab D11 (1130), Fab D5 (1131), Fab G1 (1132), Fab M10 (1133), Fab M12 (1134), Fab M15 (1135), Fab S10 (1136), Fab S6 (1137), Fab S8 (1138), Fab S9 (1139), Fab T3 (1140), Md-1 (1141), 1281 (1142)
cluster III	Fab A9 (1143), Fab G15 (1144), Fab G5 (1145), Fab L1 (1146), Fab L11 (1147), Fab L2 (1148)
cytoplasmic domain	Chessie 8 (1149)
gp120-CD4 complex	8F101 (1150), 8F102 (1151), CG-10 (1152), CG-25 (1153), CG-4 (1154), CG-76 (1155), CG-9 (1156)
immunodominant region	3D6 (698), 105-518 (1157)
p24+gp41	31A1 (1158), 39A64 (1159), 39B86 (1160), 9303 (1161)
six-helix bundle	167-D (706), polyclonal (1055), 1281 (1142), NC-1 (1162)
Nef	
C-term	AE6 (1203), AG11 (1204), EH1 (1205), AE6 (1213)

IV-B-2 Alphabetical listing of MAbs

Cross reference of MAb names and their order of appearance in the tables. Alphanumeric sorting is symbols, digits and letters.

MAb ID	No.
	280
	632
	633
	750
	751
	752
	753
	754
	1047
	1086
	1214
α(566-586)	628
μ5.5	510
0.5β	535
1-B-7	68
1-E-4	57
1-E-9	58
1.152 B3	182
1.153 G10	190
1.158 E2	183
1.160 B3	194
1.17.3	89
1.2	266
10-E-7	59
10-G-9	60
10.1	298
10/36e	531
10/46c	959
10/54	532
10/76b	381
1006-15D	477
1006-30-D	404
1008-D	755
101-342	935
101-451	936
102-135	756
1024	956
1025	757
1026	538
1027-15D	480
1027-30-D	960
1034	539
105-134	758
105-306	612
105-518	1157
105-732	697
106/01	116
108/03	110
1088	1069
10E3	542
10E7	174
10E9	759
10F10	454
11	358
11-C-5	61
11/41e	382
11/4b	383
11/4c	385
11/65	354
11/68b	1062
11/75a/21/41	1117
11/85b	533
110-B	1070
110.1	400
110.1	608
110.3	520
110.4	521
110.5	522
110.6	529
110.C	423
110.D	560
110.E	422
110.I	553
110.J	1087
110/015	111
1108	1120
1109/01	49
111/052	46
111/073	55
111/182	36
112/021	37
112/047	38
1125H	760
1125H	961
113/038	56
113/072	74
1131-A	620
115.8	672
11C10B10	105
11D11F2	106
11H9	24
12	232
12-B-4	102
120-1	937
120-16	702
120-1B1	962
1202-D	963
126-50	761
126-6	1127
1281	1142
12b	387
12G-A8g2	18
12G-D7h11	19
12G-H1c7	20
12G10	359
12H-D3b3	17
12H2	762
12I-D12g2	21
13	233
13-102-100	76
13.10	763
13/035	1166
13/042	1165
13/058	1176
1324-E	446
133/11	316
133/192	324
133/237	314
133/290	315
1331A	623
1331E	964
1334-D	1088
1342	1128
135/9	360
1357	1071
1361	1072
1367	1126
1379	1129
1393A	1073
13B5	115
13E1	176
13H8	580
14	234
14D4E11	50
14D9	709
15-21	31
1570	965
1575	740
1576	727
1577	747
1578	728
1579	729
1583	730
1595	966
1599	967
15e	968
15F8C7	45
16	235
16/4/2	134
1662	583
1663	584
1664	585
167-7	704
167-D	706
1696	173
1697	586
17	216
178.1	460
1794	587
1795	571
17b	1048
1804	588
1807	589
1808	590
181-D	665
183-H12-5C	135
187.2.1	344
1899	731
19	223
1907	732
1908	733
1909	734
19b	489
1A1	624
1A7	90
1B1	764
1B2C12	86
1B8.env	686
1C1	596
1C12B1	236
1C4	205
1D10	322
1D2F11	273
1D4A3	192
1D9	27
1D9D5	267
1E8	180
1F11	634
1F6	91
1F7	765
1G10	304
1G5C8	51
1G7	305
1H5	635
2-19	224
2-E-4	62
2-H-4	63
2.2B	766
2/11c	949

LH-104-G	119	MAG 6B	832	NF1A1	1200	polyclonal	257	polyclonal	474
LH-104-I	118	MAG 72	1030	NF2B2	1209	polyclonal	258	polyclonal	485
LH-104-K	87	MAG 86	1031	NF3A3	1210	polyclonal	259	polyclonal	488
loop 2	511	MAG 95	944	NF8B4	1211	polyclonal	263	polyclonal	524
M-1	673	MAG 96	1032	NM-01	537	polyclonal	264	polyclonal	530
M-11	674	MAG 97	945	NT2/4D5.24	278	polyclonal	269	polyclonal	534
M-13	675	Md-1	1141	NT3/2D1.1	265	polyclonal	270	polyclonal	541
M-2	676	MF119.1	348	P1/D12	502	polyclonal	271	polyclonal	543
M-22	677	MF169.1	406	P35	838	polyclonal	272	polyclonal	562
M-24	678	MF170.1	407	P4/D10	503	polyclonal	277	polyclonal	570
M-25	679	MF39.1	343	P43110	839	polyclonal	279	polyclonal	582
M-28	680	MF4.1	349	P5-3	840	polyclonal	283	polyclonal	591
M-29	681	MF46.1	363	p7	947	polyclonal	284	polyclonal	592
M-36	682	MF49.1	330	PC5009	629	polyclonal	285	polyclonal	607
M-4	683	MF53.1	350	polyclonal	2	polyclonal	286	polyclonal	617
M-6	684	MF58.1	351	polyclonal	22	polyclonal	287	polyclonal	619
M12	122	MF77.1	352	polyclonal	42	polyclonal	288	polyclonal	631
M12	1022	MF87.1	408	polyclonal	47	polyclonal	289	polyclonal	640
M13	1023	MN215	493	polyclonal	54	polyclonal	290	polyclonal	641
m18	848	MO101/V3,C4	549	polyclonal	79	polyclonal	291	polyclonal	642
M25	831	MO101/V3,C4	550	polyclonal	82	polyclonal	292	polyclonal	656
M38	605	MO101/V3,C4	551	polyclonal	95	polyclonal	293	polyclonal	658
M6	1024	MO28	833	polyclonal	157	polyclonal	294	polyclonal	659
M77	484	MO30	834	polyclonal	158	polyclonal	313	polyclonal	660
M85	308	MO43	835	polyclonal	159	polyclonal	366	polyclonal	663
M86	312	MO86/C3	579	polyclonal	160	polyclonal	395	polyclonal	687
M89	413	MO9.42.2	97	polyclonal	161	polyclonal	426	polyclonal	688
M90	941	MO9.50.2	98	polyclonal	162	polyclonal	427	polyclonal	696
M91	594	MO96/V3	509	polyclonal	163	polyclonal	429	polyclonal	708
M92	311	MO97/V3	428	polyclonal	164	polyclonal	433	polyclonal	710
M96	347	MO99/V3	448	polyclonal	165	polyclonal	434	polyclonal	714
MAb 35	231	MTW61D	1033	polyclonal	166	polyclonal	435	polyclonal	715
MAG 104	942	multiple Fabs	849	polyclonal	167	polyclonal	436	polyclonal	716
MAG 109	442	multiple MAbs	850	polyclonal	168	polyclonal	438	polyclonal	717
MAG 116	1025	multiple MAbs	851	polyclonal	169	polyclonal	439	polyclonal	721
MAG 12B	1026	multiple MAbs	852	polyclonal	170	polyclonal	440	polyclonal	744
MAG 29B	1027	N11-20	544	polyclonal	171	polyclonal	441	polyclonal	745
MAG 3B	1028	N2-4	836	polyclonal	181	polyclonal	447	polyclonal	748
MAG 45	943	N70-1.9b	546	polyclonal	189	polyclonal	452	polyclonal	853
MAG 49	443	N70-2.3a	837	polyclonal	195	polyclonal	453	polyclonal	854
MAG 53	444	NC-1	1162	polyclonal	250	polyclonal	457	polyclonal	855
MAG 55	1029	ND-15G1	705	polyclonal	251	polyclonal	459	polyclonal	856
MAG 56	445	Nea 9301	494	polyclonal	252	polyclonal	472	polyclonal	857

polyclonal	858	polyclonal	901	polyclonal	1115	T2.1	353
polyclonal	859	polyclonal	902	polyclonal	1116	T20	842
polyclonal	860	polyclonal	903	polyclonal	1121	T22	1054
polyclonal	861	polyclonal	904	polyclonal	1122	T26	843
polyclonal	862	polyclonal	905	polyclonal	1164	T27	844
polyclonal	863	polyclonal	906	polyclonal	1173	T3	845
polyclonal	864	polyclonal	907	polyclonal	1174	T30	846
polyclonal	865	polyclonal	908	polyclonal	1179	T32	670
polyclonal	866	polyclonal	909	polyclonal	1186	T34	671
polyclonal	867	polyclonal	910	polyclonal	1187	T4	847
polyclonal	868	polyclonal	911	polyclonal	1188	T49	1036
polyclonal	869	polyclonal	912	polyclonal	1201	T52	1066
polyclonal	870	polyclonal	913	polyclonal	1212	T54	1067
polyclonal	871	polyclonal	914	polyclonal	1215	T56	1037
polyclonal	872	polyclonal	915	polyclonal	1216	T7.1	332
polyclonal	873	polyclonal	916	polyclonal	1217	T9	333
polyclonal	874	polyclonal	917	polyclonal	1218	T9	946
polyclonal	875	polyclonal	918	polyclonal	1219	TA9	260
polyclonal	876	polyclonal	919	polyclonal	1220	TB12	268
polyclonal	877	polyclonal	920	polyclonal	1221	TC15	282
polyclonal	878	polyclonal	921	polyclonal	1222	TD84	261
polyclonal	879	polyclonal	922	polyclonal	1223	TE135	262
polyclonal	880	polyclonal	923	polyclonal α577-596	630	TG001	255
polyclonal	881	polyclonal	924	polyclonal α598-609	685	TG002	254
polyclonal	882	polyclonal	925	polyclonal HIVIG	172	TH-Ab1	713
polyclonal	883	polyclonal	926	RC25	527	TH1	1108
polyclonal	884	polyclonal	927	RL4.72.1	77	TH9	1038
polyclonal	885	polyclonal	928	RSD-33	384	V10	99
polyclonal	886	polyclonal	929	RT-4	246	V10-9	657
polyclonal	887	polyclonal	930	RT6H	193	V107	100
polyclonal	888	polyclonal	931	RT7O	247	V7-8	154
polyclonal	889	polyclonal	932	RT7U	248	W1	355
polyclonal	890	polyclonal	933	RTMAb8	191	W2	604
polyclonal	891	polyclonal	934	RV110026	611	X5	1053
polyclonal	892	polyclonal	955	S1-1	1034	Z13	719
polyclonal	893	polyclonal	1045	sc-FV p17	33		
polyclonal	894	polyclonal	1055	SC258	1081		
polyclonal	895	polyclonal	1068	SP.BAL114	486		
polyclonal	896	polyclonal	1110	SP.SF2:104	487		
polyclonal	897	polyclonal	1111	T1.1	331		
polyclonal	898	polyclonal	1112	T11	356		
polyclonal	899	polyclonal	1113	T13	1035		
polyclonal	900	polyclonal	1114	T15G1	841		

IV-B-3 MAbs by order of appearance in tables

No.	MAb ID
p17	
1	L14.17
2	polyclonal
3	32/5.8.42
4	HyHIV-1
5	HyHIV-2
6	HyHIV-3
7	HyHIV-4
8	HyHIV-5
9	HyHIV-6
10	32/1.24.89
11	3B10
12	3E11
13	8H10
14	HyHIV-21
15	B4f8
16	HyHIV-22
17	12H-D3b3
18	12G-A8g2
19	12G-D7h11
20	12G-H1c7
21	12I-D12g2
22	polyclonal
23	32/5.8.42
24	11H9
25	3-H-7
26	C5126
27	1D9
28	4C9
29	4H2B1
30	9G5
31	15-21
32	31-11
33	sc-FV p17
34	HyHIV-15
p17-p24	
35	3A6
p24	
36	111/182
37	112/021
38	112/047
39	ID8F6
40	F5-2
41	CB-13/5
42	polyclonal
43	3D3
44	CD-4/1
45	15F8C7
46	111/052
47	polyclonal
48	91-5
49	1109/01
50	14D4E11
51	1G5C8
52	47-2
53	714/01
54	polyclonal
55	111/073
56	113/038
57	1-E-4
58	1-E-9
59	10-E-7
60	10-G-9
61	11-C-5
62	2-E-4
63	2-H-4
64	8-D-2
65	8-G-9
66	8-H-7
67	C5123
68	1-B-7
69	3-B-7
70	6-D-12
71	6-E-7
72	8-D-5
73	FF1
74	113/072
75	25.3
76	13-102-100
77	RL4.72.1
78	406/01
79	polyclonal
80	38:9.6K
81	EB1A9
82	polyclonal
83	30:3E5
84	EF7
85	LH-104-E
86	1B2C12
87	LH-104-K
88	LH-104-A
89	1.17.3
90	1A7
91	1F6
92	23A5G4
93	23A5G5
94	3D10G6
95	polyclonal
96	F5-4
97	MO9.42.2
98	MO9.50.2
99	V10
100	V107
101	LH-104-C
102	12-B-4
103	C5122
104	9A4C4
105	11C10B10
106	11D11F2
107	CD12B4
108	BE3
109	L14
110	108/03
111	110/015
112	32:32K
113	C5200
114	FH2
115	13B5
116	106/01
117	LH-104-B
118	LH-104-I
p24-p2p7p1p6	
119	LH-104-G
p2p7p1p6	
120	i5B11
121	EC6
122	M12
123	DG8
124	EB5
125	HH3
126	AD2
127	CA5
128	DF3
129	EC3
130	FC12
131	GE4
132	JB7
133	JF11
Gag	
134	16/4/2
135	183-H12-5C
136	241-D
137	2A6
138	5E2.A3k
139	71-31
140	91-6
141	98-4.3
142	98-4.9
143	AC2
144	BC1071
145	BE10
146	CD9
147	CH9B2
148	ED8
149	EH12E1
150	G11G1
151	G11H3
152	HyHIV-19
153	IE8G2
154	V7-8
155	anti-p24
156	human sera
157	polyclonal
158	polyclonal
159	polyclonal
160	polyclonal
161	polyclonal
162	polyclonal
163	polyclonal
164	polyclonal
165	polyclonal
166	polyclonal
167	polyclonal
168	polyclonal
169	polyclonal
170	polyclonal
171	polyclonal
172	polyclonal HIVIG
Protease	
173	1696
174	10E7
175	F11.2.32
176	13E1
177	8B11
178	8C10
179	8G5
RT	
180	1E8
181	polyclonal
182	1.152 B3
183	1.158 E2
184	31D6
185	31G8
186	32E7
187	33D5
188	5B2
189	polyclonal
190	1.153 G10
191	RTMAb8
192	1D4A3
193	RT6H
194	1.160 B3
195	polyclonal
196	C2003

197 5B11
198 6B10
199 6E9
200 E-4
201 6B9
202 5F
203 5G
204 7C4
Integrase
205 1C4
206 2C11
207 2E3
208 3E11
209 3F9
210 5F8
211 6G5
212 7B6
213 7C6
214 6C5
215 8G4
216 17
217 4D6
218 7-16
219 4F6
220 anti-K159
221 5D9
222 8-6
223 19
224 2-19
225 8-22
226 4-20
227 6-19
228 7C3
229 7F11
230 8E5
231 MAb 35
Pol
232 12
233 13
234 14
235 16
236 1C12B1
237 21
238 32
239 35
240 3D12
241 3F10
242 4
243 6B9
244 7C4
245 F-6
246 RT-4
247 RT7O
248 RT7U
249 anti-HIV-1 RT
250 polyclonal
251 polyclonal
252 polyclonal
253 33
Vif
254 TG002
255 TG001
256 J4
257 polyclonal
Vpr
258 polyclonal
Tat
259 polyclonal
260 TA9
261 TD84
262 TE135
263 polyclonal
264 polyclonal
265 NT3/2D1.1
266 1.2
267 1D9D5
268 TB12
269 polyclonal
270 polyclonal
271 polyclonal
272 polyclonal
273 1D2F11
274 2D9E7
275 4B4C4
276 5G7D8
277 polyclonal
278 NT2/4D5.24
279 polyclonal
280
281 L-anti-Tat
282 TC15
283 polyclonal
284 polyclonal
285 polyclonal
286 polyclonal
287 polyclonal
288 polyclonal
289 polyclonal
290 polyclonal
291 polyclonal
292 polyclonal
293 polyclonal
294 polyclonal
295 2D9D5
Rev
296 4G9
297 Ab2
298 10.1
299 3H6
300 8E7
301 9G2
302 Ab4
303 3G4
304 1G10
305 1G7
306 Ab3
307 2G2
gp160
308 M85
309 7E2/4
310 4D4#85
311 M92
312 M86
313 polyclonal
314 133/237
315 133/290
316 133/11
317 D/3G5
318 D/6A11
319 D/5E12
320 L5.1
321 4A7C6
322 1D10
323 B242
324 133/192
325 489.1(961)
326 5B3
327 B10
328 B2
329 C6
330 MF49.1
331 T1.1
332 T7.1
333 T9
334 GV4D3
335 B27
336 B9
337 B35
338 D/4B5
339 D/5A11
340 D/6B2
341 B18
342 B20
343 MF39.1
344 187.2.1
345 37.1.1(ARP 327)
346 6D8
347 M96
348 MF119.1
349 MF4.1
350 MF53.1
351 MF58.1
352 MF77.1
353 T2.1
354 11/65
355 W1
356 T11
357 GV1A8
358 11
359 12G10
360 135/9
361 7C10
362 C4
363 MF46.1
364 6D5
365 B33
366 polyclonal
367 35D10/D2
368 40H2/C7
369 43A3/E4
370 43C7/B9
371 45D1/B7
372 46E3/E6
373 58E1/B3
374 64B9/A6
375 69D2/A1
376 82D3/C3
377 2H1B
378 697-D
379 6C4/S
380 C108G
381 10/76b
382 11/41e
383 11/4b
384 RSD-33
385 11/4c
386 8.22.2
387 12b
388 G3-136
389 G3-4
390 BAT085
391 60b
392 74
393 38/12b
394 38/60b
395 polyclonal
396 322-151
397 3D3.B8
398 4C11.D8
399 493-156
400 110.1
401 GV4H3
402 J1
403 J3
404 1006-30-D

405 847-D
406 MF169.1
407 MF170.1
408 MF87.1
409 213.1
410 B12
411 B13
412 C13
413 M89
414 B21
415 B23
416 B24
417 B25
418 B3
419 B26
420 B29
421 B36
422 110.E
423 110.C
424 IIIB-V3-26
425 IIIB-V3-21
426 polyclonal
427 polyclonal
428 MO97/V3
429 polyclonal
430 55/11
431 8/38c
432 8/64b
433 polyclonal
434 polyclonal
435 polyclonal
436 polyclonal
437 9284
438 polyclonal
439 polyclonal
440 polyclonal
441 polyclonal
442 MAG 109
443 MAG 49
444 MAG 53
445 MAG 56
446 1324-E
447 polyclonal
448 MO99/V3
449 C311E
450 907
451 924
452 polyclonal
453 polyclonal
454 10F10
455 2C4
456 412-D
457 polyclonal
458 CGP 47 439
459 polyclonal
460 178.1
461 257-D
462 311-11-D
463 41148D
464 391/95-D
465 Aw
466 Bw
467 DO142-10
468 Dv
469 Fv
470 Gv
471 Hv
472 polyclonal
473 50.1
474 polyclonal
475 BAT123
476 838-D
477 1006-15D
478 782-D
479 908-D
480 1027-15D
481 F19.26-4
482 F19.48-3
483 F19.57-11
484 M77
485 polyclonal
486 SP.BAL114
487 SP.SF2:104
488 polyclonal
489 19b
490 4G10
491 5F7
492 G3-523
493 MN215
494 Nea 9301
495 4117C
496 419-D
497 453-D
498 504-D
499 83.1
500 5023B
501 F58/D1
502 P1/D12
503 P4/D10
504 IIIB-13 V3
505 IIIB-34 V3
506 A47/B1
507 D59/A2
508 G44/H7
509 MO96/V3
510 μ5.5
511 loop 2
512 268-D
513 386-D
514 5042A
515 5042B
516 418-D
517 5021
518 5025B
519 5042
520 110.3
521 110.4
522 110.5
523 58.2
524 polyclonal
525 537-D
526 5020
527 RC25
528 5023A
529 110.6
530 polyclonal
531 10/36e
532 10/54
533 11/85b
534 polyclonal
535 0.5β
536 Cβ1, 0.5β
537 NM-01
538 1026
539 1034
540 59.1
541 polyclonal
542 10E3
543 polyclonal
544 N11-20
545 5025A
546 N70-1.9b
547 902
548 694/98-D
549 MO101/V3,C4
550 MO101/V3,C4
551 MO101/V3,C4
552 9205
553 110.I
554 anti-HIV-2 polyclonal
555 IIIB-V3-01
556 D/6D1
557 4D7/4
558 36.1(ARP 329)
559 C12
560 110.D
561 B32
562 polyclonal
563 B15
564 B34
565 7F11
566 E51
567 5C2E5
568 G3-211
569 G3-537
570 polyclonal
571 1795
572 ICR38.1a
573 G3-299
574 G3-42
575 G3-508
576 G3-519
577 G3-536
578 ICR38.8f
579 MO86/C3
580 13H8
581 G45-60
582 polyclonal
583 1662
584 1663
585 1664
586 1697
587 1794
588 1804
589 1807
590 1808
591 polyclonal
592 polyclonal
593 CRA1(ARP 323)
594 M91
595 9201
596 1C1
597 3F5
598 5F4/1
599 660-178
600 9301
601 B221
602 8C6/1
603 H11
604 W2
605 M38
606 Chim 1
607 polyclonal
608 110.1
609 42F
610 43F
611 RV110026
612 105-306
613 GV1G2
614 750-D
615 450-D
616 670-D
617 polyclonal
618 722-D
619 polyclonal

620 1131-A
621 858-D
622 989-D
623 1331A
624 1A1
625 24G3
626 25C2
627 5F3
628 α(566-586)
629 PC5009
630 polyclonal α577-596
631 polyclonal
632
633
634 1F11
635 1H5
636 3D9
637 4B3
638 4D4
639 4G2
640 polyclonal
641 polyclonal
642 polyclonal
643 2A2/26
644 50-69
645 9-11
646 98-43
647 41-1
648 41.4
649 Fab A1
650 Fab A4
651 Fab M12B
652 Fab M26B
653 Fab M8B
654 Fab T2
655 86
656 polyclonal
657 V10-9
658 polyclonal
659 polyclonal
660 polyclonal
661 2F11
662 246-D
663 polyclonal
664 9G5A
665 181-D
666 240-D
667 F240
668 D49
669 D61
670 T32
671 T34
672 115.8
673 M-1
674 M-11
675 M-13
676 M-2
677 M-22
678 M-24
679 M-25
680 M-28
681 M-29
682 M-36
683 M-4
684 M-6
685 polyclonal α598-609
686 1B8.env
687 polyclonal
688 polyclonal
689 clone 3
690 4
691 41-6
692 41-7
693 68.1
694 68.11
695 75
696 polyclonal
697 105-732
698 3D6
699 F172-D8
700 D50
701 5-21-3
702 120-16
703 98-6
704 167-7
705 ND-15G1
706 167-D
707 2F5
708 polyclonal
709 14D9
710 polyclonal
711 5B2
712 9G11
713 TH-Ab1
714 polyclonal
715 polyclonal
716 polyclonal
717 polyclonal
718 4E10
719 Z13
720 B30
721 polyclonal
722 41S-2
723 447-52D
724 C8
725 B31
726 B33
727 1576
728 1578
729 1579
730 1583
731 1899
732 1907
733 1908
734 1909
735 41-1
736 41-2
737 41-3
738 ED6
739 LA9 (121-134)
740 1575
741 88-158/02
742 88-158/022
743 88-158/079
744 polyclonal
745 polyclonal
746 B8
747 1577
748 polyclonal
749 DZ

Env

750
751
752
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754
755 1008-D
756 102-135
757 1025
758 105-134
759 10E9
760 1125H
761 126-50
762 12H2
763 13.10
764 1B1
765 1F7
766 2.2B
767 30D
768 31710B
769 38B5/C9
770 39H10/A11
771 3D5
772 3H6
773 40D3/C11
774 49B11/A1
775 4KG5
776 52G5/B9
777 55E4/H1
778 56C4/C8
779 57B6/F1
780 57H5/D7
781 63G4/E2
782 65B12/C5
783 6E10
784 7-1054
785 7B2
786 85G11/D8
787 87E4/A8
788 97B1/E8
789 A1g8
790 A9
791 AG10H9
792 AH48
793 Ag1211
794 B4
795 B4a1
796 B4e8
797 B5
798 B6
799 BAT267
800 BAT401
801 BAT509
802 C31
803 D1
804 D12
805 D16
806 D4
807 D43
808 F223
809 F285
810 F7
811 FG39
812 Fab A12
813 Fab A2
814 Fab L9
815 Fbb14
816 Fbb21
817 Fbb21
818 G12
819 G2
820 H2
821 H8
822 HBW4
823 HIVIG
824 IVI-4G6
825 Ia3
826 Ia7
827 IgA6/30lambda
828 IgA6/5k
829 IgA6/L4
830 K14
831 M25
832 MAG 6B
833 MO28

834 MO30
835 MO43
836 N2-4
837 N70-2.3a
838 P35
839 P43110
840 P5-3
841 T15G1
842 T20
843 T26
844 T27
845 T3
846 T30
847 T4
848 m18
849 multiple Fabs
850 multiple MAbs
851 multiple MAbs
852 multiple MAbs
853 polyclonal
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932 polyclonal
933 polyclonal
934 polyclonal
935 101-342
936 101-451
937 120-1
938 212A
939 522-149
940 L19
941 M90
942 MAG 104
943 MAG 45
944 MAG 95
945 MAG 97
946 T9
947 p7
948 L100
949 2/11c
950 A32
951 C11
952 L81
953 2F19C
954 B2C
955 polyclonal
956 1024
957 23A
958 D7324
959 10/46c
960 1027-30-D
961 1125H
962 120-1B1
963 1202-D
964 1331E
965 1570
966 1595
967 1599
968 15e
969 21h
970 28A11/B1
971 2G6
972 35F3/E2
973 38G3/A9
974 428
975 448-D
976 46D2/D5
977 48-16
978 50-61A
979 5145A
980 558-D
981 559/64-D
982 55D5/F9
983 588-D
984 654-D
985 67G6/C4
986 729-D
987 830D
988 9CL
989 BM12
990 D20
991 D21
992 D24
993 D25
994 D28
995 D35
996 D39
997 D42
998 D52
999 D53
1000 D60
1001 DA48
1002 DO8i
1003 F105
1004 F91
1005 GP13
1006 GP44
1007 GP68
1008 HF1.7
1009 HT5
1010 HT6
1011 HT7
1012 ICR 39.13g
1013 ICR 39.3b
1014 IgG1b12
1015 IgGCD4
1016 L28
1017 L33
1018 L41
1019 L42
1020 L52
1021 L72
1022 M12
1023 M13
1024 M6
1025 MAG 116
1026 MAG 12B
1027 MAG 29B
1028 MAG 3B
1029 MAG 55
1030 MAG 72
1031 MAG 86
1032 MAG 96
1033 MTW61D
1034 S1-1
1035 T13
1036 T49
1037 T56
1038 TH9
1039 anti-CD4BS summary
1040 b11
1041 b13
1042 b14
1043 b3
1044 b6
1045 polyclonal
1046 D33
1047
1048 17b

1049 21c
1050 23e
1051 48d
1052 49e
1053 X5
1054 T22
1055 polyclonal
1056 2A2
1057 AC4
1058 AD3
1059 AD3
1060 ID6
1061 ID6
1062 11/68b
1063 62c
1064 CRA-6
1065 L15
1066 T52
1067 T54
1068 polyclonal
1069 1088
1070 110-B
1071 1357
1072 1361
1073 1393A
1074 66a
1075 66c
1076 684-238
1077 830A
1078 CRA-3
1079 CRA-4
1080 L17
1081 SC258
1082 L25
1083 L39
1084 L40
1085 L78
1086
1087 110.J
1088 1334-D
1089 2182
1090 2191
1091 2219
1092 2412
1093 2442
1094 2456
1095 39F
1096 55/68b
1097 5G11
1098 6.1
1099 6.7
1100 8.27.3
1101 8E11/A8
1102 9305
1103 AG1121
1104 D47
1105 F5.5
1106 G3-1472
1107 K24
1108 TH1
1109 anti-gp120/V3
1110 polyclonal
1111 polyclonal
1112 polyclonal
1113 polyclonal
1114 polyclonal
1115 polyclonal
1116 polyclonal
1117 11/75a/21/41
1118 41.1
1119 55/45a/1l
1120 1108
1121 polyclonal
1122 polyclonal
1123 D27
1124 D56
1125 2G12
1126 1367
1127 126-6
1128 1342
1129 1379
1130 Fab D11
1131 Fab D5
1132 Fab G1
1133 Fab M10
1134 Fab M12
1135 Fab M15
1136 Fab S10
1137 Fab S6
1138 Fab S8
1139 Fab S9
1140 Fab T3
1141 Md-1
1142 1281
1143 Fab A9
1144 Fab G15
1145 Fab G5
1146 Fab L1
1147 Fab L11
1148 Fab L2
1149 Chessie 8
1150 8F101
1151 8F102
1152 CG-10
1153 CG-25
1154 CG-4
1155 CG-76
1156 CG-9
1157 105-518
1158 31A1
1159 39A64
1160 39B86
1161 9303
1162 NC-1

Nef

1163 4H4
1164 polyclonal
1165 13/042
1166 13/035
1167 A6
1168 A7
1169 25/03
1170 26/76
1171 3F2
1172 3D12
1173 polyclonal
1174 polyclonal
1175 3G12
1176 13/058
1177 26/028
1178 2E3
1179 polyclonal
1180 AM5C6
1181 AM5C6
1182 F14.11
1183 31/03
1184 F4
1185 F2
1186 polyclonal
1187 polyclonal
1188 polyclonal
1189 F3
1190 F8
1191 F1
1192 2F2
1193 E9
1194 3E6
1195 E5
1196 2A3
1197 2E4
1198 2H12
1199 3A2
1200 NF1A1
1201 polyclonal
1202 E7
1203 AE6
1204 AG11
1205 EH1
1206 3B4B
1207 3H3E
1208 6.1
1209 NF2B2
1210 NF3A3
1211 NF8B4
1212 polyclonal
1213 AE6

HIV-1

1214
1215 polyclonal
1216 polyclonal
1217 polyclonal
1218 polyclonal
1219 polyclonal
1220 polyclonal
1221 polyclonal
1222 polyclonal
1223 polyclonal

IV-C

HIV Antibodies Tables

All HIV MAbs and polyclonal Abs that bind to linear epitopes 30 amino acids or less in length arranged by protein position. The table entries are sorted in a nested way—first by protein, then by HXB2 start location, then by antibody type and finally by antibody name. Abs that bind to conformational epitopes or with unknown epitopes are listed at the end of each protein section.

IV-C-1 p17 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1	L14.17	p17 (11–25)	p17 (11–25 BRU)	GELDRWEKIRLRPGG	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* viral lysate *Strain:* B clade BRU *HIV component:* HIV-1 **References** Robert-Hebmann1992a, Robert-Hebmann1992b, Tatsumi1990					
2	polyclonal	p17 (11–25)	p17 (11–25 LAI)	GELDRWEKIRLRPGG	N	Vaccine	mouse
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Truong1997 • An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a differentantigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. [Truong1997]					
3	32/5.8.42	p17 (12–19 + 100–105)	p17 (12–19 IIIB)	ELDRWEKI+ALDKIE	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* viral lysate **References** Papsidero1989 • 32/5.8.42: Binds to two discontinuous regions, positions 12-19 and 100-105, peptides ELDRWEKI and ALDKIE – inhibited infectivity of cell free virus. [Papsidero1989]					
4	HyHIV-1	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998b, Liu1995 • HyHIV-1: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. [Ota1998b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
5	HyHIV-2	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998b, Liu1995 • HyHIV-2: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. [Ota1998b]					
6	HyHIV-3	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998b, Liu1995 • HyHIV-3: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. [Ota1998b]					
7	HyHIV-4	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY?	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998b, Ota1998a, Liu1995 • HyHIV-4: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. [Ota1998b] • HyHIV-4: epitope uncertain, based on the best estimate from JMH1 sequence– Ka is 1.8 x 10^7 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface. [Ota1998a]					
8	HyHIV-5	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998b, Liu1995 • HyHIV-5: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. [Ota1998b]					
9	HyHIV-6	p17 (12–29)	p17 (12–29 JMH1)	ELDKWEKIRLRPGGKTLY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998b, Liu1995 • HyHIV-6: This paper compares the results of affinity constant (Ka) measurements of anti-p17 MAbs using double Ab methods versus the faster, isotope-free BIAcore system, and results were found to be similar for HyHIV-(1-6) – six MAbs all bind to the first alpha helix of p17, a functional domain for both membrane binding and nuclear localization. [Ota1998b]					
10	32/1.24.89	p17 (17–22)	p17 (17–22 IIIB)	EKIRLR	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* viral lysate **References** Papsidero1989 • 32/1.24.89: Inhibited infectivity of cell free virus. [Papsidero1989]					
11	3B10	p17 (19–38)	p17 (19–38 SIVmac)	IRLPGGKKKYMLKHVVWAA	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1 **References** Otteken1992					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 3B10: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) , SIVagm, HIV-1, and SIVmnd, demonstrating that the matrix protein of all nine HIV and SIV isolates tested in this study expresses at least one conserved immunogenic epitope recognized serologically. [Otteken1992]					
12	3E11	p17 (19–38)	p17 (19–38 SIVmac)	IRLPGGKKKYMLKHVVWAA	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1 **References** Nilsen1996, Otteken1992					
		• 3E11: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H), SIVagm, HIV-1, and SIVmnd, demonstrating that the matrix protein of all nine HIV and SIV isolates tested in this study expresses at least one highly conserved immunogenic epitope. [Otteken1992] • 3E11: There is another MAb with this ID that recognizes integrase. [Nilsen1996]					
13	8H10	p17 (30–52)	p17 (30–52 JMH1)	KLKHIVWASRELERFAVNPGLLE		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* peptide *Strain:* B clade JMH-1 *HIV component:* p17 Gag *Adjuvant:* BSA **References** Ota1999b, Ota1999a					
		• 8H10: Inhibits viral replication of the HIV-1 infected MT-4 cells by decreasing p17 DNA levels in the infected cells, and the effect of growing the 8H10 hybridoma in co-culture with HIV-1 infected MT-4 cells was studied. [Ota1999b] • 8H10: The p17 MAb also can bind to the V3 loop. [Ota1999a]					
14	HyHIV-21	p17 (30–52)	p17 (30–52 JMH1)	KLKHIIWASRELERFAVNPGLLE	no	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998a, Liu1995					
		• HyHIV-21: epitope uncertain, based on the best estimate from JMH1 sequence – Ka is 3.6 x 10^6 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface –inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture. [Ota1998a]					
15	B4f8	p17 (51–65)	p17 (51–65)	LETSEGCRQILGQLQ	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Shang1991					
		• -B4f8: Did not bind live infected cells, only cells that had been made permeable with acetone. [Shang1991]					
16	HyHIV-22	p17 (52–83)	p17 (53–87 JMH1)	ETSEGCRQILGQRQPSLQTGSEELR-SLYNTIH	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998a, Liu1995					
		• HyHIV-22: epitope uncertain, based on the best estimate from JMH1 sequence – stains the surface of infected cells indicating the antigen is exposed at the cell surface – Ka is 2.3 x 10^5 M-1 for rec p17. [Ota1998a]					
17	12H-D3b3	p17 (62–78)	p17 (62–78)	GQLQPSLQTGSEELRSL	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Shang1991					
		• 12H-D3b3: Did not bind live infected cells, only cells that had been made permeable with acetone. [Shang1991]					
18	12G-A8g2	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Maksiutov2002, Shang1991					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 12G-A8g2: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein(T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. [Maksiutov2002] • 12G-A8g2: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. [Shang1991]					
19	12G-D7h11	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Maksiutov2002, Shang1991 • 12G-D7h11: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. [Maksiutov2002] • 12G-D7h11: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. [Shang1991]					
20	12G-H1c7	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Maksiutov2002, Shang1991 • 12G-H1c7: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. [Maksiutov2002] • 12G-H1c7: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. [Shang1991]					
21	12I-D12g2	p17 (86–115)	p17 (86–115)	YCVHQRIEIKDTKEALDKIEEEQNK-SKKKA	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Maksiutov2002, Shang1991 • 12I-D12g2: This epitope is similar to a fragment of the human protein CD40 ligand TNF-related activation protein (T-cell antigen GP39) (CD154), LDKIEDERN, as well as to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. [Maksiutov2002] • 12I-D12g2: Bound to 30-mer, but not to internal peptides – did not bind live infected cells – antigenic domain known as HPG30. [Shang1991]					
22	polyclonal	p17 (86–115)	p17 (86–115)	YSVHQRIDVKDTKEALEKIEEEQNK-SKKKA	L	Vaccine	mouse (IgA)
		Vaccine *Vector/Type:* peptide *HIV component:* p17 Gag *Adjuvant:* Cholera toxin (CT) **References** Bukawa1995 • Polyclonal secretory IgA antibody raised by oral mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to the V3, CD4 or HPG30 component of the multicomponent peptide immunogen. [Bukawa1995]					
23	32/5.8.42	p17 (87–19 + 100–105)	p17 (IIIB)	ELDRWEKI+ALDKIE	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* viral lysate *HIV component:* HIV-1 **References** Papsidero1989 • 32/5.8.42: Inhibited infectivity of cell free virus – bound to two peptides, ELDRWEKI and ALDKIE, at positions 12-19 + 100-105. [Papsidero1989]					
24	11H9	p17 (101–115)	p17 (101–115 SF2)	LEKIEEEQNKSKKKA?		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Maksiutov2002, Ferns1989, Ferns1987					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 11H9: UK Medical Research Council AIDS reagent: ARP344. • 11H9: This epitope is similar to a fragment of Lens-epithelium-derived growth factor, DIITEEDKSKKKGQ. [Maksiutov2002] • 11H9: Reactive against p18 and p55. [Ferns1987]					
25	3-H-7 (3H7)	p17 (113–122)	p17 (113–122 BH10)	KKAQQAAADT	L	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB **References** Levin1997, Robert-Hebmann1992a, Robert-Hebmann1992b, Niedrig1989 • 3-H-7: Called 3H7 – using a bicistronic vector, an intracellular Fab intrabody, 3H7, can inhibit HIV-1 infection when expressed in the cytoplasm of dividing CD4+ T cells – HXBIIIB and SI primary isolate virions from 3H7 expressing cells were far less infectious – 3H7 intrabody acts both at the stage of nuclear import and virus particle assembly. [Levin1997] • 3-H-7: No cross-reactivity with HIV-2 ROD or SIV MAC by immunoblot. [Niedrig1989]					
26	C5126	p17 (113–122)	p17 (113–122 HXB2)	KKAQQAAADT	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* viral lysate *HIV component:* HIV-1 **References** Hinkula1990 • C5126: Defined epitope by peptide blocking of binding to native protein – WB reactive with p53 and p17. [Hinkula1990]					
27	1D9	p17 (119–132)	p17 (121–134 SF2)	AAGTGNSSQVSQNY		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • 1D9: UK Medical Research Council AIDS reagent: ARP316. • 1D9: Reactive against p18, but not p55. [Ferns1987]					
28	4C9	p17 (119–132)	p18 (121–134 SF2)	AAGTGNSSQVSQNY		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • 4C9: UK Medical Research Council AIDS reagent: ARP342. • 4C9: Reactive against p18, but not p55. [Ferns1987]					
29	4H2B1	p17 (119–132)	p17 (121–134 SF2)	AAGTGNSSQVSQNY			mouse (IgG1)
		Research Contact R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • 4H2B1: UK Medical Research Council AIDS reagent: ARP315. • 4H2B1: Reactive against p18 and p55 of multiple isolates. [Ferns1987]					
30	9G5	p17 (119–132)	p17 (121–134 SF2)	AAGTGNSSQVSQNY		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • 9G5: UK Medical Research Council AIDS reagent: ARP343. • 9G5: Reactive against p18, but not p55. [Ferns1987]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
31	15-21	p17 (121–132)	p17 (121–132 BRU)	DTGHSSQVSQNY	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade BRU					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
32	31-11	p17 (121–132)	p17 (121–132 BRU)	DTGHSSQVSQNY	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade BRU					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
33	sc-FV p17	p17 (121–132)	p17 (121–132 BRU)	DTGHSSQVSQNY	L	Vaccine	mouse (IgG1κ)
		Vaccine *Strain:* B clade BRU					
		Ab type C-term **Research Contact** Paul Zhou, NIH, Bethesda, MD, USA					
		References Tewari1998, Robert-Hebmann1992a					
		• A single chain Ab (sc-FV) was made from an anti-p17 MAb, and intracellular binding of sc-FV resulted in inhibition of viral replication that was more pronounced when the sc-FV was expressed in the cytoplasm instead of the nucleus. [Tewari1998]					
34	HyHIV-15	p17 (122–115)	p17 (87–115 JMH1)	SVHQRIDVKDTKEALEKIEEEQNKS-KKKA?	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag					
		References Ota1998a, Liu1995					
		• HyHIV-15: epitope uncertain, based on the best estimate from JMH1 sequence – Ka is 1.4 x 10^7 M-1 for rec p17 – stains the surface of infected cells indicating the antigen is exposed at the cell surface – inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture. [Ota1998a]					

IV-C-2 p17-p24 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
35	3A6	p17-p24 (122–17)	p24 (122–149 BH10)	TGHSSQVSQNYPIVQNIQGQMVHQA-ISP	no	HIV-1 infection	human (IgG1κ)

References Buchacher1994, Buchacher1992

- 3A6: Human MAbs against HIV generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994]
- 3A6: The reactive peptide spans the p17/p24 border of gag. [Buchacher1994]

IV-C-3 p24 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
36	111/182	p24 (1–20)	p24 (134–153 IIIB)	PIVQNIQGQMVHQAISPRTL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 111/182: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC. [Niedrig1991]					
37	112/021	p24 (1–20)	p24 (134–153 IIIB)	PIVQNIQGQMVHQAISPRTL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 112/021: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC. [Niedrig1991]					
38	112/047	p24 (1–20)	p24 (134–153 IIIB)	PIVQNIQGQMVHQAISPRTL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 112/047: Test specific evidence of cross-reactivity between HIV-1, HIV-2 and SIV MAC. [Niedrig1991]					
39	ID8F6	p24 (11–25)	p24 (143–157 BRU)	VHQAISPRTLNAWVK	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • ID8F6: UK Medical Research Council AIDS reagent: ARP348. • ID8F6: Reacted with both p55 and p24 – showed less than 75% homologous inhibition. [Ferns1987]					
40	F5-2	p24 (14–23)	p24 (14–23 HXB2)	AISPRTLNAW	no		mouse
		References Kusk1992, Kusk1988 • F5-2: In HIV-1+ individuals, antibody to AISPRTLNAW is associated with CD4 T-cell decline. [Kusk1988, Kusk1992]					
41	CB-13/5 (CB-mab-p24/13-15)	p24 (21–25)	p24 (152–156)	NAWVK	no		mouse (IgG1κ)
		References Glaser1996, Kuttner1992, Franke1992, Grunow1990 • CB-13/5: Epitope described as VHQAISPRTLNAWVK – binding not affected by bound MAb CB-4/1. [Glaser1996] • CB-13/5: Inhibits spread of HIV-1 in cell cultures. [Franke1992] • CB-13/5: Called CB-mab-p24/13-15 – the VDJ H and VJ L regions of CB-mab-p24/13-15 were sequenced. [Kuttner1992] • CB-13/5: It is not clear whether the MAbs CD-13/5 and CB-mab-p24/13-15 are the same, but from the shared references in the primary articles they seem to be (database note)					
42	polyclonal	p24 (44–60)	p24 (176–192 LAI)	SEGATPQDLNTMLNTVG	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Truong1997 • An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. [Truong1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
43	3D3	p24 (45–50)	p24 (177–182 LAI)	EGATPQ		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • 3D3: UK Medical Research Council AIDS reagent: ARP314. • 3D3: Most broadly reactive of all the antibodies in this study. [Ferns1987]				
44	CD-4/1 (CB-4/1/1/F6)	p24 (46–56)	p24 (182–197)	GATPQDLNTML	no	Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *HIV component:* p24 Gag **References** Ehrhard1996, Glaser1996, Hohne1993, Franke1992, Grunow1990 • CD-4/1: Modification of p24 lysine residues by maleic anhydrid increased the affinity of CD-4/1, presumably due to conformational changes exposing a cryptic epitope. [Ehrhard1996] • CD-4/1: Unusual p24-MAb binding kinetics, with biphasic association – probably due to conformational changes in p24, not to p24 dimerization. [Glaser1996] • CD-4/1: Affinity of CB-4/1 to native p24 is lower than to peptide or denatured p24 – proposed that the peptide binds in a loop conformation. [Hohne1993] • CD-4/1: Inhibits spread of HIV-1 in cell cultures. [Franke1992]				
45	15F8C7	p24 (47–56)	p24 (183–197)	ATPQDLNTML	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1992, Janvier1990 • 15F8C7: Mapped to aa209-217 through Pepscan method – cross-reacts with HIV-2 [Janvier1990] – maps to aa203-217 through EIA pentadecapeptide [Janvier1992]. [Janvier1990, Janvier1992]				
46	111/052	p24 (51–60)	p24 (183–192 IIIB)	DLNTMLNTVG	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 111/052: Weak cross-reaction with HIV-2 on WB, otherwise not cross-reactive with HIV-2 or SIV MAC. [Niedrig1991]				
47	polyclonal	p24 (51–82)	Gag (dis 183–214 LAI)	DLNTMLNTVGGHQAAMQMLKETINE-EAAEWDR	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* B clade LAI *HIV component:* p24 Gag *Adjuvant:* QS21 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – only 4/28 had Ab responses to peptide G1, 4/28 had proliferative responses, and no patient had a CTL response. [Pialoux2001]				
48	91-5	p24 (64–75)	p24 (196–207)	AAMQMLKETINE	no	HIV-1 infection	human (IgG1λ)
		References Gorny1998, Robinson1990b, Tyler1990, Gorny1989 • 91-5: NIH AIDS Research and Reference Reagent Program: 1238. • 91-5: Did not enhance HIV-1 IIIB infection. [Robinson1990b] • 91-5: Synthesized by immortalization of peripheral blood cells with Epstein-Barr virus. [Gorny1989]				
49	1109/01	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
50	14D4E11	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* purified HIV-1					
		References Robert-Hebmann1992a, Robert-Hebmann1992b, Janvier1992, Janvier1990					
		• 14D4E11: Mapped to aa209-217 through Pepscan method (original paper, AAEWDRVHP) – cross-reacts with HIV-2 [Janvier1990] and to aa203-217 through EIA pentadecapeptide [Janvier1992]. [Janvier1990, Janvier1992]					
51	1G5C8	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* p24 Gag					
		References Robert-Hebmann1992a, Robert-Hebmann1992b, Janvier1992, Janvier1990					
		• 1G5C8: Mapped to aa209-217 through Pepscan method (original paper, AAEWDRVHP) [Janvier1990] and to aa203-217 through EIA pentadecapeptide [Janvier1992]. [Janvier1990, Janvier1992]					
52	47-2	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade BRU					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
53	714/01	p24 (69–86)	p24 (201–218 BRU)	LKETINEEAAEWDRVHPV	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
54	polyclonal	p24 (69–86)	p24 (201–218 LAI)	LKETINEEAAEWDRVHPV	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)					
		References Truong1997					
		• An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. [Truong1997]					
55	111/073	p24 (71–81)	p24 (203–213 IIIB)	ETINEEAAEWD	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag					
		References Niedrig1991					
		• 111/073: cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple assays. [Niedrig1991]					
56	113/038	p24 (71–81)	p24 (203–213 IIIB)	ETINEEAAEWD	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag					
		References Niedrig1991					
		• 113/038: cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple assays. [Niedrig1991]					
57	1-E-4	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989					
		• 1-E-4: One of nine MAbs that bind to this peptide. [Niedrig1989]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
58	1-E-9	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989					
		• 1-E-9: One of nine MAbs that bind to this peptide. [Niedrig1989]					
59	10-E-7	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989, Niedrig1988					
		• 10-E-7: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD and SIV MAC. [Niedrig1989]					
		• 10-E-7: Cross reactive between HIV-1, HIV-2 and SIV. [Niedrig1988]					
60	10-G-9	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989, Niedrig1988					
		• 10-G-9: One of nine MAbs that bind to this peptide. [Niedrig1989]					
		• 10-G-9: HIV-1 specific. [Niedrig1988]					
61	11-C-5	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989, Niedrig1988					
		• 11-C-5: One of nine MAbs that bind to this peptide. [Niedrig1989]					
		• 11-C-5: HIV-1 specific. [Niedrig1988]					
62	2-E-4	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG2a)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989, Niedrig1988					
		• 2-E-4: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD. [Niedrig1989]					
		• 2-E-4: Cross reactive between HIV-1, HIV-2 and SIV by ELISA, HIV-1 and HIV-2 by WB. [Niedrig1988]					
63	2-H-4	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989, Niedrig1988					
		• 2-H-4: One of nine MAbs that bind to this peptide – cross-reactive with HIV-2 ROD. [Niedrig1989]					
		• 2-H-4: Cross reactive between HIV-1, HIV-2 and SIV by ELISA, HIV-1 and HIV-2 by WB. [Niedrig1988]					
64	8-D-2	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG2a)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Robert-Hebmann1992a, Robert-Hebmann1992b, Niedrig1989, Niedrig1988					
		• 8-D-2: One of nine MAbs that bind to this peptide. [Niedrig1989]					
		• 8-D-2: HIV-1 specific. [Niedrig1988]					
65	8-G-9	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989					
		• 8-G-9: One of nine MAbs that bind to this peptide. [Niedrig1989]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
66	8-H-7	p24 (71–85)	p24 (203–217)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG3)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Robert-Hebmann1992a, Robert-Hebmann1992b, Niedrig1989, Niedrig1988					
		• 8-H-7: One of nine MAbs that bind to this peptide. [Niedrig1989]					
67	C5123	p24 (71–85)	p24 (203–217 HXB2)	ETINEEAAEWDRVHP	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* viral lysate *HIV component:* HIV-1					
		References Hinkula1990					
		• C5123: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
68	1-B-7	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB					
		References Niedrig1989, Niedrig1988					
		• 1-B-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 and SIV MAC. [Niedrig1989]					
69	3-B-7	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB					
		References Niedrig1989, Niedrig1988					
		• 3-B-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2. [Niedrig1989]					
70	6-D-12	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB					
		References Niedrig1989, Niedrig1988					
		• 6-D-12: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2. [Niedrig1989]					
71	6-E-7	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB					
		References Niedrig1989, Niedrig1988					
		• 6-E-7: Reacts with two overlapping peptides, region of overlap is given – reacted with HIV-2 and SIV MAC. [Niedrig1989]					
72	8-D-5	p24 (76–85)	p24 (208–217 BH10)	EAAEWDRVHP	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB					
		References Niedrig1989, Niedrig1988					
		• 8-D-5: Reacts with two overlapping peptides, region of overlap is given – bound only HIV-1. [Niedrig1989]					
73	FF1	p24 (76–90)	p24 (208–222 HXB2)	EAAEWDRVHPVHAGP	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* inactivated HIV					
		References Hinkula1990					
		• FF1: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
74	113/072	p24 (81–90)	p24 (213–222 IIIB)	DRVHPVHAGP	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag					
		References Niedrig1991					
		• 113/072: Weak cross-reaction with HIV-2 on WB, otherwise not cross-reactive with HIV-2 or SIV MAC. [Niedrig1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
75	25.3	p24 (82–102)	p24 (82–102)	RVHPVHAGPIAPGQMREPRGS	no		mouse (IgG1κ)
		References Momany1996					
		• 25.3: Crystal structure of the CA protein bound to Fab 25.3 was solved – monomers form 7 alpha-helices arranged in a coiled-coil – Fab binds to a long antigenic peptide that separates the longest helices, with a salt bridge at CA 82 R, and interactions as far away as positions 100 and 102. [Momany1996]					
76	13-102-100	p24 (84–94)	p24 (102–112 IIIB)	HPVHAGPIAPG			mouse (IgG)
		Research Contact Advanced Technologies, Inc., Columbia, MD					
		References Qian1998, Parker1996					
		• 13-102-100: Affinity capillary electrophoresis was used to fine map this epitope, and the optimal peptide was defined as VHAGPIAPGIAP – this method uses migration time shifts to probe relative affinities of Abs – the antibody binds to the cyclophilin A binding domain. [Qian1998]					
		• 13-102-100: Binding site (HPVHAGPIAPG) defined by epitope footprinting – first binding p24 to MAb, then allowing proteolytic cleavage to take place to cleave unprotected residues, then performing mass spectrometry to identify protected residues of epitope. [Parker1996]					
77	RL4.72.1	p24 (87–101)	p24 (219–233 BRU)	HAGPIAPGQMREPRG	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* D clade NDK *HIV component:* HIV-1					
		References Robert-Hebmann1992a, Robert-Hebmann1992b, Tatsumi1990					
		• RL4.72.1: Immunized with inactivated HIV NDK, D clade, reacts with B clade peptide. [Robert-Hebmann1992a]					
78	406/01	p24 (101–121)	p24 (233–253 BRU)	GSDIAGTTSTLQEQIGWMTNN	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade IIIB					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
79	polyclonal	p24 (101–121)	p24 (233–253 LAI)	GSDIAGTTSTLQEQIGWMTNL	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)					
		References Truong1997					
		• An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. [Truong1997]					
80	38:9.6K (38:96K)	p24 (121–130)	p24 (253–262 HXB2)	NPPIPVGEIY	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag					
		References Hinkula1990					
		• 38:9.6K: UK Medical Research Council AIDS reagent: ARP365.					
		• 38:9.6K: Called 38:96K – epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
81	EB1A9	p24 (121–135)	p24 (253–267 LAI)	NPPIPVGEIYKRWII		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1					
		Research Contact R. B. Ferns and R. S. Tedder					
		References Ferns1989, Ferns1987					
		• EB1A9: UK Medical Research Council AIDS reagent: ARP345.					
		• EB1A9: Reacted with both p55 and p24 – showed less than 75% homologous inhibition. [Ferns1987]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
82	polyclonal	p24 (121–152)	Gag (dis 253–284 LAI)	NPPIPVGEIYKRWIILGLNKIVRMY-SPTSILD	no	Vaccine	human (IgG)
	Vaccine *Vector/Type:* lipopeptide *Strain:* B clade LAI *HIV component:* p24 Gag *Adjuvant:* QS21 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – 25/28 had Ab responses to peptide G2, 14/28 had proliferative responses, and CTL responses were detected. [Pialoux2001]					
83	30:3E5	p24 (141–170)	p24 (273–302 HXB2)	IVRMYSPTSILDIRQGPKEPFRDYV-DRFYK		Vaccine	mouse (IgG1λ)
	Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **Research Contact** B. Wahren **References** Hinkula1990 • 30:3E5: UK Medical Research Council AIDS reagent: ARP367. • 30:3E5: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]						
84	EF7	p24 (141–170)	p24 (273–302 HXB2)	IVRMYSPTSILDIRQGPKEPFRDYV-DRFYK		Vaccine	mouse (IgG1κ)
	Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **References** Lundin1996, Hinkula1990 • EF7: UK Medical Research Council AIDS reagent: ARP366. • EF7: Included as a control. [Lundin1996] • EF7: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53. [Hinkula1990]						
85	LH-104-E	p24 (143–148)	p24 (275–280 BRU)	RMYSPT	no	Vaccine	mouse (IgG1κ)
	Vaccine *Vector/Type:* peptide *Strain:* B clade BRU **References** Haaheim1991 • LH-104-E: UK Medical Research Council AIDS reagent: ARP319. • LH-104-E: Reacts with both p24 and p55. [Haaheim1991]						
86	1B2C12	p24 (149–154)	p24 (273–292 IIIB)	SILDIR	no	Vaccine	mouse (IgG1)
	Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1992, Janvier1990 • 1B2C12: Reacts with HIV-1 and HIV-2 – mapped to aa281-286 through Pepscan method [Janvier1990], and to aa273-292 through EIA pentadecapeptide method [Janvier1992]. [Janvier1990, Janvier1992]						
87	LH-104-K	p24 (149–154)	p24 (281–286 BRU)	SILDIR	no	Vaccine	mouse (IgG1κ)
	Vaccine *Vector/Type:* peptide *Strain:* B clade BRU **References** Haaheim1991 • LH-104-K: UK Medical Research Council AIDS reagent: ARP322. • LH-104-K: Binds exclusively with p24 (not p55) [Haaheim1991]						
88	LH-104-A	p24 (152–157 + 219–224)	p24 (BRU)	DIRQGP+QGVGGP	no	Vaccine	mouse (IgG1κ)
	Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag						

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Haaheim1991 • LH-104-A: UK Medical Research Council AIDS reagent: ARP307. • LF-104-A: A 104 amino acid peptide was used to immunize mice – hexapeptide scans revealed two reactive p24 peptides – cross-competition studies indicated the region 270-286. [Haaheim1991]					
89	1.17.3	p24 (152–172)	p24 (152–172 SIVmac)	CVKQGPKEPFQSYVDRFYKSL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1 **References** Otteken1992 • 1.17.3: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd. [Otteken1992]					
90	1A7	p24 (152–172)	p24 (152–172 SIVmac)	CVKQGPKEPFQSYVDRFYKSL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1 **References** Otteken1992 • 1A7: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd. [Otteken1992]					
91	1F6	p24 (152–172)	p24 (152–172 SIVmac)	CVKQGPKEPFQSYVDRFYKSL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade AGM TYO-7 *HIV component:* HIV-1 **References** Otteken1992 • 1F6: Recognized an epitope present on HIV-2/SIVmac (MAC251/32H) and HIV-2smmH4, but not SIVagmTYO-1, HIV-1 IIIB or SIVmnd. [Otteken1992]					
92	23A5G4	p24 (153–172)	p24 (285–304 IIIB)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p24 Gag **References** Janvier1996, Janvier1992, Janvier1990 • 23A5G4: A few sera which were able to bind the linear sequence 178-192, but not sequence 288-302 in an indirect peptide ELISA inhibited the binding of 23A5G4 to the native p24. [Janvier1996] • 23A5G4: Mapped to aa209-217 through Pepscan method [Janvier1990] and to aa285-304 through EIA pentadecapeptide method [Janvier1992]. [Janvier1990, Janvier1992]					
93	23A5G5	p24 (153–172)	p24 (285–304 BRU)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Robert-Hebmann1992a, Robert-Hebmann1992b					
94	3D10G6	p24 (153–172)	p24 (285–304 IIIB)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* purified HIV-1 **References** Janvier1992, Janvier1990 • 3D10G6: Epitope cross-reacts with HIV-1 and HIV-2 – mapped to aa260-267 through Pepscan method [Janvier1990] and to aa285-304 through EIA pentadecapeptide method. [Janvier1990, Janvier1992]					
95	polyclonal	p24 (153–172)	p24 (285–304 LAI)	IRQGPKEPFRDYVDRFYKTL	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* Gag, p17 Gag, p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Truong1997					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• An ELISA assay was used to study a panel of Gag peptides – mature p24 CA epitopes mapped to residues 176-192, 201-218, 233-253, 285-304, and were recognized by antibodies elicited by rp24CA – one p17MA epitope, residues 11-25, and one p24CA epitope, residues 176-192, were recognized by antibodies raised against anti-p55 virus-like particles, suggesting a different antigenic properties for p24CA and p17MA antibodies depending on whether they are produced against the mature soluble protein or the immature assembled form of the gag proteins. [Truong1997]					
96	F5-4	p24 (153–175)	p24 (153–174 HXB2)	IRQGPKEPFRDYVDRFYKTLRAE	no		mouse
		References Kusk1992, Kusk1988					
		• F5-4: Binds to a location in the most hydrophilic region of p24. [Kusk1988, Kusk1992]					
97	MO9.42.2	p24 (153–178)	p24 (285–310 BRU)	IRQGPKEPFRDYVDRFYKTLRAEQAS	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* virus *Strain:* HIV-2 ROD *HIV component:* HIV-1					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
		• MO9.42.2: Reacts with HIV-1s, HIV-2s, and SIVs in rec protein ELISA. [Robert-Hebmann1992b]					
98	MO9.50.2	p24 (153–178)	p24 (285–310 BRU)	IRQGPKEPFRDYVDRFYKTLRAEQAS	no	Vaccine	mouse (IgG)
		Vaccine *Strain:* HIV-2 ROD					
		References Robert-Hebmann1992a, Robert-Hebmann1992b					
		• MO9.50.2: Reacts with HIV-1s, HIV-2s, and SIVs in rec protein ELISA. [Robert-Hebmann1992b]					
99	V10	p24 (155–169)	p24 (289–303 IIIB)	QGPKEPFRDYVDRFY	no	virus	mouse
		References Matsuo1992					
		• V10: Reacts with HIV-1 and SIV AGM analogous peptides. [Matsuo1992]					
100	V107	p24 (155–177)	p24 (289–311 IIIB)	QGPKEPFRDYVDRFYKTLRAEQA	no	virus	mouse
		References Matsuo1992					
		• V107: Reacts with FIV, HIV-1 and SIV AGM analogous peptides. [Matsuo1992]					
101	LH-104-C	p24 (156–161 + 219–224)	p24 (BRU)	GPKEPF+QGVGGP	no	Vaccine	mouse (IgG3κ)
		Vaccine *Vector/Type:* peptide *HIV component:* p24 Gag					
		References Haaheim1991					
		• LH-104-C: UK Medical Research Council AIDS reagent: ARP309.					
		• LF-104-C: A 104 amino acid peptide was used to immunize mice – hexapeptide scans revealed two reactive p24 peptides – cross-competition studies indicated the region 351-373. [Haaheim1991]					
102	12-B-4	p24 (161–170)	p24 (293–302 IIIB)	FRDYVDRFYK	no	Vaccine	mouse (IgG1)
		Vaccine *Strain:* B clade IIIB *HIV component:* HIV-1					
		References Niedrig1989, Niedrig1988					
		• 12-B-4: Epitope is defined as the overlap between two HIV-1 reactive peptides – cross-reacts with HIV-2 ROD and SIV MAC. [Niedrig1988, Niedrig1989]					
103	C5122	p24 (161–170)	p24 (293–302 HXB2)	FRDYVDRFYK	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* viral lysate *HIV component:* HIV-1					
		References Hinkula1990					
		• C5122: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
104	9A4C4	p24 (170–188)	p24 (303–317 IIIB)	KTLRAEQASQEVKNWMTET	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Robert-Hebmann1992a, Robert-Hebmann1992b, Janvier1992, Janvier1990 • 9A4C4: Mapped to aa260-267 through Pepscan method [Janvier1990] – and to aa303-317 through EIA pentadecapeptide method [Janvier1992]. [Janvier1990, Janvier1992]					
105	11C10B10	p24 (171–185)	p24 (303–317 IIIB)	TLRAEQASQEVKNWM	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p24 Gag **References** Janvier1992, Janvier1990 • 11C10B10: Mapped to aa260-267 through Pepscan method [Janvier1990] and to aa303-317 through EIA pentadecapeptide method [Janvier1992]. [Janvier1990, Janvier1992]					
106	11D11F2	p24 (171–185)	p24 (303–317 IIIB)	TLRAEQASQEVKNWM	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p24 Gag **References** Janvier1992, Janvier1990 • 11D11F2: Mapped to aa260-267 through Pepscan method [Janvier1990] and to aa303-317 through EIA pentadecapeptide method [Janvier1992]. [Janvier1990, Janvier1992]					
107	CD12B4	p24 (171–185)	p24 (303–317 LAI)	TLRAEQASQEVKNWM		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • CD12B4: UK Medical Research Council AIDS reagent: ARP346. • CD12B4: Reacted with both p55 and p24 – strain-specific binding. [Ferns1987]					
108	BE3	p24 (176–190)	p24 (308–322 HXB2)	QASQEVKNWMTETLL	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **Research Contact** B. Wahren **References** Hinkula1990 • BE3: UK Medical Research Council AIDS reagent: ARP368. • BE3: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
109	L14	p24 (176–190)	p24 (308–322 HXB2)	QASQEVKNWMTETLL	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **Research Contact** B. Wahren **References** Hinkula1990 • L14: UK Medical Research Council AIDS reagent: ARP369. • L14: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
110	108/03	p24 (181–190)	p24 (313–322 IIIB)	VKNWMTETLL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 108/03: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests. [Niedrig1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
111	110/015	p24 (181–190)	p24 (313–322 IIIB)	VKNWMTETLL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 110/015: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests. [Niedrig1991]					
112	32:32K	p24 (199–222)	p24 (331–354 HXB2)	KTILKALGPAATLEEMMTACQGVG		Vaccine	mouse (IgG1λ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **References** Hinkula1990 • 32:32K: UK Medical Research Council AIDS reagent: ARP368. • 32:32K: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
113	C5200	p24 (199–222)	p24 (331–354 HXB2)	KTILKALGPAATLEEMMTACQGVG		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* viral lysate **References** Hinkula1990 • C5200: Epitope defined by peptide blocking of binding to native protein. [Hinkula1990]					
114	FH2	p24 (201–215)	p24 (333–347 HXB2)	ILKALGPAATLEEMM	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **References** Hinkula1990 • FH2: Defined by peptide blocking of binding to native protein – WB reactive with p53 and p24. [Hinkula1990]					
115	13B5	p24 (205–214)	p24 (205–213)	LGPAATLEEM		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* p24 Gag **Ab type** C-term **Research Contact** bioMerieux **References** Berthet-Colominas1999 • 13B5: Fab which was bound to p24 capsid for crystallization and study of p24's structure. [Berthet-Colominas1999]					
116	106/01	p24 (211–230)	p24 (343–362 IIIB)	LEEMMTACQGVGGPGHKARV	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* beta-galactosidase fusion protein *Strain:* B clade IIIB *HIV component:* p24 Gag **References** Niedrig1991 • 106/01: Cross-reactive between HIV-1, HIV-2 and SIV MAC by multiple tests. [Niedrig1991]					
117	LH-104-B	p24 (225–230)	p24 (357–362 BRU)	GHKARV	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BRU **References** Haaheim1991 • LH-104-B: UK Medical Research Council AIDS reagent: ARP308. • LH-104-B: Binds exclusively with p55 (not p24), in contrast to LH-104-I. [Haaheim1991]					
118	LH-104-I	p24 (226–231)	p24 (358–363 BRU)	HKARVL	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BRU **References** Haaheim1991 • LH-104-I: UK Medical Research Council AIDS reagent: ARP321. • LH-104-I: Binds exclusively with p24 (not p55), in contrast to LH-104-B. [Haaheim1991]					

IV-C-4 p24-p2p7p1p6 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
119	LH-104-G	p24-p2p7p1p6 (231–5)	p24 (363–368 BRU)	LAEAMS	no	Vaccine	mouse (IgG1κ)

Vaccine *Vector/Type:* peptide *Strain:* B clade BRU
References Haaheim1991

- LH-104-G: UK Medical Research Council AIDS reagent: ARP320.
- LH-104-G: This epitope overlaps the p24-p2 cleavage site, database note.
- LH-104-G: Reacts with both p24 and p55, in contrast to LH-104-I. [Haaheim1991]

IV-C-5 p2p7p1p6 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
120	i5B11	p2p7p1p6 (19–28)	p7 (5–14)	NFRNQRKIVK	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995, Tanchou1994, Otake1994 • i5B11: MAb reacts with NCp7, NCp15, and partially inhibits NCp7-tRNA interaction. [Tanchou1995] • i5B11: Epitope mapped by ELISA and BIAcore – inhibits NCp7 primer tRNA binding. [Tanchou1994] • i5B11: i5B11 and 15B11 may be two names for the same MAb.					
121	EC6	p2p7p1p6 (45–54)	p15 (408–417 HXB2)	PRKKGCWKCG	no	Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **References** Hinkula1990 • EC6: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53. [Hinkula1990]					
122	M12	p2p7p1p6 (45–54)	p15 (408–417 HXB2)	PRKKGCWKCG	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* p24-p15 Gag **References** Hinkula1990 • M12: Epitope defined by peptide blocking of binding to native protein – WB reactive with p53. [Hinkula1990] • M12: There is a p15 and a gp120 MAb both called M12.					
123	DG8	p2p7p1p6 (66–81)	p7 (52–67)	RQANFLGKIWPSYKGR		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • DG8: Binds proximal to the second zinc-finger, inhibits NCp7-tRNA interaction. [Tanchou1995]					
124	EB5	p2p7p1p6 (66–81)	p7 (52–67)	RQANFLGKIWPSYKGR		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • EB5: Binds proximal to the second zinc-finger – mutation at position 59 (Lys to Ser) results in 10-fold reduction in reactivity. [Tanchou1995]					
125	HH3	p2p7p1p6 (66–81)	p7 (52–67)	RQANFLGKIWPSYKGR	no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995, Tanchou1994 • HH3: Binds proximal to the second zinc-finger. [Tanchou1995] • HH3: Epitopes mapped by ELISA and BIAcore – does not inhibit NCp7 primer tRNA binding. [Tanchou1994]					
126	AD2	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • AD2: Binds at C term of NCp7. [Tanchou1995]					
127	CA5	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• CA5: Binds at C term of NCp7. [Tanchou1995]					
128	DF3	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • DF3: Binds at C term of NCp7. [Tanchou1995]					
129	EC3	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • EC3: Binds at C term of NCp7. [Tanchou1995]					
130	FC12	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • FC12: Binds at C term of NCp7, reacts with NCp15, inhibits NCp7-tRNA interaction. [Tanchou1995]					
131	GE4	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • GE4: Binds at C term of NCp7. [Tanchou1995]					
132	JB7	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • JB7: Binds at C term of NCp7. [Tanchou1995]					
133	JF11	p2p7p1p6 (78–86)	p7 (64–72)	YKGRPGNFL	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995, Tanchou1994 • JF11: Binds at C term of NCp7. [Tanchou1995] • JF11: Epitopes mapped by ELISA and BIAcore – does not inhibit NCp7 primer tRNA binding. [Tanchou1994]					

IV-C-6 Gag Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
134	16/4/2	Gag	p24		no	Vaccine	
		Vaccine *Vector/Type:* DNA with CMV promotor, DNA with CMV/MCK hybrid promotor, DNA with MCK promotor					
		References Bojak2002a					
		• 16/4/2: The ability of three different promoters to induce Gag specific immune responses was compared. The cytomegaliovirus (CMV) early gene promoter, which allows constitutive expression in different cells of host tissue, the tissue specific muscle creatine kinase (MCK) promoter, which may be restricted to differentiated, multinucleated myofibers and so safer, and a hybrid MCK/CMV promoter – intramuscular immunization of BALB/c mice utilizing the MCK promoter in combination with a codon optimized gag gene generated humoral (IgG1 (Th1) and IgG2a (Th2)) and CTL immune responses against HIV-1 Gag, however, the quantified immune parameters were clearly reduced as compared to CMV promotor-driven Gag expression. [Bojak2002a]					
135	183-H12-5C	Gag	p24		no		mouse (IgG1)
		Research Contact Bruce Chesebro and Kathy Wehrly, Rocky Mountain Laboratories, Hamilton, Montana					
		References Wehrly1997, Toohey1995, Chesebro1992					
		• 183-H12-5C: NIH AIDS Research and Reference Reagent Program: 3537.					
		• 183-H12-5C: Cross-reacts with HIV1 and HIV-2 p24, and SIV p27. [Wehrly1997]					
		• 183-H12-5C: Used as antigen capture reagent for p24 ELISA. [Chesebro1992, Toohey1995]					
136	241-D	Gag	p24		no		human (IgG1λ)
		Research Contact Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					
		References Robinson1991, Tyler1990, Gorny1989					
		• 241-D: MH AIDS Research and Reference Reagent program: 1244.					
		• 241-D: An antibody by this name is available in the NIH AIDS Research and Reference Reagent Program, and they refer to the papers [Gorny1989, Tyler1990, Robinson1991], but no p24 MAb by this name is discussed in these papers. [Gorny1989, Robinson1991, Tyler1990]					
137	2A6	Gag	p17				
		Research Contact A. O. Arthur, Frederick Cancer Research and Development Center, Frederick, MD					
		References Pincus1998					
		• 2A6: Part of a panel of 17 MAbs used as controls testing for the dual specificity of MAb G11H3 for both p17 and mycoplasma. [Pincus1998]					
138	5E2.A3k	Gag	p24 (1–158 SF2)		no		mouse (IgG1)
		Research Contact Biodesign International, Kennebunk, Maine, USA					
		References Hochleitner2000a					
		• 5E2.A3k: The Ab binding site was studied with epitope excision (protein is bound in native conformation to immobilized MAb, then digested with proteolytic enzymes) and extraction (protein is digested then allowed to react with Ab), followed by mass spectroscopy, as well as lysine modification – the epitope is discontinuous, but involves the highly conserved N-term proline, and the antibody recognizes SIVs and HIV-2 as well as HIV-1 p24. [Hochleitner2000a]					
139	71-31	Gag	p24		no		human (IgG1λ)
		References Bandres1998, Gorny1998, Gorny1997, Spear1993, Robinson1991, Robinson1990b, Gorny1989					
		• 71-31: NIH AIDS Research and Reference Reagent Program: 530.					
		• 71-31: Included as a negative control in studies that demonstrate that CXCR4 can bind to gp120 in the absence of CD4-gp120 interactions, and that this binding can be enhanced by Env deglycosylation. [Bandres1998]					
		• 71-31: Did not mediate deposition of complement component C3 on HIV infected cells. [Spear1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 71-31: No enhancing or neutralizing activity. [Robinson1991] • 71-31: Did not enhance HIV-1 IIIB infection. [Robinson1990b]					
140	91-6	Gag	p24 (121–240 IIIB)		no	HIV-1 infection	human (IgG1λ)
		References Robinson1990b, Gorny1989 • 91-6: NIH AIDS Research and Reference Reagent Program: 1239. • 91-6: No enhancing activity for HIV-1 IIIB. [Robinson1990b]					
141	98-4.3	Gag	p24		no	HIV-1 infection	human (IgG1λ)
		References Robinson1991 • 98-4.3: No enhancing or neutralizing activity. [Robinson1991]					
142	98-4.9	Gag	p24		no	HIV-1 infection	mouse (IgG3λ)
		References Gorny1989					
143	AC2	Gag	p7		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • AC2: Binds NCp7 independent of Zn fingers, does not react with NCp15. [Tanchou1995]					
144	BC1071	Gag	p24		no	HIV-1 infection	mouse
		Research Contact Aalto BioReagents **References** Schonning1999 • BC1071: The stoichiometry of MAb neutralization was tested and MAb BC1071 was used in this study for virion quantification. [Schonning1999]					
145	BE10	Gag	p7		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • BE10: Binding NCp7 requires Zn fingers, does not react with NCp15, inhibits NCp7-tRNA interaction. [Tanchou1995]					
146	CD9	Gag	p7		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • CD9: Binds NCp7 independent of Zn fingers, does not react with NCp15. [Tanchou1995]					
147	CH9B2	Gag	p17			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • CH9B2: UK Medical Research Council AIDS reagent: ARP349. • CH9B2: Reactive against p18 and p55. [Ferns1987]					
148	ED8	Gag	p7		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* p7 Gag **References** Tanchou1995 • ED8: Binds NCp7 independent of Zn fingers, does not react with NCp15. [Tanchou1995]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
149	EH12E1	Gag	p24			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • EH12E1: UK Medical Research Council AIDS reagent: ARP313. • EH12E1: Reacted with p55 and p24 in WB. [Ferns1987]				
150	G11G1	Gag	p17				rat
		References Pincus1996, Shang1991 • G11G1: Immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but only if the antigen was expressed at the cell surface – ricin-G11G1 did not mediate cell killing. [Pincus1996]					
151	G11H3	Gag	p17				
		References Pincus1998, Shang1991 • G11H3: This MAb is cross-reactive between p17 and mycoplasma – this antibody binds strain specifically to the variable lipoprotein (Vlp) F of M. hyorhinis, in the region of the carboxy-terminal repeat CGGSTPTPEQGNNQGGSTPTPEQGNSQVSK – the p17 epitope is discontinuous, but p17 and Vlp F share the tetrapeptide SQVS. [Pincus1998]					
152	HyHIV-19	Gag	p17 (JMH1)		no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* p17 Gag **References** Ota1998a, Liu1995 • HyHIV-19: Does not react with p17 peptides – Ka is 3.7 x 10^6 M-1 for rec p17 – inhibited growth of HIV-1 JMH1 in MT-4 cells when added 24 hours after the initial culture. [Ota1998a]					
153	IE8G2	Gag	p24			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade CBL-1 *HIV component:* HIV-1 **Research Contact** R. B. Ferns and R. S. Tedder **References** Ferns1989, Ferns1987 • IE8G2: UK Medical Research Council AIDS reagent: ARP347. • IE8G2: Reacted with both p55 and p24 – broadly reactive – showed less than 75% homologous inhibition. [Ferns1987]					
154	V7-8	Gag	p24		no	HIV-1 infection	mouse (IgG3κ)
		References Montefiori1991, Robinson1990b • V7-8: NIH AIDS Research and Reference Reagent Program: 381. • V7-8: Reacted with HIV-1IIIB, RF, and MN. [Montefiori1991] • V7-8: Did not enhance HIV-1 IIIB infection. [Robinson1990b]					
155	anti-p24	Gag	p24			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *HIV component:* Gag, gp120, Nef, Pol **Research Contact** Intracel Co **References** Buonaguro2001 • anti-p24: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames, as well as gp120 of the clade A isolate 94UG018, were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 Abs were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP. [Buonaguro2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
156	human sera	Gag	p24			HIV-1 infection	human (IgG)
		References Binley1997b					
		• Retention of anti-Env antibodies and loss of anti-Gag antibodies during progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule. [Binley1997b]					
157	polyclonal	Gag	Gag (LAI)			Vaccine	mouse
		Vaccine *Vector/Type:* DNA prime with protein boost *Strain:* B clade LAI *HIV component:* Gag, Nef, Tat *Adjuvant:* IL-18					
		References Billaut-Mulot2001					
		• DNA vaccinated BALB/c mice primed and boosted with a multiepitopic vaccine with IL18 showed lymphoproliferative and CTL responses – co-administration of IL18 increased T-cell responses but decreased anti-HIV Ab levels. [Billaut-Mulot2001]					
158	polyclonal	Gag	p24		no	Vaccine	rat
		Vaccine *Vector/Type:* gp120 depleted whole killed virus *Strain:* AG recombinant HZ321 *HIV component:* virus *Adjuvant:* Complete Freund's Adjuvant (CFA), CpG immunostimulatory sequence (ISS)					
		References Moss2000					
		• Lewis rats co-immunized with HIV-1 antigen in Freund's and with immunostimulatory sequences CpG stimulated increased IFNγ expressing CD4+ and CD8+ T cells and anti-p24 antibodies relative to antigen in Freund's without CpG. [Moss2000]					
		• Different HIV strains were used for different regions: subtype A env, subtype G gag.					
159	polyclonal	Gag	p24 (SF2)			Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* gp120, p24 Gag *Adjuvant:* MF59, PLG					
		References O'Hagan2000					
		• Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF-59 had the highest Ab response and also induced p24 specific CTL. [O'Hagan2000]					
160	polyclonal	Gag	Gag (SF2)			Vaccine	macaque, guinea pig, mouse
		Vaccine *Vector/Type:* DNA, protein *Strain:* B clade SF2 *HIV component:* Gag *Adjuvant:* aluminum phosphate, MF59, PLG					
		References O'Hagan2001					
		• DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59. [O'Hagan2001]					
161	polyclonal	Gag	p24		no	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade *HIV component:* p24 Gag					
		References Gupta2001					
		• Gag p24 is the mostly widely used HIV protein for serological based diagnostic kits — phage display libraries of HIV-1 p24 identified 2 epitope-rich regions: 70% of the clones that were identified using immunized rabbit sera had DNA fragments from the N-terminal region spanning 150–240 of Gag, and 30% from the carboxy-terminal region of p24 containing amino acids 310–360 — subtype B and C comparisons were made. [Gupta2001]					
162	polyclonal	Gag	p55		no	Vaccine	mouse
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* CD4BS, Gag, V3					
		References Truong1996					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly. [Truong1996]					
163	polyclonal	Gag	p24 (LAI)			Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide, virion, baculovirus, E. Coli recombinant protein *Strain:* B clade LAI *HIV component:* p24 Gag *Adjuvant:* Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA) **References** Devito2000c					
		• To compare vaccine strategies, rabbits were immunized with virion HIV-1/Lai, baculovirus recombinant p24, E. coli recombinant p24-15, and p24-derived peptides – the rabbit immunized with peptides had the broadest linear epitope responses – the capture ELISA method using anti-p24 IgG preparations was shown to capture isolates from HIV-1 subtypes or clades A to G – only immunization with virion HIV-1/Lai and baculovirus recombinant p24 developed IgG that was capable of efficiently capturing HIV-1 p24 in ELISA producing Abs able to recognise native configurations. [Devito2000c]					
164	polyclonal	Gag				Vaccine	mouse
		Vaccine *Vector/Type:* DNA *Adjuvant:* CpG immunostimulatory sequence (ISS), phosphorothioate oligodeoxynucleotides (ODNs) **References** Deml2001					
		• Immunization mice with a codon-optimized Gag was compared with a non-optimized Rev dependent Gag expression vector – Gag expression was at higher levels and Rev independent with the codon-optimized Gag, and i.m. immunization gave a stronger Th1-driven humoral and cellular immune response – intradermal immunization with either Gag DNA induced a Th2 response and no CTL. [Deml2001]					
165	polyclonal	Gag			yes	HIV-1 infection	human
		References Montefiori2001					
		• In 7/9 patients in whom HAART was initiated during early seroconversion, NAbs to autologous strains were not found immediately following treatment interuption after 1-3 years, and Env and Gag Abs were low or undetected by ELISA indicating, that early HAART suppresses the normal antibody response to HIV-1, presumably by limiting the concentration of viral antigens needed to drive B-cell maturation – in 3 patients with a viral rebound autologous NAbs rapidly appeared and correlated with spontaneous down-regulation of viremia – prolonged control of viremia after stopping treatment persisted in the absence of detectable NAbs, suggesting that cellular immune responses alone can control viremia under certain circumstances – these results support the notion that virus-specific B-cell priming, combined with CD8+ CTL induction, may be beneficial for HIV-1 vaccines that aim to suppress viremia in the absence of complete protection to prevent disease and reduce the rate of virus transmission. [Montefiori2001]					
166	polyclonal	Gag				Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* Env, Gag *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Lebedev2000					
		• Virus-like particles (VLPs) in the form of spherical particles with yeast dsRNA enveloped in a polysaccharide matrix carrying the protein TBI, that contains fragments of HIV Env and Gag, were used to immunize BALB/c mice and induced specific Abs against HIV-1 as measured by ELISA with TBI. [Lebedev2000]					
167	polyclonal	Gag			no	Vaccine	mouse (IgG1, IgG2a)
		Vaccine *Vector/Type:* DNA with CMV promotor, DNA with CMV/MCK hybrid promotor, DNA with MCK promotor **References** Bojak2002a					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• The ability of three different promoters to induce Gag specific immune responses was compared. The cytomegaliovirus (CMV) early gene promoter, which allows constitutive expression in different cells of host tissue, the tissue specific muscle creatine kinase (MCK) promoter, which may be restricted to differentiated, multinucleated myofibers and so safer, and a hybrid MCK/CMV promoter – intramuscular immunization of BALB/c mice utilizing the MCK promoter in combination with a codon optimized gag gene generated humoral (IgG1 (Th1) and IgG2a (Th2)) and CTL immune responses against HIV-1 Gag, however, the quantified immune parameters were clearly reduced as compared to CMV promotor-driven Gag expression. [Bojak2002a]					
168	polyclonal	Gag	p24		no	HIV-1 infection	human
		References Meles2002 • Indeterminant WB in Ethiopians: of 12,124 specimens blood specimens from Ethiopia, 1,437 (11.9%) were HIV-1-positive for antibody, and 91 (0.8%) gave equivocal results, most often due to p24 reactivity – subsequent testing confirmed many of the indeterminants were HIV-negative – the American Red Cross diagnostic criteria was more accurate than CDC or WHO, which would have given some false positive results. [Meles2002]					
169	polyclonal	Gag	Gag (p24)		yes	Vaccine	mouse
		Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* A clade UG5.94UG018 *HIV component:* Gag, gp120 **References** Buonaguro2002 **Keywords** inter-clade comparisons. **Country** Uganda. • BALB/c mice were immunized with VLPs carrying a subtype A gp120. Humoral immune responses directed against B-clade derived Gag (p24) peptides or gp120-Env V3 loop peptide were readily induced following a multi-dose immunization with VLP particles presenting a gp120 molecule from a HIV-1 isolate of clade A. VLP-immunized mice showed autologous and heterologous (against B-clade HIV-1 IIIB strain) neutralization activity. Proliferative responses and CTL were also observed. [Buonaguro2002] (**inter-clade comparisons**)					
170	polyclonal	Gag	Gag			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* DNA *HIV component:* Gag **References** Bojak2002b **Keywords** Th1. • Balb/c mice vaccinated by syngag, a DNA plasmid expressing HIV-1 Gag modified for human/mammalian codon usage, gave stronger and longer lasting immune responses than wild type gag. Gag-specific antibody and cellular immune responses were both increased, with a clear T-helper 1 polarization. There was a better IgG1/IgG2 response to intramuscular (i.m.) as compared to subcutaneous (s.c.) vaccination. [Bojak2002b] (**Th1**)					
171	polyclonal	Gag	Gag			Vaccine	macaque
		Vaccine *Vector/Type:* DNA, protein, virus-like particle (VLP), PLG microparticle *Adjuvant:* E. coli heat labile enterotoxin **References** Otten2003 • This study evaluates different vaccine technologies that avoid live vectors including plasmid DNA, recombinant p55Gag protein or gag-pol administered by polylactide coglycolide (PLG) microparticles, LTK63 as adjuvant, VLP, and plasmid DNA. 4/4 macaques primed with Gag-PLG and LTK63 showed strong antibody responses after the fourth immunization at week six. The best CTL responses were found for gag DNA, the best Th and Ab were obtained using Gag protein on PLG microparticles; Gag DNA priming with a PLG-protein boost gave high level CTL, Th and Ab responses. [Otten2003]					
172	polyclonal HIVIG	Gag	p24		P	HIV-1 infection	human
		References Nichols2002 • NYBC-HIVIG derived from patients with high NAb titers and NABI-HIVIG derived from patients with high anti-p24 Ab titers were compared in neutralizing assay against a panel of six primary isolates—both could neutralize all isolates tested but the NYBC-HIVIG dose required for 50% neutralization was of 3.2 fold lower, showing that the source plasmas influence the effective concentration of NAb present in HIVIG. [Nichols2002]					

IV-C-7 Protease Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
173	1696	Protease (1–7)	Protease (1–7 BH10)	PQIYLWQ		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **Ab type** N-term **References** Lescar2003, Rezacova2002, Rezacova2001, Lescar1999 **Keywords** review, structure. • 1696: Review of the implications of antibody structure and antigen peptide binding for the mechanisms of inhibition of protease activity by two MABs with different binding sites in protease. [Rezacova2002] (**review**, **structure**) • 1696: Study compares the crystal structure of the scFv-1696 in the non-complexed form compared to the complexed Fab-1696 and the Ag-bound scFv-1696 structures. Changes in the three conformational tertiary structures of CDR-H3 as well as in the different relative orientations of the light-chain variable domains of the different structures were observed, deomnstrating plasticity in the antibody binding site. [Lescar2003] (**structure**) • 1696: The crystal structure of the single chain Fv fragment of 1696 bound to a cross-reactive peptide (PQITLWQRR) was obtained. This sturcture suggests that 1696 inhibits portease activity by favoring dissociation of the active homodimer. [Rezacova2001] (**structure**) • 1696: MAb binds to HIV-1 and HIV-2, putative epitopes are PQIYLWQ and PQFSLWK respectively – Pro1 is critical, QIYLWQR residues 2-8, does not compete - MAb disrupts catalytic activity – crystal structure of the ligand-free Fab at 3 A resolution reveals a deep cavity lined by acidic and hydrophobic residues – the binding region is located within the region required for dimerization and the Fab structure could serve as a basis for drug design targeting this region. [Lescar1999] (**structure**)			
174	10E7	Protease (36–46)	Protease (38–45 HXB2)	MSLPGRWKPKM	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **References** Bjorling1992, Croix1993 • 10E7: Immunodominant region of protease in Armenian hamster (but only weakly reactive in people, see: [Bjorling1992]) – peptide MSLPGRWKP blocks protease binding [Croix1993]. [Bjorling1992, Croix1993]					
175	F11.2.32	Protease (36–46)	Protease (36–46 BH10)	MSLPGRWKPKM		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* Protease **Ab type** flap region **References** Rezacova2002, Lescar1999, Lescar1997, Lescar1996 **Keywords** review, structure. • F11.2.32: Review of the implications of antibody structure and antigen peptide binding for the mechanisms of inhibition of protease activity by two MABs with different binding sites in protease. [Rezacova2002] (**review**, **structure**) • F11.2.32: Crystal strucutre of a Fab peptide complex was obtained. Distortion may occur in the flap region of the protein, important for regulating access of substrate to the catalytic site. [Lescar1999] (**structure**) • F11.2.32: Binding leads to significant inhibition in proteolytic activity – crystal structure of Fab-peptide was determined to 2.2 A resolution – bound peptide shows no structural similarity to the corresponding segment in native protease suggesting binding may distort protein structure. [Lescar1997] (**structure**)			
176	13E1	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **References** Croix1993 • 13E1: Binds to MSLPGRWKPKM with sightly higher affinity. [Croix1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
177	8B11	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **References** Croix1993 • 8B11: Binds to MSLPGRWKPKM with sightly higher affinity. [Croix1993]					
178	8C10	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **References** Croix1993 • 8C10: Binds to MSLPGRWKPKM with sightly higher affinity. [Croix1993]					
179	8G5	Protease (38–45)	Protease (38–45 HXB2)	LPGRWKPK	no	Vaccine	hamster (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Protease **References** Croix1993 • 8G5: Binds to MSLPGRWKPKM with sightly higher affinity. [Croix1993]					

IV-C-8 RT Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
180	1E8	RT (65–73)	RT (65–73)	KKDSTKWRK	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* RT *Adjuvant:* nitrocellulose **References** Gu1996, Wu1993 • 1E8: Significantly inhibits DNA polymerase activity of RT by hindering binding of dNTPs – additive or synergistic RT inhibition with nevirapine and delavirdine. [Gu1996] • 1E8: Inhibits RT activity, binding site overlaps with two AZT resistance mutations. [Wu1993]					
181	polyclonal	RT (249–263)	RT (dis 249–263)	KDSWTVNDIQKLVGK		Vaccine, in vitro stimulation or selectio	human (IgG)
		Vaccine *Vector/Type:* peptide presented on icosahedral protein scaffold *HIV component:* RT *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Ab type** C2 **References** Domingo2003 **Keywords** vaccine antigen design. • A virus-like protein scaffold, called E2DISP, derived from pyruvate dehydrogenase multienzyme from Bacillus stearothermophilus has been engineered to display 60 copies of one or more epitopes on a single molecule. An E2DISP scaffold which displayed pep23, a 15-residue B and T helper HIV-1 RT epitope elicited a pep23-specific T-helper response *in vitro*. The E2DISP scaffold displaying peptide RT2, which is a CTL HIV-1 RT epitope, was able to elicit a CD8+ T cell response *in vitro* and in a vaccinated HLA-A2 transgenic mouse. Thus the E2DISP scaffold allows cell-entry and access to both the class I and class II processing pathways. The Th response in vaccinated mice supported Pep23-specific IgG responses. [Domingo2003] (**vaccine antigen design**)					
182	1.152 B3	RT (294–302)	RT (294–302)	PLTEEAELE	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* RT **References** Orvell1991 • 1.152 B3: Weakly positive by immunofluorescence – binding inhibits RT enzymatic activity. [Orvell1991]					
183	1.158 E2	RT (294–302)	RT (294–302)	PLTEEAELE	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* RT **References** Orvell1991 • 1.158 E2: Negative by immunofluorescence – binding inhibits RT enzymatic activity. [Orvell1991]					
184	31D6	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 31D6: Strong inhibitor of RT, > 50% inhibition. [Szilvay1992]					
185	31G8	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992 • 31G8: Weak inhibitor of RT, reactive by immunofluorescence. [Szilvay1992]					
186	32E7	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT **References** Szilvay1992					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 32E7: Weak inhibitor of RT, reactive by immunofluorescence. [Szilvay1992]					
187	33D5	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT					
		References Szilvay1992					
		• 33D5: Weak inhibitor of RT, reactive by immunofluorescence. [Szilvay1992]					
188	5B2	RT (294–318)	RT (294–319)	PLTEEAELELAENREILKEPVHGVY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* E. coli Trp fusion protein *HIV component:* RT					
		References Szilvay1992					
		• 5B2: UK Medical Research Council AIDS reagent: ARP3018.					
		• 5B2: Weak inhibitor of RT, reactive by immunofluorescence. [Szilvay1992]					
		• 5B2: There is an RT specific Ab [Szilvay1992] and a gp41 specific Ab [Tian2001] both called 5B2. [Szilvay1992]					
189	polyclonal	RT (295–304)	RT (295–304 PV22)	LTEEAELELA	no	HIV-1 infection	human (IgG)
		References Grimison1995					
190	1.153 G10	RT (350–354)	RT (350–354)	KTGKY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* RT					
		References Orvell1991					
191	RTMAb8	RT (376–383)	RT (532–539)	TTESIVIW	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* RT					
		References Ferns1991, Tisdale1988					
192	1D4A3	RT (384–387)	RT (540–543)	GKIP	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* RT					
		References Ferns1991					
193	RT6H	RT (384–387)	RT (540–543)	GKIP	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* RT					
		References Ferns1991					
194	1.160 B3	RT (442–450)	RT (442–450)	VDGAANRET	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* RT					
		References Orvell1991					
195	polyclonal	RT (521–531)	RT (521–531 PV22)	IIEQLIKKEKV	no	HIV-1 infection	human (IgG)
		References Grimison1995					
196	C2003	RT (536–549)	RT (703–716 BH10)	VPAHKGIGGNEQVD	no	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10					
		References DeVico1991					
		• C2003: Inhibits polymerase activity from a variety of retroviruses – RT protected from inhibition by preincubation with template primer. [DeVico1991]					
197	5B11	RT	RT (BH-10)			HIV-1 infection	human
		Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal					
		References Herschhorn2003					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

Keywords antibody generation, antibody sequence, variable domain, immunotherapy.

- 5B11: One of five a human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. [Herschhorn2003] (**antibody generation**, **immunotherapy**, **antibody sequence, variable domain**)

198 6B10 RT RT (BH-10) HIV-1 infection human

Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn2003
Keywords antibody generation, antibody sequence, variable domain.

- 6B10:One of five a human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (DDDP and RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. In contrast, 6B10 seemed to enhance DDDP activity and did not effect RDDP. [Herschhorn2003] (**antibody generation**, **antibody sequence, variable domain**)

199 6E9 RT RT (BH-10) in vitro stimulation or selectio human

Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn2003
Keywords antibody generation, antibody sequence, variable domain, immunotherapy.

- 6E9: One of five a human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. [Herschhorn2003] (**antibody generation**, **immunotherapy**, **antibody sequence, variable domain**)

200 E-4 RT RT (BH-10) HIV-1 infection human

Research Contact Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn2003
Keywords antibody generation, antibody sequence, variable domain.

- E-4:One of five a human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. In contrast, E-4 seemed to enhance RDDP. [Herschhorn2003] (**antibody generation**, **antibody sequence, variable domain**)

201 6B9 RT RT (dis 155–250) yes Vaccine mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade HXB2 *HIV component:* RT
Ab type palm domain
References Ohba2001, Chiba1997, Chiba1996

- 6B9: In contrast to MAb 7C4, which binds to the thumb region of RT, 6B9 binds to the palm subdomain and does not inhibit RT activity. [Chiba1996]

202 5F RT RT (252–335) yes Vaccine mouse

Vaccine *Vector/Type:* vaccinia *Strain:* B clade HXB2 *HIV component:* RT
Ab type thumb domain
References Ohba2001

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 5F: BALB/c mice were vaccinated with vaccinia carrying RT and a phage display library was produced and panned with RT – Fabs 5F and 5G were cloned, both recognizing an immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain also recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related. [Ohba2001]					
203	5G	RT	RT (252–335)		yes	Vaccine	mouse
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade HXB2 *HIV component:* RT **Ab type** thumb domain **References** Ohba2001 • 5G: BALB/c mice were vaccinated with vaccinia carrying RT and a phage display library was produced and panned with RT – Fabs 5F and 5G were cloned, both recognizing an immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain also recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related. [Ohba2001]					
204	7C4	RT	RT (dis 252–335)		yes	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade HXB2 *HIV component:* RT **Ab type** thumb domain **References** Ohba2001, Chiba1997, Chiba1996 • 7C4: Fabs 5F and 5G both recognize the same immunodominant neutralizing RT epitope in the region of the template primer-binding site in the thumb domain recognized by MAb 7C4 – sequencing revealed the heavy chains and light chains of 7C4, 5G and 7C4 are related. [Ohba2001] • 7C4: 7C4 inhibits RT from HIV-1 strains IIIB, Bru, and IMS-1 but not HIV-2 strains GH-1 and LAV-2, SIV MAC, nor SIV MND. [Chiba1997] • 7C4: 7C4 was produced from a hybridoma cell line derived from a BALB/c mouse repeatedly immunized with RT in a vaccinia construct, and was found to inhibit RT through binding to the template primer-binding site, a possible target for RT inhibitors. [Chiba1996]					

IV-C-9 Integrase Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
205	1C4	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996, Haugan1995 • 1C4: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996] • 1C4: MAb interferes with integrase binding to DNA. [Haugan1995]					
206	2C11	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996 • 2C11: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996]					
207	2E3	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Ovod1992, Nilsen1996 • 2E3: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996] • 2E3: There are two MAbs called 2E3 – the other one binds to Nef. [Ovod1992]					
208	3E11	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996, Otteken1992 • 3E11: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996] • 3E11: Recognized an epitope present on HIV-2/SIVmac, SIVagm, HIV-1, and SIVmnd. [Otteken1992] • 3E11: There is another MAb with this ID that recognizes p17. [Otteken1992]					
209	3F9	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996 • 3F9: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996]					
210	5F8	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Nilsen1996, Haugan1995 • 5F8: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996] • 5F8: MAb interferes with integrase binding to DNA. [Haugan1995] • 5F8: There is another MAb with this ID that recognizes and unknown protein in HIV.					
211	6G5	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996 • 6G5: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996]					
212	7B6	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996 • 7B6: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996]					
213	7C6	Integrase (1–16)	Integrase (1–16 HXB2)	FLDGIDKAQDEHEKYH	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996 • 7C6: One of a large set of MAbs that interact with the N-terminal part of integrase: 1C4, 2C11, 2E3, 3E11, 3F9, 5F8, 6G5, 7B6, 7C6 – these MAbs inhibit end processing and DNA joining, but had little effect on integration activities. [Nilsen1996]					
214	6C5	Integrase (17–38)	Integrase (17–38 HXB2)	SNWRAMASDFNLPPVVAKEIVA	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996, Haugan1995 • 6C5: This MAb inhibits end processing and DNA joining, but had little effect on integration activities. [Nilsen1996] • 6C5: MAb interferes with integrase binding to DNA. [Haugan1995]					
215	8G4	Integrase (22–31 + 82–101)	Integrase (12–42 HXB2)	MASDFNLPPV+GYIEAEVIPAETGQ-ETAYFI?	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **References** Nilsen1996, Haugan1995 • 8G4: MAb interferes with integrase binding to DNA. [Haugan1995] • 8G4: This MAb reacted strongly with peptides IN(12-31) and IN(22-42), and less strongly with peptide IN(82-101) – it did not react with a deletion mutant of positions 17-38 – this MAb inhibits end processing and DNA joining, but had little effect on integration activities. [Nilsen1996]					
216	17 (mAb17)	Integrase (25–35)	Integrase (25–35)	DFNLPPVVAKE	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Int **References** Yi2000b, Levy-Mintz1996, Bizub-Bender1994					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 17: Epitope mapped to helix-turn-helix motif in the N-term domain of Integrase, positions 25-35 – Zn binding stabilizes the Integrase-mAb17 complex – both MAb and Fab form of mAb17 inhibit Integrase activity – epitope region likely to be involved in protein-protein interaction. [Yi2000b] • 17: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. [Levy-Mintz1996] • 17: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 14 and 17 form a competition group. [Bizub-Bender1994]					
217	4D6	Integrase (42–55)	Integrase (42–55 HXB2)	KCQLKGEAMHGQVD	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** N-term **References** Nilsen1996, Haugan1995 • 4D6: This MAb inhibits end processing and DNA joining, and reduces reintegration activity. [Nilsen1996] • 4D6: MAb interferes with integrase binding to DNA. [Haugan1995]					
218	7-16 (7-19)	Integrase (50–159)	Integrase (50–159 HXB2)		no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int **Ab type** Integrase catalytic core **Research Contact** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 7-16: Binds to the central catalytic domain – the paper seems to sometimes call this antibody 7-16, sometimes 7-19, a possible typo. [Ishikawa1999]					
219	4F6	Integrase (56–102)	Integrase (56–102 HXB2)	CSPGIWQLDCTHLEGKVILVAVHVA-SGYIEAEVIPAETGQETAYFLL	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** Integrase catalytic core **References** Nilsen1996, Haugan1995 • 4F6: MAb interferes with integrase binding to DNA. [Haugan1995] • 4F6: MAb binding had minimal effects on IN *in vitro* activities. [Nilsen1996]					
220	anti-K159	Integrase (151–163)	Integrase (163–175)	VESMNKELKKIIG		Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* Int **References** Maksiutov2002, Maroun1999 • anti-K159: This epitope is similar to a fragment of the human protein Apoptosis regulator BCL-W (KIAA0271), ESVNKEMEPLVGQV. [Maksiutov2002] • anti-K159: Both the peptide K159, SQGVVESMNKELKKIIGQVRDQAEHLKTA, and the Abs raised against this peptide inhibit Integrase activity – K159 was found to fulfill condition of minimal number of helical heptads to achieve the formation of a stable coiled-coil structure – Integrase is proposed to function as a dimer interacting in this region. [Maroun1999]					
221	5D9	Integrase (186–250)	Integrase (186–250 HXB2)		no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **Ab type** Integrase DNA binding domain **References** Nilsen1996, Haugan1995 • 5D9: While C-term and N-term anti-Integrase MAbs interfere with Integrase-DNA binding, 5D9 which binds more centrally, does not. [Haugan1995] • 5D9: MAb binding had minimal effects on IN *in vitro* activities. [Nilsen1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
222	8-6	Integrase (211–227)	Integrase (211–227 HXB2)	KELQKQITKIQNFRVYY	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int **Research Contact** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 8-6: Antibody binds proximal to the DNA binding region. [Ishikawa1999]					
223	19 (2-19, scAb2-19)	Integrase (228–236)	Integrase (228–236 LAI)	RDSRNPLWK	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Int **References** Kitamura1999, Levy-Mintz1996, Bizub-Bender1994 • 19: Called 2-19, scAb2-19 is a single-chain Ab made from MAb 2-19 –acts intra-cellularly to block infection at low MOI by binding to integrase – scAb interfered with the folding of Gag-Pol polyprotein, the Ab did not affect viral production in LAI transfected cells, but the virus produced was less infectious – authors suggest that the epitope may be conformational. [Kitamura1999] • 19: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – 19 has a low binding affinity. [Bizub-Bender1994]					
224	2-19	Integrase (228–236)	Integrase (228–236 HXB2)	RDSRNPLWK	no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int **Ab type** Integrase DNA binding domain **Research Contact** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 2-19: MAb inhibits RT-Integrase interaction, and the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. [Ishikawa1999]					
225	8-22	Integrase (237–252)	Integrase (237–252 HXB2)	GPAKLLWKGEGAVVIQ	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int **Ab type** Integrase DNA binding domain **Research Contact** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 8-22: MAb inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. [Ishikawa1999]					
226	4-20	Integrase (253–261)	Integrase (253–261 HXB2)	DNSDIKVVP	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int **Ab type** Integrase DNA binding domain **Research Contact** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 4-20: Inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. [Ishikawa1999]					
227	6-19	Integrase (262–270)	Integrase (261–270 HXB2)	RRKAKIIRD	no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* chimeric maltose binding protein (MBP) *Strain:* B clade IIIB *HIV component:* Int					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type Integrase DNA binding domain **Research Contact** Yoshihiro Kitamura, Div of Mol Genetics, Nat Inst of Infectious Diseases, Musashimurayama, Japan **References** Ishikawa1999 • 6-19: Inhibits the terminal cleavage and strand transfer functions of Integrase, but not the disintegration activity. [Ishikawa1999]					
228	7C3	Integrase (262–271)	Integrase (262–271 HXB2)	RRKAKIIRDY	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **References** Nilsen1996, Haugan1995 • 7C3: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration. [Nilsen1996] • 7C3: MAb interferes with integrase binding to DNA. [Haugan1995]					
229	7F11	Integrase (262–271)	Integrase (262–271 HXB2)	RRKAKIIRDY	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **References** Lasky1987, Nilsen1996 • 7F11: There is another MAb with this name that binds to gp120. [Lasky1987] • 7F11: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration. [Nilsen1996]					
230	8E5	Integrase (262–271)	Integrase (262–271 HXB2)	RRKAKIIRDY	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade HXB2 *HIV component:* Int **References** Nilsen1996, Haugan1995 • 8E5: A set of three MAbs recognize an epitope in this region, 7C3, 7F11, and 8E5 – all three HIV-1 MAbs cross-react with HIV-2 IN – these MAbs inhibit end-processing, DNA joining and reintegration, and had little effect on disintegration. [Nilsen1996] • 8E5: MAb interferes with integrase binding to DNA. [Haugan1995]					
231	MAb 35	Integrase (264–273)	Integrase (264–273)	KAKIIRDYGK	no	Vaccine	mouse (IgGκ)
		Vaccine *Vector/Type:* protein *HIV component:* Int **References** Acel1998, Barsov1996 • MAb 35: Integrase was shown to have intrinsic DNA polymerase activity that can catalyze gap repair – MAb 35 inhibits this activity. [Acel1998] • MAb 35: Although MAb 35 does not inhibit HIV-1 IN, Fab 35 inhibits 3'-end processing, strand transfer and disintegration. [Barsov1996] • MAb 35: There appears to be two different IN Abs with similar names: MAb 35 and 35. [Barsov1996]					

IV-C-10 Pol Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
232	12	Pol	Integrase (1–58)		no	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* Int					
		References Levy-Mintz1996, Bizub-Bender1994					
		• 12: Used for the creation of single-chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. [Levy-Mintz1996]					
		• 12: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group. [Bizub-Bender1994]					
233	13	Pol	Integrase (1–58)		no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Int					
		References Bizub-Bender1994					
		• 13: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group. [Bizub-Bender1994]					
234	14	Pol	Integrase (1–58)		no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Int					
		References Bizub-Bender1994					
		• 14: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 14 and 17 form a competition group. [Bizub-Bender1994]					
235	16	Pol	Integrase		no	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* Int					
		References Bizub-Bender1994					
		• 16: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized. [Bizub-Bender1994]					
236	1C12B1	Pol	RT (431–521)			Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* RT					
		References Ferns1991					
		• 1C12B1: UK Medical Research Council AIDS reagent: ARP384.					
		• 1C12B1: Recognized both p66 and p51 in Western blot, binds to C terminus. [Ferns1991]					
237	21	Pol	Integrase (58–141)		no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* Int					
		References Levy-Mintz1996, Bizub-Bender1994					
		• 21: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. [Levy-Mintz1996]					
		• 21: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized. [Bizub-Bender1994]					
238	32 (mAb32, Fab32)	Pol	Integrase (223–266)		no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* Int					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Yi2002, Yi2000a, Bizub-Bender1994 • 32: Called mAb32 – mAb33 and mAb32 compete for binding to the C-term domain of Integrase – while mAb32 only weakly inhibits IN activity, mAb33 inhibits strongly, mAb32 has a lower affinity than mAb33, and Fab32 does not inhibit at all while Fab33 inhibits DNA binding a catalytic activity. [Yi2002] • 32: Limited proteolysis combined with mass spectrometric analysis indicates Fab32 binds to two strands of the beta sheet, beta1 223F, 224R, 226Y, and 228R and beta5 264K and 266K. [Yi2000a] • 32: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – MAbs 32 and 33 form a competition group. [Bizub-Bender1994]				
239	35	Pol	Integrase (1–58)		no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* Int **References** Bizub-Bender1994 • 35: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – the Zn finger motif is in the binding region – MAbs 12, 13 and 35 form a competition group. [Bizub-Bender1994] • 35: There appears to be two IN Abs with similar names: MAb 35 and 35. [Bizub-Bender1994]					
240	3D12	Pol	RT			Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT **References** Chiba1997 • 3D12: There is an anti-Nef MAb that also has this name (see [Chiba1997]) [Chiba1997]					
241	3F10	Pol	RT			Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT **References** Chiba1997					
242	4	Pol	Integrase (141–172)		no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* Int **References** Levy-Mintz1996, Bizub-Bender1994 • 4: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. [Levy-Mintz1996] • 4: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – 4 has a low binding affinity. [Bizub-Bender1994] • 4: There is another MAb with this ID that reacts with gp41. [Bizub-Bender1994]					
243	6B9	Pol	RT			Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT **References** Chiba1997					
244	7C4	Pol	RT			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* vaccinia *HIV component:* RT **References** Chiba1997 • 7C4: Dose-dependent inhibition of polymerase activity of RT of strains IIIB, Bru and IMS-1, but not HIV-2 strains GH-1 or LAV-2 or SIV strains MAC or MND. [Chiba1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
245	F-6	Pol	RT (BH-10)			in vitro stimulation or selectio	human

Ab type C-term **Research Contact** Amon Hizi, Sackler School of Medicine, Tel Aviv, Isreal
References Herschhorn2003
Keywords antibody generation, antibody sequence, variable domain, immunotherapy.

- F-6: One of five a human single chain Fv (ScFv) Abs isolated from an phage display library. F-6 was shown to bind to the carboxyl terminal segment of the p66 RT polypeptide, corresponding to RNase H. F-6 inhibited the DNA and RNA-dependent DNA polymerase (RDDP) activities of HIV-1 RT; two others, 6E9 and 5B11, inhibited RDDP and so have possible therapeutic potential. To pinpoint the mechanism of inhibition, three peptides were synthesized corresponding to the CDR3 sequences of F-6, and a cyclic version of the CDR H3 region bound to purified RT and blocked RDDP. [Herschhorn2003] (**antibody generation**, **immunotherapy**, **antibody sequence, variable domain**)

246	RT-4	Pol	RT		no		mouse (IgG2b)

References Gu1996, Li1993

- RT-4: Increased nevirapine and delavirdine inhibition, no effect on AZT inhibition. [Gu1996]

247	RT7O	Pol	RT (231–315)			Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *HIV component:* RT
Research Contact B. Ferns and R. Tedder
References Ferns1991

- RT7O: UK Medical Research Council AIDS reagent: ARP381.
- RT7O: Conformational epitope located centrally in the protein – inhibited RT enzyme activity and thus may bind close to the active site of the enzyme. [Ferns1991]

248	RT7U	Pol	RT (231–315)			Vaccine	mouse

Vaccine *Vector/Type:* protein *HIV component:* RT
Research Contact B. Ferns and R. Tedder
References Ferns1991

- RT7U: UK Medical Research Council AIDS reagent: ARP380.
- RT7U: Has a conformational epitope – reacts with p66 and p51 in WB. [Ferns1991]

249	anti-HIV-1 RT	Pol	RT				mouse (IgG)

References Wainberg1995, Maciejewski1995, diMarzo Veronese1986

- Commentary on Maciejewski *et al.* [Wainberg1995]
- anti-HIV-1 RT: Cloned heavy and light chains to express Fab intracellularly, preventing HIV infection *in vitro* – this MAb was broadly cross-reactive with clinical strains and even HIV-2. [Maciejewski1995]

250	polyclonal	Pol	p55		no	Vaccine	macaque

Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* Gag, gp120, V3
References Wagner1998b

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – gag and env CTL specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock. [Wagner1998b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
251	polyclonal	Pol	RT			Vaccine	mouse
		Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12 **References** Kim1997b • A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice, as well as Ab response detected by ELISA. [Kim1997b]					
252	polyclonal	Pol	RT (203–219)			Vaccine	mouse (IgA)
		Vaccine *Vector/Type:* Salmonella *HIV component:* RT **References** Burnett2000 • A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV RT gene fragment in the Lpp-OmpA-HIV fusion protein, induced a lymphoproliferative Th response and fecal RT-specific IgA in BALB/c mice. [Burnett2000]					
253	33 (mAb33, Fab33, 33D5, mab 33)	Pol	Integrase (223–268 HXB2)		no	Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *HIV component:* Int **Ab type** C-term **References** Yi2002, Yi2000a, Levy-Mintz1996, Bizub-Bender1994 • 33: Called mAb33 – mAb33 and mAb32 compete for binding to the C-term domain of Integrase – while mAb32 only weakly inhibits IN activity, mAb33 inhibits strongly, mAb32 has a lower affinity than mAb33, and Fab32 does not inhibit at all while Fab33 inhibits catalytic activity and DNA binding – heteronuclear NMR indicated eight residues of Integrase are immobilized upon Fab33 binding, two in the core of the protein, and 6 on the outer face that form a contiguous patch likely to contain the epitope – 223F, 224R, 226Y, 244K, 267I, and 268I, which may be a useful target for drug design – the Fab33-IN complex is far more soluble than IN alone and may be useful for crystallization. [Yi2002] • 33: Limited proteolysis combined with mass spectrometric analysis were used to define the binding site for Fab32, but Fab33 binding to the Intergrase C-term domain left it resistant to proteolytic digestion. [Yi2000a] • 33: Used for the creation of single chain variable antibody fragments (SFvs) for internal cellular expression – neutralization of IN activity prior to integration, whether the Ab is expressed in the nucleolus or the cytoplasm – relative binding affinity to IN: 12 > 17 = 33 > 21 > 4. [Levy-Mintz1996] • 33: BALBc mice were immunized with rec integrase, hybridomas expressing anti-integrase Abs were generated, and the antibodies characterized – MAbs 32 and 33 form a competition group. [Bizub-Bender1994]					

IV-C-11 Vif Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
254	TG002	Vif (34–47)	Vif (34–47)	KARGWFYRHHYESP?	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Vif **Research Contact** Transgene • TG002: NIH AIDS Research and Reference Reagent Program: 2746. • TG002: This MAb was raised in response to a rec Vif protein derived from E. coli.					
255	TG001	Vif (176–192)	Vif (176–192)	KPQKTKGHRGSHTMNGH?	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Vif **Ab type** C-term **Research Contact** Transgene • TG001: NIH AIDS Research and Reference Reagent Program: 2745. • TG001: This antibody was raised in response to a rec Vif protein derived from E. coli.					
256	J4	Vif	(HXB2)				humanized rabbit
		References Goncalves2002 • J4: The authors developed a Vif-specific intrabody single-chain FAb fragment of J4 called 14BL – when expressed intracellularly in the cytoplasm this intrabody efficiently bound Vif protein and neutralized its infectivity enhancing function – intrabody-expressing transduced cells were shown to be highly refractory to challenge with the laboratory strain NL43 and with primary isolates strains of HIV-1. [Goncalves2002]					
257	polyclonal	Vif	Vif			Vaccine	mouse
		Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12 **References** Kim1997b • A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice, as well as an Ab response detected by ELISA. [Kim1997b]					

IV-C-12 Vpr Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
258	polyclonal	Vpr	Vpr (89.6)			HIV-1 infection	human (IgG)

References Richardson2003
Keywords rate of progression.
Country France.

- Serum samples were obtained from the French GRIV (gentic resistance to HIV) cohort and tested for anti-Tat and anti-Vpr responses, as both may contribute as extracellular proteins to pathogenesis. Serum anti-Vpr IgG responses were significantly higher in stable non-progressors (CD4+ T cell counts greater than 500 cell/ul after being positive for 8 years with no ART) and unstable non-progressors (declined during a 20 month follow up), than fast progressors (CD4+ T less than 300 cells/ul within 2 years of seroconversion, some HAART). [Richardson2003] (**rate of progression**)

IV-C-13 Tat Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
259	polyclonal	Tat (1–15)	Tat (1–15 89.6)	MEPVDRPLEPWKHPG		Vaccine	macaque (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
Ab type C-term, N-term, Tat basic region
References Silvera2002
Keywords antibody binding site definition and exposure, vaccine antigen design.

- Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). [Silvera2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
260	TA9	Tat (1–20)	Tat (1–20 Lai/Bru)	MEPVDPRLEPGSQPKT		Vaccine	mouse (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Ab type N-term **Research Contact** Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard2003
Keywords inter-clade comparisons.

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TA9 is clade B specific, and does not recognize Tat from clade A, C, D, or CRF01 (AE).TA9 binds to the Tat peptide aa 1-61 strongly, and is also able to bind to Tat aa 1-20, and Tat peptide aa 8-53. [Belliard2003] (**inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
261	TD84	Tat (1–20)	Tat (1–20 Lai/Bru)	MEPVDPRLEPGSQPKT		Vaccine	mouse (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Ab type N-term **Research Contact** Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard2003
Keywords inter-clade comparisons.

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TD84 is clade B specific, and does not recognize Tat from clade A, C, D, or CRF01 (AE). It reacts strongly with aa 1-61, and is able to react with aa 1-20. [Belliard2003] (**inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
262	TE135	Tat (1–20)	Tat (1–20 Lai/Bru)	MEPVDPRLEPGSQPKT		Vaccine	mouse (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)
Ab type N-term **Research Contact** Dr. J.-L. Guesdon, Institut Pasteur, Paris
References Belliard2003
Keywords inter-clade comparisons.

- This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TE135 is clade B specific, and does not recognize Tat from clade A, C, D, or CRF01 (AE). It reacts strongly with aa 1-61, and is able to react with aa 1-20. [Belliard2003] (**inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
263	polyclonal	Tat (1–20 + 1–20)	Tat (1–20 IIIB BH10)	MEPVDPRLEPWKHPGSQPKT?		Vaccine	mouse (IgA, IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2)
References Borsutzky2003

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Keywords adjuvant comparison, genital and mucosal immunity, immunodominance, mucosal immunity, Th1, Th2, vaccine-induced epitopes. • Intranasal immunization of BALB/c mice Tat with MALP-2 induced stronger immune responses than i.p. vaccination of Tat with IFA. Also i.n. MALP-2 vaccination favored Th1 responses, while i.p IFA favored Th2. Ab, T help and CTL responses were observed. MALP-2 enhanced Tat-specific IgA responses in the lung and in the genital tract. Three linear Ab epitopes were recognized. The most frequent response (80% of vaginal lavage, 100% of sera and lung lavage) was to Tat peptide 1-20. The second strongest to Tat 46-60 (20% of vaginal lavage, 50% of lung lavage, 50% of sera. Finally, 50% of the sera of Tat+ IFA i.p. immunized mice recognized Tat 73-86. [Borsutzky2003] (**adjuvant comparison**, **genital and mucosal immunity**, **vaccine-induced epitopes**, **immunodominance**, **mucosal immunity**, **Th1**, **Th2**)					
264	polyclonal	Tat (1–24)	Tat (1–24)	MEPVDPRLEPWKHPGSQPKTACTN		HIV-1 infection, Vaccine	human (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade *HIV component:* Tat *Adjuvant:* Montanide (ISA 51) **Ab type** N-term **References** Noonan2003 **Keywords** immunotherapy, vaccine-specific epitope characteristics. • Intramuscular injection of Tat-toxoid induced high titers of nti-Tat reactivity in serum samples of six HIV-1 positive and in four HIV negative study subjects. Anti-Tat antibodies successfully blocked extracellular Tat from transactivating HIV Tat-sensitive promotors. The anti-Tat IgG response in sera from two healthy and HIV infected patients inhibited cell entry of synthetic Tat, thus blocking its functional activity. Additionally, the anti-Tat antibodies inhibited intercellular Tat transfer as demonstrated by a co-culture cell system. All HIV-1 infected patients had Ab responses to the N-term region of Tat, and 4/4 HIV-1+ and 5/6 HIV-1 negative patients responded to the basic domain. Several additional peptides were recognized either exclusively or more commonly in the HIV+ people. The N-terminus region of Tat mediates binding to CD26, that may be involved in modulation of chemokine function, and may also mediate T-cell apotosis. [Noonan2003] (**vaccine-specific epitope characteristics**, **immunotherapy**)					
265	NT3/2D1.1	Tat (2–15)	Tat	EPVDPNLEPWNHPS		Vaccine	mouse (IgG1a)
		Vaccine *Vector/Type:* peptide *HIV component:* Tat **Ab type** N-term **References** Dingwall1989 • NT3/2D1.1: UK Medical Research Council AIDS reagent: ARP352. • NT3/2D1.1: Immunoprecipitates and immunoblots HIV-1 tat protein. [Dingwall1989]					
266	1.2	Tat (2–17)	Tat (1–16)	EPVDPRLEWKHPGSQ			
		References Ranki1995, Ovod1992 • 1.2: Weak expression of Tat observed in HIV+ brain tissue sample, in contrast to Nef. [Ranki1995]					
267	1D9D5	Tat (2–21)	Tat	EPVDPRLEWKHPGSQPKTA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Tat **Ab type** N-term **References** Valvatne1996, Mhashilkar1995 • 1D9D5: Exogenously delivered Tat can efficiently transactivate an HIV-LTR-CAT construct in HeLa cells in the presence of 1D9D5, suggesting when considered with the results of [Mhashilkar1995], that free Tat and not Ab bound is taken up by cells [Valvatne1996]. [Mhashilkar1995, Valvatne1996] • 1D9D5: Single chain antibodies, intrabodies, were engineered that can be stably expressed in the cytoplasm of mammalian cells – co-expression of an N-term intrabody can inhibit transactivation of an HIV LTR-CAT construct and block import into nucleus, but intrabody specific for exon 2 did not inhibit activity. [Mhashilkar1995]					
268	TB12	Tat (44–60)	Tat (44–61 Lai/Bru)	GISYGRKKRRQRRPPQG		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type Tat basic region **Research Contact** Dr. J.-L. Guesdon, Institut Pasteur, Paris **References** Belliard2003 **Keywords** inter-clade comparisons. • This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. TB12 is clade B and D specific, and does not recognize Tat from clade A, C, or CRF01 (AE). It reacts strongly with aa 1-61, and is also able to react with aa 44-61, in the basic region involved in Tat uptake. [Belliard2003] (**inter-clade comparisons**)					
269	polyclonal	Tat (46–60)	Tat (46–60 IIIB BH10)	SYGRKKRRQRRRAHQ?		Vaccine	mouse (IgA, IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2) **References** Borsutzky2003 **Keywords** adjuvant comparison, genital and mucosal immunity, immunodominance, mucosal immunity, Th1, Th2, vaccine-induced epitopes. • Intranasal immunization of BALB/c mice Tat with MALP-2 induced stronger immune responses than i.p. vaccination of Tat with IFA. Also i.n. MALP-2 vaccination favored Th1 responses, while i.p IFA favored Th2. Ab, T help and CTL responses were observed. MALP-2 enhanced Tat-specific IgA responses in the lung and in the genital tract. Three linear Ab epitopes were recognized. The most frequent response (80% of vaginal lavage, 100% of sera and lung lavage) was to Tat peptide 1-20. The second strongest to Tat 46-60 (20% of vaginal lavage, 50% of lung lavage, 50% of sera. Finally, 50% of the sera of Tat+ IFA i.p. immunized mice recognized Tat 73-86. [Borsutzky2003] (**adjuvant comparison**, **genital and mucosal immunity**, **vaccine-induced epitopes**, **immunodominance**, **mucosal immunity**, **Th1**, **Th2**)					
270	polyclonal	Tat (46–60)	Tat (46–60 89.6)	SYGRKKRRQRRRAHQ		Vaccine	macaque (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Ab type** C-term, N-term, Tat basic region **References** Silvera2002 **Keywords** antibody binding site definition and exposure, vaccine antigen design. • Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). [Silvera2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)					
271	polyclonal	Tat (46–60)	Tat (46–60 89.6)	SYGRKKRRQRRRAHQ		Vaccine	macaque (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Ab type** C-term, N-term, Tat basic region **References** Silvera2002 **Keywords** antibody binding site definition and exposure, vaccine antigen design. • Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). [Silvera2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
272	polyclonal	Tat (47–60)	Tat (46–60)	YGRKKRRQRRRPPQ		HIV-1 infection, Vaccine	human (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade *HIV component:* Tat *Adjuvant:* Montanide (ISA 51)
Ab type Tat basic region
References Noonan2003
Keywords immunotherapy, vaccine-specific epitope characteristics.

- Intramuscular injection of Tat-toxoid induced high titers of anti-Tat reactivity in serum samples of six HIV-1 positive and in four HIV negative study subjects. Anti-Tat Abs successfully blocked extracellular Tat from transactivating HIV Tat-sensitive promotors. The anti-Tat IgG response in sera from two healthy and HIV infected patients inhibited cell entry of synthetic Tat, thus blocking its functional activity. Additionally, the anti-Tat Abs inhibited intercellular Tat transfer in a co-culture cell system. All HIV-1 infected patients had Ab responses to the N-term region of Tat, and 4/4 HIV-1+ and 5/6 HIV-1 negative patients responded to the basic domain. Several additional peptides were recognized either exclusively or more commonly in the HIV+ people. The basic region of Tat mediates binding to VEGFR2 on Kaposi's sarcoma cells and endothelial cells, and HIV patients with Kaposi's sarcoma lack Abs to this domain.. [Noonan2003] (**vaccine-specific epitope characteristics**, **immunotherapy**)

273	1D2F11	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *HIV component:* Tat
Ab type C-term
References Valvatne1996

- 1D2F11: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat. [Valvatne1996]

274	2D9E7	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *HIV component:* Tat
Ab type C-term
References Valvatne1996

- 2D9E7: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat, but less efficiently than MAbs 1D2F11 or 4B4C4. [Valvatne1996]

275	4B4C4 (4B4)	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *HIV component:* Tat
Ab type C-term
References Jensen1997, Valvatne1996

- 4B4C4: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat. [Valvatne1996]

276	5G7D8	Tat (49–86)	Tat	RKKRRQRRRPPQGSQTHQVSLSKQP-TSQSRGDPTGPKE		Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *HIV component:* Tat
Ab type C-term
References Valvatne1996

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 5G7D8: MAb did not bind shorter peptides – this MAb inhibited exogenously delivered Tat transactivation of an HIV-LTR-CAT construct in HeLa cells by inhibition of cellular uptake of Tat, but less efficiently than 1D2F11 or 4B4C4. [Valvatne1996]					
277	polyclonal	Tat (73–86 + 73–86)	Tat (73–86 IIIB BH10)	PTSQPRGDPTGPKE?		Vaccine	mouse (IgA, IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), macrophage activating lipopeptide-2 (MALP-2) **References** Borsutzky2003 **Keywords** adjuvant comparison, genital and mucosal immunity, immunodominance, mucosal immunity, Th1, Th2, vaccine-induced epitopes. • Intranasal immunization of BALB/c mice Tat with MALP-2 induced stronger immune responses than i.p. vaccination of Tat with IFA. Also i.n. MALP-2 vaccination favored Th1 responses, while i.p IFA favored Th2. Ab, T help and CTL responses were observed. MALP-2 enhanced Tat-specific IgA responses in the lung and in the genital tract. Three linear Ab epitopes were recognized. The most frequent response (80% of vaginal lavage, 100% of sera and lung lavage) was to Tat peptide 1-20. The second strongest to Tat 46-60 (20% of vaginal lavage, 50% of lung lavage, 50% of sera. Finally, 50% of the sera of Tat+ IFA i.p. immunized mice recognized Tat 73-86. [Borsutzky2003] (**adjuvant comparison**, **genital and mucosal immunity**, **vaccine-induced epitopes**, **immunodominance**, **mucosal immunity**, **Th1**, **Th2**)					
278	NT2/4D5.24	Tat (73–86)	Tat	PTSQPRGDPTGPKE		Vaccine	mouse
		Vaccine *Vector/Type:* peptide *HIV component:* Tat **Ab type** C-term **References** Dingwall1989 • NT2/4D5.24: Immunoprecipitates and immunoblots HIV-1 tat protein. [Dingwall1989]					
279	polyclonal	Tat (76–90)	Tat (76–90 89.6)	QPRGDPTGPKQKKK		Vaccine	macaque (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade 89.6, B clade HXBc2 *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA) **Ab type** C-term, N-term, Tat basic region **References** Silvera2002 **Keywords** antibody binding site definition and exposure, vaccine antigen design. • Anti-Tat and Tat toxoid responses were raised in rhesus macaques using HxBc2 and 89.6P Tat, and Tat toxoids.High anti-Tat IgG responses were observed in all animals, and helper responses were detected in 8/16, and IFN gamma CTL in 11/16.. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response. The most consistent reactions to the vaccinations were to peptides in regions: N-term, 1-15 (MEPVDRPLEPWKHPG), basic domain 46-60 (SYGRKKRRQRRRAHQ), and 61-91, particularly C-term 76-90 (QPRGDPTGPKQKKK). [Silvera2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)					
280		Tat	Tat			Vaccine	human
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), Montanide (ISA 51) **References** Gringeri1998 **Keywords** immunotherapy. • 14 HIV-1 infected individuals were vaccinated with inactivated Tat (called Tat-toxoid), with the intent of enhancing Tat Ab levels to suppress the negative impact of secreted Tat on immune function. Tat vaccinations were safe and patients developed increased levels of Tat-specific Abs; some patients had increased Tat-specific proliferative responses. CD4 T cells tended to increase a small but significant amount after immunization, and in several patients viral load decreased. [Gringeri1998] (**immunotherapy**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
281	L-anti-Tat	Tat	Tat		L P (when lipidated)	Vaccine	mouse (IgG1)
	Vaccine *Vector/Type:* protein *HIV component:* Tat **Research Contact** AGMED, Inc., Bedford, MA USA **References** Cruikshank1997 • L-anti-Tat: Lipidated antibody can be taken up by cells and effectively block IIIB and primary virus HIV-1 replication in actively and latently infected cells. [Cruikshank1997]						
282	TC15	Tat	Tat (Lai/Bru)			Vaccine	mouse (IgG)
	Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA) **Ab type** N-term **Research Contact** Dr. J.-L. Guesdon, Institut Pasteur, Paris **References** Belliard2003 **Keywords** inter-clade comparisons. • TC15: This is one of 5 anti-Tat murine monoclonal antibodies generated in this study. It is conformational reacting only with intact protein. It reacts with B and D clade Tat proteins, and not recognize Tat from clade A, C, or CRF01 (AE). [Belliard2003] (**inter-clade comparisons**)						
283	polyclonal	Tat	Tat			HIV-1 infection	human (IgG)
	References Belliard2003 **Keywords** inter-clade comparisons, rate of progression. **Country** France. • Sera from 20 HIV-1 positive individuals were tested for their ability to react with Tat proteins from different clades, and were found to react with subtype A, B, and D, but not with subtype C or CRF01 (AE). Sera from 101 slow progressors and 42 fast progressors were tested for responses to Tat peptides, and compared to responses to gp41 peptide, as anti-Tat antibodies have been shown by others to be elevated in slow progressors. In this study, overall levels of Tat antibodies were not different in the two groups, however relative levels of antibodies to different Tat and gp41 peptides were observed. [Belliard2003] (**inter-clade comparisons**, **rate of progression**)						
284	polyclonal	Tat	Tat (Lai/Bru)			SHIV infection, Vaccine	macaque (IgG)
	Vaccine *Vector/Type:* peptide *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* aluminum phosphate, CpG immunostimulatory sequence (ISS), Montanide (ISA 720) **Ab type** N-term **References** Belliard2003 **Keywords** rate of progression. • Macaques were immunized with different combinations of Tat peptides. Serum from these animals was able to inhibit Tat-induced apoptosis, and Tat antibodies are associated with long term survival. Anti-Tat antibodies generated in infected macaques tended to be restricted to the peptide 44-61, while sera from infected humans could react with several different peptides. [Belliard2003] (**rate of progression**)						
285	polyclonal	Tat	Tat (Lai/Bru)			SHIV infection, Vaccine	rabbit (IgG)
	Vaccine *Vector/Type:* peptide *Strain:* B clade BRU *HIV component:* Tat *Adjuvant:* BSA, Complete Freund's Adjuvant (CFA) **Ab type** N-term **References** Belliard2003 **Keywords** rate of progression.						

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 12 rabbits were immunized with different combinations of Tat peptides. Abs raised against peptide aa 8-53 did not react with the peptide 19-53, suggesting that the N-terminal region is important. Serum from these animals was able to inhibit Tat-induced apoptosis, and Tat antibodies in humans are associated with long term survival. [Belliard2003] (**rate of progression**)					
286	polyclonal	Tat	Tat		yes	Vaccine	mouse (IgG1, IgG2a, IgG3)
		Vaccine *Vector/Type:* protein *HIV component:* Tat *Adjuvant:* Complete Freund's Adjuvant (CFA), red blood cells **References** Dominici2003 **Keywords** adjuvant comparison, immunotherapy, Th1, Th2. • BALB/c mice were immunized intra-peritineally with Tat protein bound to red blood cells via biotin-avidin conjugation. This antigen delivery system was successfully internalized by dendritic cells, and induced more consistent anti-Tat NAbs responses and sightly increased Tat-specific CTL responses relative to Tat protein with CFA. RBC-Tat immunization induced Th1 (IgG2a)and Th2 (IgG1 and IgG3)type immune responses. (**adjuvant comparison**, **immunotherapy**, **Th1**, **Th2**)					
287	polyclonal	Tat	Tat			Vaccine	mouse (IgA, IgG)
		Vaccine *Vector/Type:* chitosan nanoparticles *HIV component:* Tat *Adjuvant:* adjuvant oily structure (IMS) **References** Le Buanec2001 **Keywords** adjuvant comparison, mucosal immunity. • Mice were immunized with Tat toxoid (Tat detoxified by carboxamidation) either intranasally or orally using either adjuvant oily structure (IMS), nanoparticles of chitosan, or microparticles of polylactide-co-glycolide. Each of these strategies triggered IgG and IgA that inhibited Tat activity. [Le Buanec2001] (**adjuvant comparison**, **mucosal immunity**)					
288	polyclonal	Tat	Tat (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Tat *Adjuvant:* Cholera toxin (CT), E. coli mutant heat labile enterotoxin (LT-R72), E. coli heat labile enterotoxin **References** Marinaro2003 **Keywords** adjuvant comparison, mucosal immunity. • Intranasal immunization of BALB/c mice with Tat and e.coli heat-labile enterotoxin (LT) and non-toxic LT-R72 LT induced strong antigen-specific IgG Abs which remained stable for one year. Tat-specific IgA reponses were measured in vaginal and intestinal secretions. Immunization of BALB/c mice with native Tat (aa1-86) induced serum IgG directed against an immunodominant epitope (aa1-20) and against a second epitope (aa 46-60). CTL responses were also observed. Anti-Tat serum Abs neutralized Tat activity in a dose-independent manner. C57BL/6 remained unresponsive to Tat immunizations when Tat was co-adminstered with LT or cholera toxin (CT) as adjuvant; BALB/c mice are H-2d, C57BL/6 are H-2b. Congenic BALB.B mice that express H-2b rather than H-2d also could not respond to Tat, suggesting the repsonse to Tat is constrained by the haplotype. [Marinaro2003] (**adjuvant comparison**, **mucosal immunity**)					
289	polyclonal	Tat	Tat			Vaccine	macaque (IgG)
		Vaccine *Vector/Type:* protein, vaccinia *Strain:* B clade MN *HIV component:* gp160, Tat *Adjuvant:* Incomplete Freund's Adjuvant (IFA), polyphosphazene **References** Pauza2000 • 16 Macaques mulatta were immunized with Tat toxoid, or with Tat plus gp160, and challenged with the SHIV 89.6PD isolate. Sera from 14/16 animals neutralized Tat *in vitro*. 8 macaques developed both cellular and humoral responses to Tat, and 7/8 of these had low viral set points after rectal challenge with SHIV89.6PD. CD4+ T cells in Tat vaccinated infected animals had lower IFN-alpha and chemokine receptor expression, features of infection associated with extracellular Tat. [Pauza2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
290	polyclonal	Tat	Tat (IIIB, 89.6, CMU08)			HIV-1 infection, Vaccine	human (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade *HIV component:* Tat
Ab type C-term, N-term, Tat basic region
References Richardson2003
Keywords antibody binding site definition and exposure, inter-clade comparisons, rate of progression, vaccine-specific epitope characteristics.
Country France.

- Serum samples were obtained from the French GRIV (gentic resistance to HIV) cohort and tested for anti-Tat and anti-Vpr responses as both may contribute as extracellular proteins to pathogenesis. Serum anti-Tat IgG responses were significantly higher and maintained for up to 20 months in stable non-progressors (CD4+ T cell counts greater than 500 cell/ul after being positive for 8 years with no ART) compared to unstable non-progressors and fast progressors (CD4+ T less than 300 cells/ul within 2 years of seroconversion, some HAART). Anti-Tat IgG from GRIV stable non-progressors recognized linear epitopes located within the N-terminal, basic and the C-terminal domains of Tat. Humoral responses of fast-progressors and of one unstable non-progressor were restricted to the basic region of Tat. Tat toxoid vaccinees from Milan tended to recognize N-terminal and C-terminal domains. Sera from some GRIV and Tat toxoid vaccinees cross-reacted in an ELISA assay with a truncated 89.6 S/HIV 89.6P Tat, 89.6P Tat, HIv-1 subtype E (CMU08) and with SIVmac251 Tat (one sample). [Richardson2003] (**antibody binding site definition and exposure**, **vaccine-specific epitope characteristics**, **inter-clade comparisons**, **rate of progression**)

291	polyclonal	Tat	Tat			Vaccine	macaque (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade 89.6, B clade IIIB *HIV component:* Tat
Ab type C-term, N-term, Tat basic region
References Richardson2002
Keywords antibody binding site definition and exposure, vaccine antigen design, variant cross-recognition or cross-neutralization.

- Anti-Tat responses were raised in rhesus macaques using IIIB Tat, SHIV89.6P Tat, carboxymethylated Tat and 89.6P Tat toxoids. Tat IgG responses to the vaccine were cross-reactive with subtype E and MAC 251. Ab and proliferative responses were observed, and the trucated 86 amino acid IIIB Tat was more immunogenic than the full 102 amino acid Tat. Tat vaccinated animals when challenged with SHIV89.6 were infected despite a robust immune response and were not distinguishable from controls. [Richardson2002] (**antibody binding site definition and exposure**, **vaccine antigen design**, **variant cross-recognition or cross-neutralization**)

292	polyclonal	Tat	Tat (IIIB, 89.6, CMU08)			HIV-1 infection, Vaccine	human (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade *HIV component:* Tat
Ab type C-term, N-term, Tat basic region
References Richardson2003
Keywords antibody binding site definition and exposure, inter-clade comparisons, rate of progression, vaccine-specific epitope characteristics.
Country France.

- Serum samples were obtained from the French GRIV (gentic resistance to HIV) cohort and tested for anti-Tat and anti-Vpr responses as both may contribute as extracellular proteins to pathogenesis. Serum anti-Tat IgG responses were significantly higher and maintained for up to 20 months in stable non-progressors (CD4+ T cell counts greater than 500 cell/ul after being positive for 8 years with no ART) compared to unstable non-progressors and fast progressors (CD4+ T less than 300 cells/ul within 2 years of seroconversion, some HAART). Anti-Tat IgG from GRIV stable non-progressors recognized linear epitopes located within the N-terminal, basic and the C-terminal domains of Tat. Humoral responses of fast-progressors and of one unstable non-progressor were restricted to the basic region of Tat. Tat toxoid vaccinees from Milan tended to recognize N-terminal and C-terminal domains. Sera from some GRIV and Tat toxoid vaccinees cross-reacted in an ELISA assay with a truncated 89.6 S/HIV 89.6P Tat, 89.6P Tat, HIv-1 subtype E (CMU08) and with SIVmac251 Tat (one sample). [Richardson2003] (**antibody binding site definition and exposure**, **vaccine-specific epitope characteristics**, **inter-clade comparisons**, **rate of progression**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
293	polyclonal	Tat	Tat			Vaccine	macaque (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120, Nef, Tat *Adjuvant:* AS02A (oil-in-water emulsion, 3D-monophosphoryl lipid A, QS21), AS06 (CpG, aluminum hydroxide)
References Voss2003
Keywords adjuvant comparison, variant cross-recognition or cross-neutralization.

- Monkeys were immunized with different combinations of gp120/NefTat/SIV-Tat three times over a three-month time period and intravenously challenged with SHIV 89.6P four weeks after the last immunzation. Vaccination induced anti-Tat, -Nef and -gp120 Ab responses which decreased until challenge. Neutralizing Ab responses against HIV-1 MN and HIV-1 W61D were observed. Vaccination with the combination of all three proteins reduced viral load and kept animals from a CD4+ T cell decline, preventing AIDS for more than 2.5 years. The adjuvant AS02A elicited NAbs and protected from disease, while AS06 did not. gp120 alone or TatNef/SIV-Tat without gp120 could not protect from disease. [Voss2003] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)

294	polyclonal	Tat	Tat			HIV-1 infection	human

References Zagury1998
Keywords immunotherapy, rate of progression.
Country France.

- Comparing 67 fast progressors with 182 non-progressors in the GRIV cohort, only anti-Tat Ab levels, not Abs to Env, Gag, or Nef, were correlated as a serological indicator of rate of progression. This suggests that raising Tat Abs may be beneficial as immunotherapy or in a vaccine. [Zagury1998] (**immunotherapy**, **rate of progression**)

295	2D9D5	Tat	Tat			Vaccine	mouse (IgG)

Vaccine *Vector/Type:* protein *HIV component:* Tat
Ab type C-term
References Mhashilkar1995

- 2D9D5: Single chain antibodies, intrabodies, were engineered that can be stably expressed in the cytoplasm of mammalian cells – co-expression of C-term intrabody did not inhibit transactivation of an HIV LTR-CAT construct, in contrast to MAb 1D9D5. [Mhashilkar1995]

IV-C-14 Rev Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
296	4G9	Rev (5–15)	Rev (5–15)	SGDSDEELIRT?		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Rev **References** Jensen1997 • 4G9: Mapped binding location by protein footprinting. [Jensen1997]					
297	Ab2	Rev (32–50)	Rev (32–49 BRU)	EGTRQARRNRRRWRERQR		Vaccine	(IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **Research Contact** Tony Lowe and Jonathan Karn, MRC Center, Cambridge **References** Henderson1997 • Ab2: The Ab2 binding site overlaps the nuclear localization signal – Ab2 binding to Rev was blocked by bound HIV RNA – the cellular protein importin-beta can bind in this Arg rich region – atypically, the Rev binds specifically to importin-beta, but not to the importin-beta-importin-alpha dimer. [Henderson1997]					
298	10.1	Rev (33–48)	Rev (33–48)	GTRQARRNRRRRWRER?			
		References Maksiutov2002, Ranki1995, Ranki1994, Ovod1992 • 10.1: This epitope is similar to a fragment of the human protein Complement 4 (containing C4A anaphylatoxin), GRRNRRRR. [Maksiutov2002] • 10.1: Binds to the RRE binding site – polyclonal anti-Rev Ab detected Rev in astrocytes in 4/5 brain autopsy samples, but only one of these was positive using 10.1, suggesting most Rev was bound to RRE. [Ranki1995]					
299	3H6	Rev (38–43)	Rev (38–44)	RRNRRR		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **References** Maksiutov2002, Orsini1995 • 3H6: This epitope is similar to a fragment of the human protein Complement 4 (containing C4A anaphylatoxin), GRRNRRRR. [Maksiutov2002] • 3H6: Directed against nucleolar localization/RRE binding domain – antigenic domain tentative, MAb failed to bind a RRNRRR Rev deletion mutant. [Orsini1995] • 3H6: There is another MAb with this ID that recognizes gp41.					
300	8E7	Rev (70–84)	Rev (70–84)	PVPLQLPPLERLTLD		Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **References** Maksiutov2002, Boe1998, Jensen1997, Szilvay1995, Kalland1994b, Kalland1994a • 8E7: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG. [Maksiutov2002] • 8E7: HIV-1 RNA and Rev localize to the same region in the nucleoplasm, but the splicing factor SC-35 localizes in different speckles with the nucleoplasm than Rev – intron containing beta-globin was distributed similarly to HIV-1, suggesting Rev and HIV-1 RNAs interact at putative sites of mRNA transcriptions and splicing. [Boe1998] • 8E7: Peptide interaction mapped to aa 70-84, 75-88 – protein footprint to 65-88. [Jensen1997] • 8E7: 8E7 worked in indirect immunofluorescence and also detected Rev in WB assays – used to detect localization of Rev in several compartments including the nucleoli, nucleoplasm, perinuclear zone, and cytoplasm – Rev co-localized with host cell factors known to assemble on nascent transcripts – Rev shuttles continuously between cytoplasmic and nucleoplasmic compartments. [Kalland1994a, Kalland1994b, Szilvay1995]					
301	9G2 (9G2G4D6E8)	Rev (70–84)	Rev (70–84)	PVPLQLPPLERLTLD		Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **Research Contact** Anne Marie Szilvay					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Maksiutov2002, Jensen1997, Kalland1994a • 9G2: Called 9G2G4D6E8: UK Medical Research Council AIDS reagent: ARP3058. • 9G2: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG. [Maksiutov2002] • 9G2: Peptide interaction mapped to aa 70-84, 75-88 – protein footprint to 65-88. [Jensen1997] • 9G2: Worked in indirect immunofluorescence and also detected Rev in WB assays – used to detect localization of Rev throughout the cell. [Kalland1994a]					
302	Ab4	Rev (72–91)	Rev (72–91 BRU)	PLQLPPLERLTLDCNEDCGT		Vaccine	(IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **Research Contact** Tony Lowe and Jonathan Karn, MRC Center, Cambridge **References** Maksiutov2002, Henderson1997 • Ab4: This epitope is similar fragments of the human protein Epidermal growth factor receptor substrate 15, EPVPMSLPPA, and Insulin-like growth factor binding protein complex acid labile chain precursor, QPPGLERLWLEGNPWDCG. [Maksiutov2002] • Ab4: The binding site overlaps the nuclear export signal – binding was not blocked by bound HIV RNA and may be accessible for protein interaction. [Henderson1997]					
303	3G4	Rev (90–116)	Rev (90–116)	GTSGTQGVGSPQILVESPTVLESGT-KE?		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **References** Orsini1995 • 3G4: Binds to a region that can be dispensed with and still retain Rev function. [Orsini1995]					
304	1G10 (IG10F4)	Rev (96–105)	Rev (95–105)	GVGSPQILVE		Vaccine	mouse (IgG2bκ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **Research Contact** Anne Marie Szilvay **References** Jensen1997, Kalland1994a • 1G10: Called IG10F4: UK Medical Research Council AIDS reagent: ARP3060. • 1G10: Peptide interaction mapped to aa 91-105, 96-110 – protein footprint to aa 10-20, and 95-105. [Jensen1997] • 1G10: Bound Rev in indirect immunofluorescence and also detected Rev in WB – used to detect localization of Rev throughout the cell. [Kalland1994a]					
305	1G7	Rev (96–105)	Rev (95–105)	GVGSPQILVE		Vaccine	mouse (IgG2bκ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **References** Jensen1997, Kalland1994a • 1G7: Peptide interaction mapped to aa 91-105, 96-110 – protein footprint to aa 95-105. [Jensen1997] • 1G7: Worked in indirect immunofluorescence and also detected Rev in WB – used to detect localization of Rev throughout the cell. [Kalland1994a]					
306	Ab3	Rev (102–116)	Rev (102–116 BRU)	ILVESPTVLESDKTE		Vaccine	(IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **Research Contact** Tony Lowe and Jonathan Karn, MRC, Cambridge **References** Henderson1997 • Ab3: This binding site is at the carboxy end of Rev – Ab3 binding was not blocked by bound HIV RNA. [Henderson1997]					
307	2G2	Rev	Rev			Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* Rev **References** Orsini1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2G2: Does not bind to any of a set of glutathione S-transferase (GST) Rev fusion proteins, or to Rev in a RIPA buffer, suggesting a conformational epitope. [Orsini1995]					

IV-C-15 gp160 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
308	M85	gp160 (30–51)	gp120 (30–51 LAI)	ATEKLWVTVYYGVPVWKEATTT	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** Fulvia di Marzo Veronese **References** Wyatt1997, Ditzel1997, Moore1996, Moore1994d, Moore1994c, diMarzo Veronese1992 • M85: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. [Wyatt1997] • M85: Binding inhibited by MAb 4D4#85, enhanced by conformationally sensitive anti-V3 MAb 5G11, and some anti-18 MAbs. [Moore1996] • M85: C1 domain – mutation 40 Y/D impairs binding – the relative affinity for denatured/native gp120 is < .01, suggesting conformational component. [Moore1994c] • M85: Immunoblot and RIP reactive for strains IIIB, 451, MN, RF, and RUTZ – binds deglycosylated gp120. [diMarzo Veronese1992]			
309	7E2/4	gp160 (31–50)	gp120 (31–50 LAI)	TEKLWVTVYYGVPVWKEATT		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** S. Ranjbar, NIBSC, UK **References** Maksiutov2002, Moore1994c • 7E2/4: UK Medical Research Council AIDS reagent: ARP3050. • 7E2/4: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. [Maksiutov2002] • 7E2/4: C1 domain – the relative affinity for denatured/native gp120 is .07, suggesting conformational component. [Moore1994c]			
310	4D4#85	gp160 (41–50)	gp120 (LAI)	GVPVWKEATT		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **Research Contact** S. Nigida and L. Arthur, NCI, Frederick, MD USA **References** Maksiutov2002, Binley1998, Wyatt1997, Moore1996, Moore1994d, Moore1994c • 4D4#85: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. [Maksiutov2002] • 4D4#85: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998] • 4D4#85: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-50, are deleted. [Wyatt1997] • 4D4#85: Inhibits binding of C1 MAb M85, C1-C5 discontinuous epitope MAbs 181 and 212A, and CD4 binding induced MAbs 48d and 17b. [Moore1996] • 4D4#85: C1 domain – the relative affinity, denatured/native gp120 is 0.1 – mutation 45 W/S impairs binding. [Moore1994c]			
311	M92	gp160 (41–50)	gp120 (31–50 LAI)	GVPVWKEATT	no	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** Fulvia di Marzo Veronese **References** Maksiutov2002, Moore1994d, Moore1994c, diMarzo Veronese1992 • M92: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. [Maksiutov2002] • M92: The relative affinity for denatured/native gp120 is 1. [Moore1994c] • M92: Immunoblot reactive, RIP negative, but precipitates deglycosylated gp120 – reacts with strains IIIB, 451, MN, RF, and RUTZ. [diMarzo Veronese1992]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
312	M86	gp160 (42–61)	gp120 (42–61 LAI)	VPVWKEATTTLFCASDAKAY	no	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *HIV component:* Env
Ab type C1 **Research Contact** Fulvia di Marzo Veronese
References Maksiutov2002, Moore1994c, diMarzo Veronese1992

- M86: This epitope has a high degree of similarity with the platelet membrane glycoprotein IIIA precursor (GLIIIA) (integrin beta- 3) (CD61): PLYKEATSTF. [Maksiutov2002]
- M86: C1 domain – the relative affinity for denatured/native gp120 is 1. [Moore1994c]
- M86: Immunoblot and RIP reactive for strains IIIB, 451, MN, RF, and RUTZ – binds deglycosylated gp120. [diMarzo Veronese1992]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
313	polyclonal	gp160 (52–71)	Env (42–61 LAI)	LFCASDAKAYDTEVHNVWAT	no	Vaccine	mouse

Vaccine *Vector/Type:* vaccinia *HIV component:* Env
Ab type C1
References Collado2000

- Vaccinia p14 can elicit NAbs and p39 tends to be immunodominant, so these two proteins were fused to regions of HIV-1 Env – reduced glycosylation was noted when p14 or p39 was placed in the N-term region of the fusion protein – chimeric proteins shifted the Env Ab response from V3 to either a C1 or C4 domain, depending on the construct – all chimeric Env proteins: 14kEnv, 39kEnv, and Env39k elicited a strong Ab response to the C1 region of gp120 (LFCASDAKAYDTEVHNVWAT), and Env39k mounted a strong response to the C4 region (KAMYAPPISGQIRCSSNITG) [Collado2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
314	133/237	gp160 (61–70)	gp120 (51–70 LAI)	YDTEVHNVWA	L	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type C1
References Moore1994d, Moore1994c, Niedrig1992b

- 133/237: The relative affinity, denatured/native gp120 is 1.4 – mutation of position 69 W/L impairs binding. [Moore1994c]
- 133/237: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains. [Niedrig1992b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
315	133/290	gp160 (61–70)	gp120 (61–70 LAI)	YDTEVHNVWA	L	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type C1 **Research Contact** M. Niedrig
References Pantophlet2003b, Yang2000, Binley1998, Wyatt1997, Binley1997a, Moore1996, Wyatt1995, Moore1994d, Moore1994c, Thali1993, Niedrig1992b
Keywords vaccine antigen design.

- 133/290: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 133/290: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000]
- 133/290: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998]
- 133/290: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. [Wyatt1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 133/290: Reciprocal binding inhibition with the antibody 522-149, that binds to a discontinuous epitope – binding is enhanced by some C5 and C1 binding site antibodies. [Moore1996] • 133/290: Used for antigen capture assay, either to bind gp120 to the ELISA plate, or to quantify bound gp120. [Wyatt1995] • 133/290: The relative affinity for denatured/native gp120 is 2.2 – mutation in position 69 W/L impairs binding. [Moore1994c] • 133/290: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains. [Niedrig1992b]					
316	133/11	gp160 (64–78)	gp120 (64–78)	EVHNVWATHACVPTD	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C1 **References** Niedrig1992b • 133/11: Region of overlap for reactive peptides is WATHA – weak neutralization of lab strains. [Niedrig1992b]					
317	D/3G5	gp160 (73–82)	gp120 (73–82 LAI)	ACVPTDPNPQ	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/3G5: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					
318	D/6A11	gp160 (73–82)	gp120 (73–82 LAI)	ACVPTDPNPQ	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/6A11: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					
319	D/5E12	gp160 (73–92)	gp120 (73–92 LAI)	ACVPTDPNPQEVVLVNVTEN	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/5E12: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					
320	L5.1	gp160 (79–93)	gp120 (89–103 IIIB)	PNPQEVVLVNVTENF		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Ab type** C1 **References** Akerblom1990					
321	4A7C6	gp160 (81–90)	gp120 (81–90 LAI)	PQEVVLVNVT		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** R. Tedder **References** Moore1996, Moore1994d, Moore1994c, Moore1993a, Thali1993, Thiriart1989 • 4A7C6: UK Medical Research Council AIDS reagent: ARP 360. • 4A7C6: Reciprocal binding inhibition with the antibody 133/192 – enhanced by anti-C5 antibodies, and C1 antibody 135/9. [Moore1996] • 4A7C6: C1 region epitope (88 N/P substitutions abrogates binding), but substitutions 380 G/F and 420 I/R also impaired binding. [Moore1994d] • 4A7C6: The relative affinity for denatured/native gp120 is 7.9 – mutation 88 N/P impairs binding. [Moore1994c] • 4A7C6: Bound preferentially to denatured IIIB gp120. [Moore1993a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
322	1D10	gp160 (81–100)	gp120 (81–100 LAI)	PQEVVLVNVTENFDMWKNDM	L	Vaccine	rat
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C1 **References** Moore1994c, Nakamura1992, Berman1991, Dowbenko1988 • 1D10: The relative affinity for denatured/native gp120 is 13 – mutation 88 N/P impairs binding. [Moore1994c] • 1D10: Cross-blocks 5B3 in IIIB-rsgp160 ELISA – type specific in rgp120 ELISA binding. [Nakamura1992]					
323	B242	gp160 (83–92)	gp120 (83–92 LAI)	EVVLVNVTEN	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp160 **Ab type** C1 **References** Bristow1994 • B242: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. [Bristow1994]					
324	133/192	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C1 **Research Contact** Matthias Niedrig **References** Pantophlet2003b, Binley1998, Binley1997a, Trkola1996a, Moore1996, Moore1994d, Moore1994c, Moore1993c, Niedrig1992b **Keywords** vaccine antigen design. • 133/192: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**) • 133/192: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998] • 133/192: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] • 133/192: Reciprocal binding inhibition with the antibody 4A7C6 – enhanced by some anti-C5 and-C1 antibodies. [Moore1996] • 133/192: C1 region – substitutions 76P/Y, 113 D/A or R, 117 K/W, 420 I/R, 427 W/S impair binding, other substitutions enhanced binding. [Moore1994d] • 133/192: The relative affinity for denatured/native gp120 is 1.8. [Moore1994c] • 133/192: Epitope seems complex, binds multiple peptides – weak neutralization of lab strain. [Niedrig1992b]					
325	489.1(961)	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **Research Contact** C. Bruck, SKB, Belgium **References** Moore1994c • 489.1(961): NIH AIDS Research and Reference Reagent Program: 961. • 489.1(961): The relative affinity for denatured/native gp120 is 1. [Moore1994c]					
326	5B3	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp160 **Ab type** C1 **References** Moore1994c, Beretta1994, Nakamura1992, Berman1991 • 5B3: The relative affinity of denatured/native gp120 is 8.3. [Moore1994c] • 5B3: Cross-blocks 1D10 in competitive IIIB-rsgp160 ELISA – no neutralization – blocks IIIB-gp120 sCD4 binding – localized binding to residues 72-106. [Nakamura1992]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 5B3: Blocks gp120 -CD4 binding. [Berman1991]					
327	B10	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Moore1994c, Abacioglu1994 • B10: There is FNM/FDM polymorphism in LAI-based peptides, and N is essential (J. P. Moore, per. comm.) • B10: The relative affinity for denatured/native gp120 is 0.4. [Moore1994c] • B10: C1 region – epitope boundaries mapped by peptide scanning, FNMW core. [Abacioglu1994]					
328	B2	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Binley1997a, Moore1994d, Moore1994c, Abacioglu1994, Thali1993 • B2: There is FNM/FDM polymorphism in LAI-based peptides, and N is essential (J. P. Moore, per. comm.) • B2: The relative affinity for denatured/native gp120 is 1.4. [Moore1994c] • B2: C1 region – epitope boundaries mapped by peptide scanning, FNMW core. [Abacioglu1994]					
329	C6 (Ch6)	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Pincus1996, Moore1994c, Abacioglu1994, Pincus1993a • C6: NIH AIDS Research and Reference Reagent Program: 810. • C6: Called Ch6 – binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. [Pincus1993a, Pincus1996] • C6: There is FNM/FDM polymorphism in LAI-based peptides – N is essential (J. P. Moore, per. comm.) • C6: The relative affinity for denatured/native gp120 is 0.9. [Moore1994c] • C6: C1 region – epitope boundaries mapped by peptide scanning, FNMW core. [Abacioglu1994]					
330	MF49.1	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • MF49.1: The relative affinity of denatured/native gp120 is 3.8. [Moore1994c]					
331	T1.1	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *HIV component:* gp160 **Ab type** C1 **References** Moore1994c, Broliden1990, Akerblom1990 • T1.1: C1 region – the relative affinity for denatured/native gp120 is 1. [Moore1994c] • T1.1: No ADCC activity – reactive peptide: NVTENFNMWKNDMVEQ, IIIB. [Broliden1990] • T1.1: Also reacted in solid phase with gp120(234-248) NGTGPCTNVSTQCT. [Akerblom1990]					
332	T7.1	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C1 **References** Moore1994d, Moore1994c, Bolmstedt1990, Akerblom1990 • T7.1: The relative affinity of denatured/native gp120 is 4.0. [Moore1994c]					
333	T9	gp160 (91–100)	gp120 (91–100 LAI)	ENFDMWKNDM		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **Research Contact** Lennart Akerblom, Britta Wahren and Jorma Hinkula **References** Binley1997a, Moore1994d, Moore1994c, Bolmstedt1990, Akerblom1990 • T9: Binds to the C1 region – 45 W/S, 88 N/P, 256 S/Y, 262 N/T, 475 M/S, 485 1.83, and 491 I/F enhanced binding, no substitution tested significantly inhibited. [Moore1994d] • T9: The relative affinity of denatured/native gp120 is 7.9. [Moore1994c] • T9: There are two HIV-Abs with the name T9, one binds to gp41, one to gp120.					
334	GV4D3	gp160 (92–100)	gp120 (92–100 IIIB)	NFNMWKNDM		Vaccine	mouse
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120-Mab complex **Ab type** C1 **Research Contact** Patricia Earl and Christopher Broder, NIH **References** Denisova1996 • GV4D3: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV4H4 and GV5F9 are homologous to GV4D3 and were generated in the same experiment. [Denisova1996]					
335	B27	gp160 (93–96)	gp120 (94–97 BH10)	FNMW	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp160 **Ab type** C1 **References** Bristow1994, Abacioglu1994 • B27: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. [Bristow1994] • B27: C1 region – epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
336	B9	gp160 (93–96)	gp120 (93–96 LAI)	FNMW		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Abacioglu1994 • B9: Binds C1 region – epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
337	B35	gp160 (93–98)	gp120 (94–99 BH10)	FNMWKN		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Abacioglu1994 • B35: C1 region – epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
338	D/4B5	gp160 (93–101)	gp120 (93–101 LAI)	FNMWKNDMV	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/4B5: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
339	D/5A11	gp160 (93–101)	gp120 (93–101 LAI)	FNMWKNDMV	no	Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/5A11: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					
340	D/6B2	gp160 (93–101)	gp120 (93–101 LAI)	FNMWKNDMV	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** C1 **References** Bristow1994 • D/6B2: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					
341	B18	gp160 (101–110)	gp120 (101–110 LAI)	VEQMHEDIIS		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Moore1994c, Abacioglu1994 • B18: The relative affinity for denatured/native gp120 is 1. [Moore1994c] • B18: C1 region – epitope boundaries mapped by peptide scanning, HEDII core. [Abacioglu1994]					
342	B20	gp160 (101–110)	gp120 (101–110 LAI)	VEQMHEDIIS		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C1 **References** Moore1994c, Abacioglu1994 • B20: The relative affinity for denatured/native gp120 is 1. [Moore1994c] • B20: C1 region – epitope boundaries mapped by peptide scanning – HEDII core. [Abacioglu1994]					
343	MF39.1 (39.1)	gp160 (101–110)	gp120 (101–110 LAI)	VEQMHEDIIS		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Cook1994, Thiriart1989 • MF39.1: The relative affinity of denatured/native gp120 is 30. [Moore1994c] • MF39.1: Called 39.1, and is probably the same as MF39.1 – MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994]					
344	187.2.1 (187.1)	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** Claudine Bruck and Clothilde Thiriart **References** Moore1994d, Moore1994c, Cook1994, Moore1993a, Thiriart1989 • 187.2.1: UK Medical Research Council AIDS reagent: ARP332. • 187.2.1: The relative affinity for denatured/native gp120 is 7 – mutations 113 D/A (not D/R) and 117 K/W impair binding. [Moore1994c] • 187.2.1: Called 187.1, and is probably the same as 187.2.1 – MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 187.2.1: Called 187.1, and is probably the same as 187.2.1 – bound preferentially to denatured IIIB gp120. [Moore1993a]					
345	37.1.1(ARP 327) (37.1)	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** Claudine Bruck **References** Moore1994c, Moore1993a, Thiriart1989 • 37.1.1: UK Medical Research Council AIDS reagent: ARP327. • 37.1.1: The relative affinity for denatured/native gp120 is 8.6 – mutations 113 D/R (not D/A) and 117 K/W impair binding. [Moore1994c] • 37.1.1: Called 37.1 – bound preferentially to denatured IIIB gp120. [Moore1993a]					
346	6D8	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	rat
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C1 **References** Moore1994c, Nakamura1992, Dowbenko1988 • 6D8: The relative affinity for denatured/native gp120 is 15 – mutations 113 D/R and 113 D/A impair binding. [Moore1994c] • 6D8: Highly cross reactive with multiple stains by rgp120 ELISA. [Nakamura1992]					
347	M96	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV	no	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** Fulvia di Marzo Veronese **References** Moore1994d, Moore1994c, diMarzo Veronese1992 • M96: C1 region – the relative affinity for denatured/native gp120 is 6. [Moore1994c] • M96: Immunoblot reactive for strains IIIB, 451, MN, RF, and RUTZ. [diMarzo Veronese1992]					
348	MF119.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • MF119.1: The relative affinity for denatured/native gp120 is 30 – mutations 113 D/A, 113 D/R, and 117 K/W impair binding. [Moore1994c]					
349	MF4.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • MF4.1: The relative affinity for denatured/native gp120 is 8. [Moore1994c]					
350	MF53.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • MF53.1: The relative affinity for denatured/native gp120 is 10. [Moore1994c]					
351	MF58.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Moore1994c, Thiriart1989					
352	MF77.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • MF77.1: The relative affinity for denatured/native gp120 is 11. [Moore1994c]					
353	T2.1	gp160 (101–120)	gp120 (101–120 LAI)	VEQMHEDIISLWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **Research Contact** Lennart Akerblom, Britta Wahren and Jorma Hinkula **References** Moore1994d, Moore1994c, Bolmstedt1990, Akerblom1990 • T2.1: The relative affinity for denatured/native gp120 is .27 – mutations 113 D/R, 106 E/A, and 117 D/A impair binding. [Moore1994c]					
354	11/65 (11/65a/5h)	gp160 (102–121)	gp120 (311–321 HXB10)	EQMHEDIISLWDQSLKPCVK		Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** C1 **References** Peet1998, McKeating1993b, McKeating1992a • 11/65: UK Medical Research Council AIDS reagent: ARP3076. • 11/65: Called 11/65a/5h – The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/65 was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998] • 11/65: Binds only soluble gp120, not virion bound – used to quantify gp120 shedding – (numbering is incorrect in original?) [McKeating1992a]					
355	W1	gp160 (102–121)	gp120 (102–121 LAI)	EQMHEDIISLWDQSLKPCVK		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **Research Contact** D. Weiner, U. Penn. **References** Moore1994c • W1: The relative affinity for denatured/native gp120 is 6 – mutations 113 D/A, 113 D/R, and 117 K/W impair binding. [Moore1994c]					
356	T11	gp160 (102–125)	gp120 (102–125)	EQMHEDIISLWDQSLKPCVKLTPL		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* oligomeric gp140 **Ab type** C1 **Research Contact** R. Doms, Univ. of Pennsylvania **References** Jagodzinski1996, Earl1994 • T11: The sulfated polysaccharide, curdlan sulfate (CRDS), binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop from gp120 results in more potent T11 inhibition by CRDS. [Jagodzinski1996] • T11: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
357	GV1A8	gp160 (105–113)	gp120 (105–113 IIIB)	HEDIISLWD		Vaccine	mouse
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120-Mab complex **Ab type** C1 **References** Denisova1996					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• GV1A8: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV7A4 and GV5H5 are homologous to GV1A8 and were generated in the same experiment. [Denisova1996]					
358	11	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • 11: The relative affinity for denatured/native gp120 is 7.8 – mutation 113 D/R impairs binding. [Moore1994c]					
359	12G10	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • 12G10: The relative affinity for denatured/native gp120 is 17 – mutation 117 K/W impairs binding. [Moore1994c]					
360	135/9 (87-135/9)	gp160 (111–120)	gp120 (111–120 LAI)	LWDQSLKPCV	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C1 **Research Contact** Matthias Niedrig **References** Yang2000, Kropelin1998, Binley1998, Binley1997a, Trkola1996a, Moore1996, Moore1994d, Moore1994c, Niedrig1992b • 135/9: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] • 135/9: Noted to bind to C1 peptide HEDIISLWDQSLK – blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998] • 135/9: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998] • 135/9: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] • 135/9: Binding is enhanced by some anti-C1 and anti-C5 antibodies – enhances binding of some anti-V3, anti-C4 and anti-V2 MAbs – 135/9 binds to predicted alpha-helix in C1. [Moore1996] • 135/9: Substitutions 106 E/A, 113 D/A or R, and 117 K/W impair binding, some substitutions enhance binding. [Moore1994d] • 135/9: The relative affinity for denatured/native gp120 is 15 – mutation 113 D/R impairs binding to native and denatured, 113 D/A only to denatured. [Moore1994c] • 135/9: Defines the epitope as gp120(114-123) MHEDIISLWD (core LWD?) – weak neutralization of lab strain. [Niedrig1992b]			
361	7C10	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • 7C10: The relative affinity for denatured/native gp120 is 5.8 – mutation 117 K/W impairs binding. [Moore1994c]					
362	C4	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C1 **Research Contact** George Lewis **References** Moore1994c, Moore1993a, Abacioglu1994 • C4: The relative affinity for denatured/native gp120 is 10. [Moore1994c] • C4: C1 region – epitope boundaries mapped by peptide scanning, BH10 core IISLW. [Abacioglu1994] • C4: Bound preferentially to denatured IIIB gp120. [Moore1993a]					
363	MF46.1	gp160 (111–120)	gp120 (101–120 LAI)	LWDQSLKPCV		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C1 **References** Moore1994c, Thiriart1989 • MF46.1: The relative affinity for denatured/native gp120 is 8.5. [Moore1994c]					
364	6D5	gp160 (122–141)	gp120 (122–141 LAI)	LTPLCVSLKCTDLKNDTNTN		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** V2 **Research Contact** S. Nigida and L. Arthur, NCI, Frederick, MD USA **References** Moore1994d, Moore1994c • 6D5: The relative affinity for denatured/native gp120 is 15 – mutations Delta119-205 and 125 L/G impair binding. [Moore1994c]					
365	B33	gp160 (123–142)	gp120 (123–142 LAI)	TPLCVSLKCTDLGNATNTNS	no	Vaccine	mouse (IgG2bκ)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp160 **Ab type** V2 **Research Contact** Daniels **References** Bristow1994, Abacioglu1994 • B33: UK Medical Research Council AIDS reagent: ARP304, gp160/41 binding. • B27: C1 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. [Bristow1994] • B33: Epitope boundaries mapped by peptide scanning. [Abacioglu1994] • B33: There are two MAbs in the literature named B33, see also gp160(727-734) [Abacioglu1994]					
366	polyclonal (VEI1)	gp160 (131–151)	Env (131–151)	CTDLKNDTNTNSSSGRMMMEK		HIV-1 infection	human
		References Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. [Carlos1999]					
367	35D10/D2	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 35D10/D2: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 35D10/D2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
368	40H2/C7	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 40H2/C7: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 40H2/C7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
369	43A3/E4	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK		Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 43A3/E4: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 43A3/E4: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
370	43C7/B9	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 43C7/B9: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 43C7/B9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
371	45D1/B7	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 45D1/B7: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 45D1/B7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
372	46E3/E6	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK		Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 46E3/E6: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 46E3/E6: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
373	58E1/B3	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 58E1/B3: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 58E1/B3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
374	64B9/A6	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 64B9/A6: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 64B9/A6: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
375	69D2/A1	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK	L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 69D2/A1: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 69D2/A1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
376	82D3/C3	gp160 (139–155)	gp120	NTKSSNWKEMDGEIK		Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** V1 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization. • 82D3/C3: In an extensive review of gp120 binding MAbs in this database, V1-specific MAbs in are noted to be unusual, but in one study transgenic mouse immunization with SF162 yeilded ten V1 MAbs with highly strain-specific autologous NAb responses, and V1 was immunodominant. Human MAbs to V1 may be difficult to isolate due to selection with heterologous strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 82D3/C3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – C-term-V1- region was immunodominant in these mice and the ten V1-specific MAbs could potently neutralize autologous strain SF162 but were highly type specific. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
377	2H1B	gp160 (155–161)	gp120 (370–376 HIV2ROD)	RNISFKA	no	Vaccine	mouse
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C3 **References** Matsushita1995 • 2H1B: Binds in WB, but binds poorly to Env on the cell surface. [Matsushita1995]					
378	697-D (697D, 697-30D)	gp160 (161–180)	gp120 (161–180 IIIB)	ISTSIRGKVQKEYAFFYKLD	P (weak)	HIV-1 infection	human (IgG1λ)
		Ab type V2 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) or Cellular Products Inc, Buffalo NY **References** Gorny2004, He2002, Maksiutov2002, Edwards2002, Nyambi2000, Hioe2000, Gorny2000a, Stamatatos1998, Nyambi1998, Parren1997c, Fouts1997, Binley1997a, Trkola1996a, Moore1995b, Forthal1995, Gorny1994 **Keywords** ADCC, antibody binding site definition and exposure, co-receptor, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 697-D: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weak with limited cross-reactivity; it weakly neutralizes some primary but not TCLA strains. 697-D is the best characterized of the anti-V2 MAbs, and binds weakly and sporadically to isolates from clades A-D. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**) • 697-D: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK. [Maksiutov2002] • 697-D: Called 697D – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A, 4117C and 697D were used as controls. [He2002] • 697-D: Called 697D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] (**antibody binding site definition and exposure**) • 697-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. [Nyambi2000] (**inter-clade comparisons**) • 697-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V2 MAb 697-D did not effect proliferation. [Hioe2000] • 697-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold. [Gorny2000a] (**antibody binding site definition and exposure**) • 697-D: Called 697-30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D. [Stamatatos1998] (**variant cross-recognition or cross-neutralization**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 697-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, and bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and weak binding to viruses from subtype A and D. [Nyambi1998] (**inter-clade comparisons**) • 697-D: Does not neutralize TCLA strains but neutralizes some primary isolates weakly. [Parren1997c] (**variant cross-recognition or cross-neutralization**) • 697-D: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 697-D bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997] (**antibody binding site definition and exposure**) • 697-D: Partial inhibition of gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**co-receptor**) • 697-D: Review: called 697/30D – neutralizes some primary, but not lab adapted strains. [Moore1995b] (**variant cross-recognition or cross-neutralization**, **review**) • 697-D: Not neutralizing, no ADCC activity, and no viral enhancing activity. [Forthal1995] (**ADCC**, **enhancing activity**) • 697-D: Conformational with weak reactivity to V2 peptide ISTSIRGKVQKEYAFFYKLD – neutralized 3/4 primary isolates, but none of 4 lab strains – V2 substitutions 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS abrogate binding – anti-C4 MAbs G3-536 and G45-60 enhance binding – mild oxidation of carbohydrate moieties inhibits binding. [Gorny1994] (**antibody binding site definition and exposure**)			
379	6C4/S	gp160 (162–169)	gp120 (BH10)	STSIRGKV		Vaccine	
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Research Contact** S. Ranjbar (NIBSC, UK) **References** Moore1993b • 6C4/S: UK Medical Research Council AIDS reagent: ARP3049.					
380	C108G	gp160 (162–169)	gp120 (162–169 HXB2)	STSIRGKV	L	HIV-1 infection	chimpanzee (IgG1κ)
		Ab type V2 **Research Contact** S. Tilley, Public Health Research Institute, NY, NY **References** Gorny2004, Alsmadi1998, Mondor1998, Ugolini1997, Warrier1996, Warrier1995, Wu1995, Warrier1994 **Keywords** ADCC, antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, review, variant cross-recognition or cross-neutralization. • C108G: This MAb is unsual among V2-directed MAbs. It is glycan dependent and can neutralize both a primary isolate (BaL and a TCLA (IIIB) strain. [Gorny2004] (**antibody binding site definition and exposure**, **review**) • C108G: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – C108G bound and directed lysis against only IIIB – this is first demonstration of ADCC directed by a V2 specific MAb. [Alsmadi1998] (**ADCC**, **variant cross-recognition or cross-neutralization**) • C108G: Inhibits HX10 binding to both CD4 positive and negative HeLa cells. [Mondor1998] • C108G: Viral binding inhibition by C108G was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997] (**antibody binding site definition and exposure**) • C108G: Synergistic neutralization of HIV-1 when combined with anti-V3 MAbs 0.5beta and C311E, or anti-CD4BS MAbs, 1125H and 5145A – neutralization further enhanced by presence of both 1125H and 0.5beta. [Warrier1996] (**antibody interactions**) • C108G: Characterization of MAb variable region. [Warrier1995] (**antibody sequence, variable domain**) • C108G: Strain specificity: LAI, BaL, HXB2 – conformational character – glycosylation site at 160 critical – mutation of conserved glycosylation site at 156 increased epitope exposure. [Wu1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • C108G: Chimps were infected with HIV-1 IIIB, and this high affinity MAb gave potent neutralization of HIV-1 IIIB – binding not affected by reduction of disulfide bonds – binding disrupted by removal of N-linked glycans – peptide binds with lower affinity than glycosylated Env. [Warrier1994] (**antibody binding site definition and exposure**, **antibody generation**)			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
381	10/76b	gp160 (162–170)	gp120 (162–171 BH10)	STSIRGKVQ	L (HXB10)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** McKeating1996b, Wu1995, Shotton1995, McKeating1993a, McKeating1993b • 10/76b: UK Medical Research Council AIDS reagent: ARP3077. • 10/76b: Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b] • 10/76b: HX10 strain specificity – binds native, deglycosylated, or denatured gp120. [Wu1995] • 10/76b: Included in cross-competition and neutralization studies. [Shotton1995] • 10/76b: Cross-competes with MAbs 10/76b and 11/4b – HXB2 neutralization escape mutant has the substitution I/T at residue 165. [Shotton1995] • 10/76b: R to L substitution abrogated binding – human sera recognize epitope. [McKeating1993b]				
382	11/41e	gp160 (162–170)	gp120 (162–171)	STSIRGKVQ	L (HXB10)	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** Wu1995, Shotton1995, McKeating1993b • 11/41e: HX10 strain specificity – binds native and deglycosylated gp120. [Wu1995] • 11/41e: Included in cross-competition and neutralization studies. [Shotton1995] • 11/41e: R to L abrogated binding – human sera recognize the epitope. [McKeating1993b]				
383	11/4b	gp160 (162–170)	gp120 (162–171)	STSIRGKVQ	L (HXB10)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** Moore1996, Wu1995, Shotton1995, McKeating1993b • 11/4b: Linear V2 epitope – reciprocal binding enhancement of anti-V2 discontinuous epitope antibodies (in contrast to BAT085) and CD4 inducible antibody 48d. Reciprocal inhibits BAT085 binding – inhibits CRA-3 binding CRA-3 does not inhibit 11/4b. [Moore1996] • 11/4b: HXB10 strain specificity – binds native, deglycosylated, or denatured gp120. [Wu1995] • 11/4b: Cross-competes with MAbs 10/76b and 11/4c – HXB2 neutralization escape mutant has the substitution I/T at residue 165. [Shotton1995] • 11/4b: A change from R to L abrogated binding – human sera recognize epitope. [McKeating1993b]				
384	RSD-33	gp160 (162–170)	gp120 (162–171)	STSIRGKVQ		Vaccine	
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Research Contact** R. Daniels (NIMR, UK) **References** Moore1993b					
385	11/4c (11/4c/1j/4j)	gp160 (162–170)	gp120 (152–181)	STSIRGKVQ	L (HXB2)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V2 **References** Peet1998, Shotton1995, Wu1995, McKeating1993b • 11/4c: UK Medical Research Council AIDS reagent: ARP3035. • 11/4c: Called 11/4c/1j/4j – The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/4c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998] • 11/4c: Cross-competes with MAbs 10/76b and 11/4b – HXB2 neutralization escape mutant has the substitution I/T at residue 165. [Shotton1995] • 11/4c: HX10 strain specificity – binds native, deglycosylated, or denatured gp120. [Wu1995] • 11/4c: R to L substitution abrogated binding – human sera recognize epitope. [McKeating1993b]				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
386	8.22.2	gp160 (162–178)	gp120	TTSIRDKVQKEYALFYK		Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Ab type V2 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny2004, Maksiutov2002, He2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 8.22.2: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. 8.22.2 weakly neutralizes SF162. [Gorny2004] (**review**)
- 8.22.2: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK. [Maksiutov2002]
- 8.22.2 : Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – several of the MAbs obtained were effective at neutralizing the autologous strain – 8.22.2 was the only V2-specific MAb created and it could cross-compete with MAb 697D – 8.22.2 could cross-react with BaL and JR-FL, two B clade R5 strains, but not B clade X4 or E clade viruses, and it could weakly neutralize autologous strain SF162. [He2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

387	12b	gp160 (162–181)	gp120 (162–181)	STSIRGKVQKEYAFFYKLDI	L (HXB10)	Vaccine	rat (IgG2a)

Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120
Ab type V2
References Maksiutov2002, McKeating1996b, Shotton1995

- 12b: This epitope is similar to a fragment of the human protein macrophage colony stimulating factor I receptor SISIRLKVQK. [Maksiutov2002]
- 12b: Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b]
- 12b: V2 MAb neutralized HXB2 – position 179-180 LD to DL abrogates binding – competes with 60b, but not 74. [Shotton1995]

388	G3-136 (G3.136)	gp160 (170–180)	gp120 (170–180 IIIB)	QKEYAFFYKLD	L	Vaccine	mouse (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type V2 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY
References Pantophlet2003b, Zwick2003, Ly2000, Stamatatos1998, Parren1998a, Wyatt1997, Ditzel1997, Stamatatos1997, Binley1997a, Poignard1996a, Moore1996, Stamatatos1995, Sattentau1995b, Yoshiyama1994, Moore1993b, Moore1993a, Thali1993, Pirofski1993, Fung1992
Keywords antibody interactions, vaccine antigen design.

- G3-136: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- G3-136: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V2 MAb used. [Zwick2003] (**antibody interactions**)
- G3-136: Called G3.136 – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- G3-136: Called G3.136 – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D. [Stamatatos1998]
- G3-136: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- G3-136: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997]
- G3-136: Called G3.136 – does not mediate gp120 virion dissociation in contrast to anti-V2 MAb G3-4 – not neutralizing for SF162 or SF128A in either primary macrophages or PBMC. [Stamatatos1997]
- G3-136: Described epitope as STSIRGKVKEYAFFYKLDI – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT123 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs. [Poignard1996a]
- G3-136: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes cell free Hx10. [Sattentau1995b]
- G3-136: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V2 loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a – anti-V2 MAbs G3-4 and G3.136 don't bind to T-cell tropic SF2. [Stamatatos1995]
- G3-136: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity. [Yoshiyama1994]
- G3-136: Binding enhanced by selected antibodies to C1, C4, C5, V3 and anti-CD4 binding site MAbs – enhances binding of selected V3, C4 and anti-CD4 binding site MAbs. [Moore1993b]
- G3-136: Marginal binding to peptide, binding inhibited by 183/184 PI/SG substitution. [Moore1993b]
- G3-136: Conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120. [Moore1993a]
- G3-136: V2 region – binds and neutralizes IIIB and RF in CEM-SS cells, but not MN – neutralization activity against a few primary isolates in PBMC – sCD4 binding inhibits binding (contrast with BAT085) – deglycosylation or reduction of gp120 by DTT diminishes reactivity. [Fung1992]

389 G3-4 (G3.4) gp160 (170–180) gp120 (170–180 BH10) QKEYAFFYKLD L Vaccine mouse (IgG2bκ)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type V2 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY
References Pantophlet2003b, Zwick2003, Srivastava2002, Ly2000, Stamatatos1998, Parren1998a, Wyatt1997, Ditzel1997, Stamatatos1997, Binley1997a, Poignard1996a, Moore1996, Jagodzinski1996, Sattentau1995b, Wu1995, Stamatatos1995, Yoshiyama1994, Thali1994, Gorny1994, Moore1994b, Moore1993b, Thali1993, Sattentau1993, Sullivan1993, Moore1993a, McKeating1992a, Fung1992, Ho1992, Ho1991a
Keywords antibody interactions, vaccine antigen design.

- G3-4: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- G3-4: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V2 MAbs used. [Zwick2003] (**antibody interactions**)
- G3-4: Called G3.4 – Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – G3.4 recognized o-gp140. [Srivastava2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G3-4: Called G3.4 – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000] • G3-4: Called G3.4 – Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V2 MAbs G3.4, G3.136, or 687-30D. [Stamatatos1998] • G3-4: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] • G3-4: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997] • G3-4: Called G3.4 – mediates gp120 virion dissociation in contrast to anti-V2 MAb G3-136 – not neutralizing for SF162 or SF128A in either primary macrophages or PBMC. [Stamatatos1997] • G3-4: Described epitope as STSIRGKVKEYAFFYKLDI – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT085 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs. [Poignard1996a] • G3-4: Binding enhanced by selected antibodies to C1, C4, C5, V3 and anti-CD4 binding site MAbs – enhances binding of selected V3, C4 and anti-CD4 binding site MAbs. [Moore1996] • G3-4: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop from gp120 results in more potent G3-4 binding inhibition by CRDS – G3-4 epitope described as 176-184 FYKLDIIPI and 191-193 YSL. [Jagodzinski1996] • G3-4: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes Hx10 cell-free virus. [Sattentau1995b] • G3-4: Reactive with BH10, RF, and MN – binds native, but not denatured or deglycosylated gp120, binds to deglycosylated V1V2 fusion protein, suggesting importance of glycans outside the V1V2 region. [Wu1995] • G3-4: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V2 loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a – anti-V2 MAbs G3-4 and G3.136 don't bind to T-cell tropic SF2. [Stamatatos1995] • G3-4: Neutralizes RF – substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity and result in neutralization escape. [Yoshiyama1994] • G3-4: gp41 mutation (582 A/T) that reduces neutralization of anti-CD4 binding site MAbs does not alter G3-4s ability to neutralize. [Thali1994] • G3-4: Weakly neutralizing, IC 50 = 53 mug/ml. [Gorny1994] • G3-4: Conformationally sensitive – sporadic cross-reactivity among, and outside, B clade gp120s. [Moore1994b] • G3-4: V2 region, marginal binding to peptide, binding inhibited by 183/184 PI/SG substitution. [Moore1993b] • G3-4: Conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120. [Moore1993a] • G3-4: Increased binding in the presence of sCD4. [Sattentau1993] • G3-4: Substitutions in residues 176 to 184 affect MAb recognition – substitutions in V2 can result in gp120-gp41 dissociation. [Sullivan1993] • G3-4: Neutralizes IIIB and RF, not MN – blocks sCD4-gp120, not as potent as MAb 15e – V2 binding MAbs BAT085 and G3-136 block G3-4 gp120 binding – sensitive to reduction of gp120 by DTT. [Ho1992] • G3-4: Binding is sensitive to removal of glycans by endo H – 50% neutralization of 4/9 primary isolates – has conformational features. [Ho1991a]					
390	BAT085 (BAT-085)	gp160 (171–180)	gp120 (170–180 IIIB)	KEYAFFYKLD	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Parren1998a, Ditzel1997, Binley1997a, Poignard1996a, Moore1996, Sattentau1995b, Wu1995, Yoshiyama1994, Gorny1994, Moore1994d, D'Souza1994, Moore1993b, Thali1993, Pirofski1993, Moore1993a, Fung1992, Fung1987 • BAT085: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] • BAT085: Epitope suggested to be QKEYAFFYKLD – binds oligomer – binding of V2 MAbs G3-136, G3-4 or BAT123 did not significantly alter gp120 dissociation from virus or expose the gp41 epitope of MAb 50-69, in contrast to anti-V3 MAbs. [Poignard1996a] • BAT085: Binding is blocked by other V2 region antibodies, enhanced by several anti-C1 MAbs, and anti-V3 MAb G511 – reciprocal enhancement of CD4i MAb 48d binding. [Moore1996] • BAT085: Bound preferentially to the monomeric rather than oligomeric form of LAI gp120 – neutralizes cell free Hx10. [Sattentau1995b] • BAT085: HXB10 strain specificity – binds native, deglycosylated, or denatured gp120. [Wu1995] • BAT085: Neutralizes RF – substitution 177 Y/H in the V2 loop of RF does not inhibit neutralization, in contrast to MAbs G3-4 and SC258. [Yoshiyama1994] • BAT085: Interacts with two overlapping peptides with region of overlap KEYAFFYKLD. [Gorny1994] • BAT085: Multi-lab study for antibody characterization and assay comparison – did not bind MN or SF2. [D'Souza1994] • BAT085: Peptide affinities of G3-136 and G3-4 are 100-fold less than BAT085, but BAT085 has lower affinity for BH10 gp120 and is weaker at neutralization. [Moore1993b] • BAT085: 7/8 V2 murine MAbs required gp120 native structure to bind, but BAT085 was the exception – type-specific. [Moore1993b] • BAT085: Called BAT-85 – conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120, and does not inhibit HIV-1 sera from binding to IIIB gp120. [Moore1993a] • BAT085: V2 region – sCD4 does not block – neutralizes IIIB and some primary isolates, but not MN or RF – binds MN – deglycosylation or DDT reduction of gp120 does not diminish reactivity. [Fung1992]			
391	60b	gp160 (172–181)	gp120 (172–181 HXB2)	EYAFFYKLDI	no	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** Shotton1995 • 60b: V2 MAb did not neutralize HXB2 – bound to rgp120 in ELISA – substitutions 179-180 LD/DL and 191-193 YSL/GSS abrogate binding, as do changes outside the minimum epitope – competes with 12b, but not 74. [Shotton1995]					
392	74	gp160 (172–181)	gp120 (172–181)	EYAFFYKLDI	no	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** Shotton1995 • 74: V2 MAb did not neutralize HXB2 – did not bind rgp120 ELISA – position 179-180 LD to DL abrogates binding, as do changes outside the minimum epitope – does not compete with 60b or 12b, and is enhanced by two conformation dependent MAbs. [Shotton1995]					
393	38/12b	gp160 (172–191)	gp120 (172–191 HXB2)	EYAFFYKLDIIPIDNDTTSY		Vaccine	rat
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** Wu1995 • 38/12b: Broad specificity: HXB2, MN, SF162 – binds native and deglycosylated gp120. [Wu1995]					
394	38/60b	gp160 (172–191)	gp120 (172–191 HXB2)	EYAFFYKLDIIPIDNDTTSY		Vaccine	rat
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **References** Wu1995 • 38/60b: Strain specificity: HXB2 – binds native and deglycosylated gp120. [Wu1995]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
395	polyclonal (VEI2)	gp160 (176–196)	Env	FYKLDIVPIDNTTTSYRLISC		HIV-1 infection	human
		References Carlos1999					
		• Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. [Carlos1999]					
396	322-151	gp160 (211–221)	gp120 (201–220 LAI)	EPIPIHYCAPA		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env					
		Research Contact G. Robey, Abbot Labs					
		References Moore1994d, Moore1994c					
		• 322-151: The relative affinity denatured/native gp120 is 30. [Moore1994c]					
397	3D3.B8	gp160 (211–221)	gp120 (211–220 LAI)	EPIPIHYCAPA		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env					
		References Moore1994c, Bolmstedt1990					
		• 3D3.B8: The relative affinity denatured/native gp120 is greater than 10. [Moore1994c]					
398	4C11.D8	gp160 (211–221)	gp120 (211–220 LAI)	EPIPIHYCAPA		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* protein *HIV component:* Env					
		References Moore1994c, Bolmstedt1990					
		• 4C11.D8: The relative affinity denatured/native gp120 is greater than 10. [Moore1994c]					
399	493-156	gp160 (211–230)	gp120 (211–230 LAI)	EPIPIHYCAPAGFAILKCNN		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* Env					
		Research Contact G. Robey, Abbot Labs					
		References Moore1994c					
		• 493-156: The relative affinity denatured/native gp120 is >10. [Moore1994c]					
400	110.1	gp160 (212–221)	gp120 (200–217)	PIPIHYCAPA	no	Vaccine	human
		Vaccine *Vector/Type:* protein *HIV component:* Env					
		References Valenzuela1998, Pincus1996, Pincus1993a					
		• 110.1: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding – 110.1-RAC did not mediate cell killing, and sCD4 has no effect. [Pincus1993a, Pincus1996]					
		• 110.1: There is another antibody with this ID that binds to Env at positions 491-500 in LAI, see.					
401	GV4H3	gp160 (219–226)	gp120 (219–226 IIIB)	APAGFAIL		Vaccine	mouse
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120-Mab complex					
		References Denisova1996					
		• GV4H3: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes. [Denisova1996]					
402	J1	gp160 (222–231)	gp120 (222–231 LAI)	GFAILKCNNK		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade LAI					
		Research Contact J. Hoxie, U. Penn.					
		References Cook1994, Moore1994d, Moore1994c					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• J1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994] • J1: The relative affinity denatured/native gp120 is 30. [Moore1994c]					
403	J3	gp160 (222–231)	gp120 (222–231 LAI)	GFAILKCNNK		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade LAI **Research Contact** J. Hoxie, U. Penn. **References** Cook1994, Moore1994c • J3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994] • J3: The relative affinity denatured/native gp120 is 30. [Moore1994c]					
404	1006-30-D	gp160 (236–245)	gp120 (241–251)	KGSCKNVSTV			human (IgG1λ)
		Ab type C2 **References** Nyambi2000, Hioe2000 • 847-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including two C2 MAbs – the binding of anti-C2 MAbs was weak to isolates from clades B, C, D, E, F, G, and they did not not bind to isolates from subtypes A and H – epitope is suggested to be in a 20 amino acid peptide KGSCKNVSTVQCTHGIRPVV. [Nyambi2000] • 1006-30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C2 MAbs 1006-30-D and 847-D did not effect proliferation. [Hioe2000]					
405	847-D	gp160 (236–245)	gp120 (241–251)	KGSCKNVSTV			human (IgG1λ)
		Ab type C2 **References** Nyambi2000, Hioe2000 • 847-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including two C2 MAbs – the binding of anti-C2 MAbs was weak to isolates from clades B, C, D, E, F, G, and they did not not bind to isolates from subtypes A and H – epitope is suggested to be in a 20 amino acid peptide KGSCKNVSTVQCTHGIRPVV. [Nyambi2000] • 847-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C2 MAbs 1006-30-D and 847-D did not effect proliferation. [Hioe2000]					
406	MF169.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **References** Moore1994d, Moore1994c, Thiriart1989 • MF169.1: The relative affinity denatured/native gp120 is 11 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding. [Moore1994c]					
407	MF170.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **References** Moore1994d, Moore1994c, Thiriart1989 • MF170.1: The relative affinity denatured/native gp120 is 15 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding to denatured and native gp120, and 262N/T, 269 E/L and 281 A/V to only native gp120. [Moore1994c]					
408	MF87.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **References** Moore1994c, Thiriart1989					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• MF87.1: The relative affinity denatured/native gp120 is 10 – mutations 252 R/W, 257 T/G, and 257 T/R impair binding. [Moore1994c]					
409	213.1	gp160 (252–261)	gp120 (242–261 LAI)	RPVVSTQLLL		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C2 **Research Contact** Claudine Bruck **References** Moore1994c, Moore1993a, Thiriart1989 • 213.1: UK Medical Research Council AIDS reagent: ARP334. • 213.1: The relative affinity denatured/native gp120 is 100 – mutations 252 R/W, 257 T/G or T/R impair binding. [Moore1994c] • 213.1: Bound preferentially to denatured IIIB and SF2 gp120. [Moore1993a]					
410	B12	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Maksiutov2002, Moore1994c • B12: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. [Maksiutov2002] • B12: C2 region – the relative affinity for denatured/native gp120 is 27 – mutations 257 T/R and 262 N/T impair binding. [Moore1994c]					
411	B13 (Bh13, Chessie B13)	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **Research Contact** George Lewis, Institute of Human Virology, Baltimore MD, USA **References** Maksiutov2002, Wang2002c, Connor1998, Pincus1996, Moore1994d, Abacioglu1994, Moore1994c, Moore1993a, Pincus1993a • B13: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. [Maksiutov2002] • B13: Called Bh13 – binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. [Pincus1993a, Pincus1996] • B13: C2 region – epitope boundaries mapped by peptide scanning, core epitope: TQLLLN. [Abacioglu1994] • B13: The relative affinity for denatured/native gp120 is 30 – mutations 257 T/R and 269 E/L impair binding. [Moore1994c] • B13: Bound preferentially to denatured IIIB gp120. [Moore1993a]					
412	C13	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **Research Contact** George Lewis **References** Maksiutov2002, Abacioglu1994, Moore1994c, Moore1993a • C13: NIH AIDS Research and Reference Reagent Program: 1209. • C13: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. [Maksiutov2002] • C13: Epitope boundary extended to RPVVSTQLLLNGSLAEEEVVIR, to take into account the effect of a point mutation. [Abacioglu1994] • C13: The relative affinity for denatured/native gp120 is 36 – mutations 257 T/R, 267 E/L, and 269 E/L impair binding. [Moore1994c] • C13: Bound preferentially to denatured IIIB gp120. [Moore1993a]					
413	M89	gp160 (252–271)	gp120 (252–271 LAI)	RPVVSTQLLLNGSLAEEEVV	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C2 **Research Contact** Fulvia di Marzo Veronese					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Maksiutov2002, Moore1994d, Moore1994c, diMarzo Veronese1992 • M89: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. [Maksiutov2002] • M89: C2 region – the relative affinity for denatured/native gp120 is >30 – mutations 257 T/R and 269 E/L impair binding. [Moore1994c] • M89: Immunoblot reactive, RIP negative, for strains IIIB, 451, MN, RF, and RUTZ. [diMarzo Veronese1992]					
414	B21	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B21: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
415	B23	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B23: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
416	B24	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B24: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
417	B25	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B25: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
418	B3	gp160 (257–262)	gp120 (257–262 BH10)	TQLLLN		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B3: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
419	B26	gp160 (257–263)	gp120 (257–263 BH10)	TQLLLNG		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B26: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
420	B29	gp160 (257–263)	gp120 (257–263 BH10)	TQLLLNG		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Abacioglu1994 • B29: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
421	B36	gp160 (257–263)	gp120 (257–263 BH10)	TQLLLNG		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C2 **References** Abacioglu1994 • B36: C2 region, epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
422	110.E	gp160 (262–281)	gp120 (262–281 LAI)	NGSLAEEEVVIRSVNFTDNA		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** C2 **Research Contact** F. Traincard **References** Maksiutov2002, Moore1994d, Moore1994c • 110.E: This epitope is similar to a fragment of human protein lymphatic endothelium-specific hyaluronan receptor LYVE-1, TTRLLVQGSLRAEE. [Maksiutov2002] • 110.E: The relative affinity for denatured/native gp120 is 7.3. [Moore1994c]					
423	110.C	gp160 (271–280)	gp120 (271–280 LAI)	VIRSVNFTDN		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** C2 **Research Contact** F. Traincard, Hybridolabs, Institut Pasteur **References** Valenzuela1998, Moore1994d, Moore1994c • 110.C: Only slightly reduces LAI viral binding or entry into CEM cells. [Valenzuela1998] • 110.C: The relative affinity for denatured/native gp120 is 1. [Moore1994c]					
424	IIIB-V3-26	gp160 (291–307)	gp120 (299–304 IIIB)	SVEINCTRPNNNTRKSI	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Ab type** V3 **References** Maksiutov2002, Laman1992 • IIIB-V3-26: This epitope is similar to a fragment of the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO- 1 antigen) (CD95 antigen), VEINCTRQN. [Maksiutov2002] • IIIB-V3-26: Binds to the base of the V3 loop on denatured gp120. [Laman1992]					
425	IIIB-V3-21 (V3-21)	gp160 (294–299)	gp120 (299–304 IIIB)	INCTRP	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Ab type** V3 **Research Contact** J. Laman **References** Maksiutov2002, Zhang2002, Valenzuela1998, Laman1993, Laman1992 • IIIB-V3-21: NIH AIDS Research and Reference Reagent Program: 1725. • IIIB-V3-21: UK Medical Research Council AIDS reagent: ARP3048. • IIIB-V3-21: This epitope is similar to a fragment of the FasI receptor precursor (Apptosis-mediating surface antigen fas) (APO- 1 antigen) (CD95 antigen), VEINCTRQN. [Maksiutov2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• IIIB-V3-21: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] • IIIB-V3-21: Does not block HIV-1 LAI binding or entry into CEM cells. [Valenzuela1998] • IIIB-V3-21: Binds to NP40 treated gp120, and epitope is probably obscured by local glycosylation. [Laman1993] • IIIB-V3-21: Binds to the base of the V3 loop on denatured gp120. [Laman1992]				
426	polyclonal	gp160 (296–327)	gp120 (MN)	CNYNKRKRIHIGPGRAFYTTKNIIG-TIC	L		rabbit (IgA, IgG)
		Ab type V3 **References** FitzGerald1998 • Polyclonal response to MN, or Thai E V3 loop inserted into Pseudomonas Exotoxin for vaccination – inserts of 14 or 26 amino acids were used from MN or a Thai E strain, constrained by disulfide bond – sera from vaccinated rabbit were reactive with strain-specific gp120 – administration to mucosal surfaces elicits IgA. [FitzGerald1998]					
427	polyclonal	gp160 (297–330)	Env (dis 303–335 LAI)	TRPNNNTRKSIHIGPGRAFYATGEI-IGDIRQAH	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* B clade LAI *HIV component:* V3 *Adjuvant:* QS21 **Ab type** V3 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28 (89%), proliferative in 19/28 (79%), and CTL in 13/24 (54%) of testable volunteers – 14/28 had non-neutralizing Ab responses to this peptide (E), 7/24 had proliferative responses, and multiple CTL responses were detected. [Pialoux2001]					
428	MO97/V3	gp160 (299–308)	gp120 (299–308 IIIB)	PNNNTRKSIR	no	in vitro stimulation or selectio	human (IgM)
		Ab type V3 **References** Gorny2004, Ohlin1992 **Keywords** review. • M097/V3: Review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains; a subset can also neutralize some primary isolates. The three IgMs, M096, M097, and M099, are non-neutralizing. [Gorny2004] (**review**) • MO97: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with rpB1 (IIIB Env 286-467) [Ohlin1992]					
429	polyclonal	gp160 (299–331)	gp120 (306–338 BH10)	PNNNTRKSIRIQRGPGRAFVTIGKI-GNMRQAHC	L	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 **Ab type** V3 **References** Neurath1990 • 21 V3 loop variant peptides spanning this region were tested and serological cross-reactivity correlated with divergence. [Neurath1990]					
430	55/11	gp160 (300–315)	gp120 (300–315)	NNNTRKRIRIQRGPGR?			
		Ab type V3					

B Cell

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Peet1998					
		• 55/1l: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/1l binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]					
431	8/38c (8/38/1c)	gp160 (300–315)	gp120 (300–315 HXB10)	NNNTRKRIRIQRGPGR	L	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120					
		Ab type V3 **Research Contact** C. Dean and C. Shotton, Institute for Cancer Research, Surrey, UK					
		References Peet1998, Parren1998a, Jeffs1996, Sattentau1995b, McKeating1992a					
		• 8/38c: UK Medical Research Council AIDS reagent: ARP3039.					
		• 8/38c: Called 8/38/1c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 8/38c binding was only diminished by V3 serine substitutions C-term to the tip of the loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]					
		• 8/38c: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]					
		• 8/38c: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. [Jeffs1996]					
		• 8/38c: Binds equally well to monomer and oligomer, less rapid association rate than other anti-V3 antibodies, and an associated less potent neutralization of lab strains. [Sattentau1995b]					
		• 8/38c: Binds to virion gp120 and neutralizes only in the presence of sCD4. [McKeating1992a]					
432	8/64b	gp160 (300–315)	gp120 (300–315 HXB10)	NNNTRKRIRIQRGPGR	L	Vaccine	rat (IgM)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120					
		Ab type V3					
		References Peet1998, McKeating1992a					
		• 8/64b: UK Medical Research Council AIDS reagent: ARP3036.					
		• 8/64b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 8/64b binding was abrogated by V3 serine substitutions C-term to the tip of the loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]					
		• 8/64b: Binds to virion gp120 and neutralizes only in the presence of sCD4. [McKeating1992a]					
433	polyclonal	gp160 (300–321)	gp120	NYNKRKRIHIGPGRAFYTTK	L	HIV-1 infection, Vaccine	human
		Vaccine *Vector/Type:* peptide *HIV component:* V3					
		Ab type V3					
		References Bartlett1998					
		• V3 peptide vaccine (MN, RF, EV91, and Can0A) with a C4 helper T cell epitope were used to vaccinate HLA-B7 HIV-infected patients – V3 Ab levels and the anti-HIV proliferative response, but no decrease in HIV-1 RNA levels or increase in CD4 levels was observed. [Bartlett1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
434	polyclonal	gp160 (300–321)	gp120	NYNKRKRIHIGPGRAFYTTK		HIV-1 exposed seronegative	human (IgA)
		Ab type V3 **References** Kaul1999 • HIV-1 Env-specific mucosal IgA found in genital track of 16/21 HIV-1 resistant chronically exposed Kenyan sex workers – 11/21 had detectable Th responses. [Kaul1999]					
435	polyclonal	gp160 (300–322)	gp120 (IIIB)	CNNTRKSIRIQRGPGRAFVTIGK	L		guinea pig (IgG)
		Ab type V3 **Research Contact** D. Bolognesi and T. Matthews, Duke University **References** Allaway1993 • Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion. [Allaway1993]					
436	polyclonal (VEI3)	gp160 (300–328)	Env	NNNTRKSIRIGPGRAFYTTGDIGNI–RQ		HIV-1 infection	human
		Ab type V3 **References** Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. [Carlos1999]					
437	9284 (NEA 9284)	gp160 (301–312)	gp120 (307–318 IIIB)	NNTRKSIRIQRG	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1 **Ab type** V3 **Research Contact** Dupont de Nemours, Les Ulis, France or Wilmington, Delaware **References** Schonning1998, Parren1998a, Binley1997a, Cao1997b, Poignard1996a, Moore1996, Fontenot1995, VanCott1995, Sattentau1995b, Sorensen1994, Okada1994, Cook1994, Thali1994, VanCott1994, Thali1993, Trujillo1993, Moore1993c, Sattentau1993, McKeating1992a, Wyatt1992, Sattentau1991, Skinner1988a, Skinner1988b • 9284: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 9284 was found to have an inaccessible epitope on the oligomeric form of Env and anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU. [Schonning1998] • 9284: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] • 9284: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4. [Cao1997b] • 9284: V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. [Poignard1996a] • 9284: Binds V3 loop – anti-C1 MAbs 133/290 and 135/9 enhance binding – reciprocal binding inhibition of other anti-V3 MAbs. [Moore1996] • 9284: Used to monitor HIV-1 Env expression in infected H9 cells, binds native and reduced gp120s similarly. [VanCott1995] • 9284: Binds equally well to monomer and oligomer, rapid association and potent neutralization of lab strains – neutralizes cell-free virus Hx10. [Sattentau1995b] • 9284: Did not neutralize infection of HIV/HTLV-I pseudotype. [Sorensen1994] • 9284: Binding domain aa 301-310: TRKSIRIQRG – mutations in the V3 loop from basic residues can destroy virus infectivity and syncytium formation: R306T, R309T and R313G can also reduce binding of V3 MAbs with two different binding sites: 9284 and 0.5beta – called NEA9284. [Okada1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 9284: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. [Cook1994] • 9284: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb. [Thali1994] • 9284: Does not bind MN gp120, just IIIB. [VanCott1994] • 9284: Peptide RIQRGPGRAFVTIGKIGNMRQA – Reacts with three human brain proteins of 35, 55, 110 kd – called NEA-9284. [Trujillo1993] • 9284: Inhibits C4 region antibodies (G3-299, G3-519) which have conformational requirements. [Moore1993c] • 9284: Increased binding in the presence of sCD4. [Sattentau1993] • 9284: Single amino acid substitutions in the C4 region (427 W/V or W/S) or at the base of the V3 loop (298 R/G) can significantly increase binding and neutralization– position 427 is also important for CD4 binding and anti-CD4 binding site MAbs. [Wyatt1992] • 9284: Two fold increase in binding to gp120 in the presence of bound sCD4. [Sattentau1991] • 9284: IIIB type-specific binding and neutralization. [Skinner1988b]			
438	polyclonal	gp160 (301–325)	gp120 (IIIB)	NNTRKSIRIQRGPGRAFVTIGKIGN	L	Vaccine	mouse (IgA)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *Adjuvant:* Cholera toxin (CT) **Ab type** V3 **References** Bukawa1995 • Polyclonal secretory IgA antibody raised by mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to V3, CD4 or HPG30 component of the multicomponent peptide immunogen. [Bukawa1995]					
439	polyclonal	gp160 (301–325)	gp120 (IIIB)	NNTRKSIRIQRGPGRAFVTIGKIGN	L	Vaccine	mouse (IgA22a)
		Vaccine *Vector/Type:* DNA *Strain:* B clade IIIB *HIV component:* Env, Rev **Ab type** V3 **References** Sasaki1998 • An anti-env response was sought, and co-expression of Rev was required – intramuscular versus nasal vaccination with DNA vaccine with a QS21 adjuvant was studied – QS21 enhanced the IgG2a response mediated via Th1 cytokines IFNgamma and IL-2. [Sasaki1998]					
440	polyclonal	gp160 (302–317)	Env (B consensus)	NTRKSIHIGPGRAF		HIV-1 infection	human
		Ab type V3 **References** Morris2001 • Ab responses before HAART therapy and after one year of therapy were measured in 8 individuals that were classified HAART successes, and 10 patients who were classified as HAART failures – V3 peptide antibody binding titers to the B-consensus and MN and SF2 variants, and neutralization of HIV-1 MN and four subtype B clinical isolates were tested – subjects with strong anti-V3 and NAb humoral immune responses before starting HAART were more likely to achieve sustained viral suppression to <500 copies RNA/ml on HAART – HIV-specific Ab responses declined after 1 year of successful viral suppression on HAART. [Morris2001]					
441	polyclonal	gp160 (302–318)	Env	NTRKSIHIGPGRAFY	L P	HIV-1 infection	human
		Ab type V3 **References** Bongertz2001 • Non-transmitting mothers had an increased frequency of high neutralizing plasma Ab titers against HIV-1 MN (1:50 dilution, >90% neutralization, 33/88 pregnant women), compared to plasma from transmitting mothers (0/8 pregnant women) – non-transmitting mothers also had more potent neutralization against primary isolates from transmitting mothers, but neutralization of autologous virus was comparable for non-transmitting (7/13) and transmitting mothers (2/4) [Bongertz2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
442	MAG 109	gp160 (302–321)	gp120 (302–321 BH10)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	mouse

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Ab type V3
References Kang1994

- MAG 109: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
443	MAG 49 (#49)	gp160 (302–321)	gp120 (302–321 BH10)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	mouse

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Ab type V3
References Moore1996, Kang1994

- MAG 49: Called #49 in this text. Binding enhanced by anti-C1 MAbs 133/290, 135/9, and by many anti-CD4 binding site MAbs – reciprocal enhancement of some anti-V2 MAbs – reciprocal binding inhibition of anti-V3 MAbs. [Moore1996]
- MAG 49: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
444	MAG 53	gp160 (302–321)	gp120 (302–321 BH10)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	mouse

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Ab type V3
References Kang1994

- MAG 53: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
445	MAG 56	gp160 (302–321)	gp120 (302–321)	NTRKSIRIQRGPGRAFVTIG	L	Vaccine	mouse

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Ab type V3
References Kang1994

- MAG 56: Binds a V3 loop peptide – sensitive to both V3 loop mutations and a mutation at the base of the V1/V2 loop structure (120/121 VK/LE) [Kang1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
446	1324-E (1324E)	gp160 (303–308)	Env (subtype CRF01)	TRTSVR	L	HIV-1 infection	human (IgG1κ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1998
Keywords antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 1324-E: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**)
- 1324-E: Called 1324E – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1324E showed poor cross-reactivity, and was the only MAb tested that was derived from a non-B clade infected patient, an E clade infection was the source of 1324E. [Nyambi2000] (**inter-clade comparisons**)
- 1324-E: MAb reacted with peptides from E clade, while B clade derived MAbs could not. [Zolla-Pazner1999b] (**inter-clade comparisons**)
- 1324-E: E clade stimulated MAb did not cross-react with B clade peptides nor did B clade derived peptides with an E clade V3 loop, but both E and B clade stimulated Abs can cross-react with some peptides from other clades – this Ab showed strong binding to several E, A and F peptides, one C peptide, and no reactivity with B peptides and most D peptides. [Zolla-Pazner1999a] (**inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1324-E: A human MAb was derived from an HIV-1 E clade infection from a US service man who had served in Thailand, selected with the consensus V3 peptide from clade E – cross-reactive with V3 peptides, and gp120 from E, C and A clades, as well as cells infected with a C-clade primary isolate, but not with B and D clade V3 peptides or rgp120 – neutralizes E clade virus adapted for growth in H9 cells, but not 5 primary E clade isolates, including the autologous isolate – kinetic parameters were measured, 1324E was comparable to 447-52D. [Gorny1998] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					
447	polyclonal	gp160 (303–319)	gp120 (subtype C)	CKRKIHIGPGQAFYT		Vaccine	mouse (IgG2a, IgG2b)
		Vaccine *Vector/Type:* peptide in ISCOM, peptide in liposome *HIV component:* V3 *Adjuvant:* Immune stimulating complexes (ISCOM) **Ab type** V3 **References** Ahluwalia1997 • A V3 loop peptide modified to resemble an Indian form (GPGQ) was incorporated into ISCOMS (immune stimulating complexes) or liposomes, and used to immunize mice – the IgG2a/IgG2b antibody response was enhanced by the presentation in the ISCOM suggestive of a Th1 response. [Ahluwalia1997]					
448	MO99/V3	gp160 (304–308)	gp120 (304–308 IIIB)	RKSIR	no	in vitro stimulation or selectio	human (IgM)
		Ab type V3 **References** Gorny2004, Ohlin1992 **Keywords** antibody binding site definition and exposure, antibody generation. • M099/V3: Review. provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains; a subset can also neutralize some primary isolates. The three IgMs, M096, M097, and M099, are non-neutralizing. [Gorny2004] • MO99: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with rpB1 (IIIB Env 286-467) [Ohlin1992] (**antibody binding site definition and exposure**, **antibody generation**)					
449	C311E	gp160 (304–313)	gp120 (309–316 MN)	RKRIHIGP	L	HIV-1 infection	chimpanzee (IgG1)
		Ab type V3 **References** Alsmadi1998, Warrier1996 • C311E: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – C311E bound and directed lysis against all four strains. [Alsmadi1998] • C311E: Chimps were infected with HIV-1 IIIB, and this resulting MAb gave synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. [Warrier1996]					
450	907	gp160 (304–314)	gp120 (309–318)	RKSIRIQRGPG	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **References** Pincus1996, Pincus1991, Pincus1989, Chesebro1988 • 907: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] • 907: Epitope sequence is based on database count of a specified location – 924-RAC immunotoxin is IIIB strain-specific. [Pincus1991] • 907: Coupled to ricin A chain (RAC), MAb 907 inhibited protein synthesis and cell growth in HIV-infected cells. [Pincus1989] • 907: Strain specific binding, and neutralization of only the LAV strain. [Chesebro1988]					
451	924	gp160 (304–314)	gp120 (309–318 IIIB)	RKSIRIQRGPG		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Ab type** V3					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Pincus1998, Pincus1996, Cook1994, Pincus1993b, Pincus1993a, Pincus1991, Chesebro1988 • 924: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] • 924: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. [Cook1994] • 924: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – MAb 924 was used as a control – infected lab workers and a vaccinia gp160 vaccine had strong V3 MAb response, but alum absorbed rec gp160 did not generate anti-V3 response. [Pincus1993b] • 924: MAb was coupled to ricin A chain (RAC) – immunotoxin efficacy was not significantly decreased by sCD4, although the efficacy of gp41 MAb immunotoxins *in vitro* increased 30-fold by sCD4. [Pincus1993a] • 924: Epitope sequence is based on database count of a specified location – 924-RAC immunotoxin is IIIB strain-specific. [Pincus1991] • 924: HIV IIIB strain specific. [Chesebro1988]				
452	polyclonal	gp160 (304–318)	gp120 (304–318 LAI)	RKSIRIQRGPGRAFV		in vitro stimulation or selectio	human (IgG, IgM)
		Ab type V3 **References** Chin1995 • Mimicking the humoral immune response *in vitro* supports isotype switching – human IgG MAbs were generated from naive donors. [Chin1995]					
453	polyclonal	gp160 (304–318)	gp120 (304–318 LAI)	RKSIRIQRGPGRAFV		Vaccine	human (IgG, IgM)
		Vaccine *Vector/Type:* peptide *Strain:* B clade LAI **Ab type** V3 **References** Zafiropoulos1997 • IgG to IgM isotype switching in response to primary and secondary peptide vaccinations was studied – the immunogen contained a V3 loop fragment and a tetanus toxin helper epitope. [Zafiropoulos1997]					
454	10F10	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* gp120 **Ab type** V3 **References** Duarte1994 • 2C4: Putative epitope lies within IHIGPGRAFYT – generated by multi-epitope polypeptide immunization – recognize MN and SC (TRSIHIGPGRAFYTT) peptides, lower affinity for SF2. [Duarte1994]					
455	2C4	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L (MN)	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* peptide *Strain:* B clade MN **Ab type** V3 **References** Duarte1994 • 2C4: Putative epitope lies within IHIGPGRAFYT – neutralizes MN, not IIIB and SF2 – generated by multi-epitope polypeptide immunization – recognize MN and SC (TRSIHIGPGRAFYTT) peptides, lower affinity for SF2. [Duarte1994]					
456	412-D (412-10D, 412, 412D)	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L	HIV-1 infection	human (IgG1κ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Nyambi1998, Gorny1998, Fontenot1995, VanCott1994, Spear1993, Gorny1993					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Keywords antibody binding site definition and exposure, binding affinity, complement, inter-clade comparisons, kinetics, review, vaccine antigen design, variant cross-recognition or cross-neutralization. • 412-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 412-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 412-D showed limited reactivity. [Nyambi2000] (**inter-clade comparisons**) • 412-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 412-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 412-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 412-D was bound only to B clade virions and to D clade MAL. [Nyambi1998] (**inter-clade comparisons**) • 412-D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 412-D has a relatively fast dissociation, thus low affinity among V3 MAbs. [Gorny1998] (**kinetics**) • 412-D: Called 412 – The tip of the V3 loop was presented in a mucin backbone – higher valency correlates with higher affinity constant. [Fontenot1995] (**vaccine antigen design**, **binding affinity**) • 412-D: Called 412-10D – relatively rapid dissociation and weak homologous neutralization. [VanCott1994] (**binding affinity**) • 412-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG. [Spear1993] (**complement**) • 412-D: Neutralizes MN, does not bind SF2 or HXB2 – not reactive with hexa or heptapeptides by Pepscan. [Gorny1993] (**variant cross-recognition or cross-neutralization**)					
457	polyclonal	gp160 (304–320)	gp120 (MN)	RKRIHIGPGRAFYTT	L (MN ALA-1)	HIV-1 infection	human
		Ab type V3 **References** Spear1994 • 40% of antibody in serum that can bind to native viral proteins on MN-infected cells can be blocked by the peptide RKRIHIGPGRAFYTT, which can also block 75-95% of the complement activation on HIV infected cells. [Spear1994]					
458	CGP 47 439	gp160 (304–322)	gp120	RKRIRIQRGPGRAFVTIGK?	L	Vaccine	human
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Jacobson1998, Gauduin1998, Gunthard1994, Safrit1993, Liou1989 • CGP 47 439: Review of passive immunotherapy, summarizing [Gunthard1994] in relation to other studies [Jacobson1998]. [Gunthard1994, Jacobson1998] • CGP 47 439: Post-exposure passive transfer of murine BAT123 can confer protection to hu-PBL-SCID mice challenged with HIV-1 LAI – this protection is not elicited by CGP 47 439, suggesting that the protection is mediated by complement – the protective ability of BAT123 is lost when mice were treated with cobra venom factor, which inactivates serum complement – in this circumstance complement activation provided a protective advantage. [Gauduin1998] • CGP 47 439: Phase I/IIA clinical trial studying multidose tolerability, immunogenicity and pharmacokinetic responses – GP 47 439 was well tolerated, serum t_1/2 was 8-16 days, and a virus burden reduction was noted in some patients. [Gunthard1994] • CGP 47 439: passive transfer to Hu-PBS-SCID mice confers protection against challenge with homologous cell-free virus – CGP 47 439 is a BAT123-human Ig chimera. [Safrit1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
459	polyclonal	gp160 (304–322)	(MN)	RKRIHIGPGRAFYTTKN		HIV-1 infection	human
		Ab type V3 **References** Cheingsong-Popov1992 • The Ab response of 829 HIV-1 infected subjects from eight geographic areas to a set of different V3 peptides was determined by ELISA and cross-inhibition studies – the Ab binding pattern was highly variable, depended on the geographic origin of the sample – 297 sera were tested in a neutralization assay – there was a correlation between Ab binding to the MN V3 loop and MN neutralizing titer, but with neutralization of IIIB or CBL-4. [Cheingsong-Popov1992]					
460	178.1 (178.1.1)	gp160 (305–309)	gp120 (305–309 BH10)	KSiRI	L	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Env **Ab type** V3 **Research Contact** C. Thiriart, Smith Kline and MRC AIDS reagent project **References** Cook1994, Moore1993a, Back1993, Thiriart1989 • 178.1: UK Medical Research Council AIDS reagent: ARP331. • 178.1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro* – binding of GalCer to gp120 inhibited but did not completely block MAb binding. [Cook1994] • 178.1: gp41 amino acid substitutions 668 (N/S) and 675 (I/M) in gp41 interfere with 5023s neutralization potency, region 662-675 is ELDKWANLWNWFNI. [Back1993] • 178.1: Called 178.1.1 – conformational, does not bind well to denatured gp120. [Moore1993a] • 178.1: Reacts to gp120 and gp160 in RIPA EIA and immunoblot. [Thiriart1989]					
461	257-D (257, 257-2-D-IV, 257-D-IV, 257, 257-2D, 257D, ARP3023)	gp160 (305–309)	gp120 (MN)	KRIHI	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Zhang2002, Vella2002, York2001, Park2000, Nyambi2000, Oggioni1999, Beddows1999, Zolla-Pazner1999b, Zolla-Pazner1999a, Stamatatos1998, Gorny1998, Yang1998, LaCasse1998, Hioe1997b, Hill1997, Stamatatos1997, Schutten1997, Schutten1996, Wisnewski1996, Fontenot1995, Schutten1995b, Schutten1995a, Zolla-Pazner1995a, D'Souza1995, Stamatatos1995, VanCott1994, D'Souza1994, Spear1993, Cavacini1993a, Gorny1993, Karwowska1992b, D'Souza1991, Gorny1991 **Keywords** antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, assay development, binding affinity, co-receptor, complement, enhancing activity, inter-clade comparisons, kinetics, review, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization. • 257-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 257-D: NIH AIDS Research and Reference Reagent Program: 1510. • 257-D: UK Medical Research Council AIDS reagent: ARP3023. • 257-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**variant cross-recognition or cross-neutralization**) • 257-D: Called ARP3023: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. [Vella2002] (**assay development**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 257-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001]
- 257-D: Called 257D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000]
- 257-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 257-D showed intermediate reactivity. [Nyambi2000] (**inter-clade comparisons**)
- 257-D: Study of a live-vector mucosal vaccine that expresses HIV-1 V3 domains using the bacterium Streptococcus gordonii which can express heterologous Ag and can colonize the oral cavity and vagina of mice – 268-D and 257-D recognized S. gordonii expressing the V3 domain of MN – the vaccine stimulated V3-specific IgG2a in mice. [Oggioni1999] (**vaccine antigen design**)
- 257-D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 257-D bound rgp120 W61D but could only neutralize the W61D isolate following T-cell line adaptation. [Beddows1999] (**vaccine antigen design**, **variant cross-recognition or cross-neutralization**, **vaccine-specific epitope characteristics**)
- 257-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**)
- 257-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**)
- 257-D: Called 257D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V3 MAbs 391-95D or 257D. [Stamatatos1998] (**vaccine antigen design**, **inter-clade comparisons**)
- 257-D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 257-D has a slow dissociation, thus the highest affinity among V3 MAbs. [Gorny1998] (**kinetics**, **binding affinity**)
- 257-D: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998] (**assay development**)
- 257-D: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized. [LaCasse1998] (**co-receptor**, **variant cross-recognition or cross-neutralization**)
- 257-D: Called 257 – gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect. [Hill1997] (**antibody binding site definition and exposure**, **co-receptor**)
- 257-D: Binds less extensively than MAb 391-95D on the surface of HIV-1 isolates SF162 and SF128A – neutralizes less potently than 391-95D – stronger neutralization of primary macrophage targets than PBMC. [Stamatatos1997] (**variant cross-recognition or cross-neutralization**)
- 257-D: Neutralized (>90%) an SI-env chimeric virus and enhanced (>200%) an NSI-env chimeric virus. [Schutten1997] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 257-D: IIIB neutralizing MAbs *in vitro* fail to neutralize in a mouse model *in vivo*. [Schutten1996]
- 257-D: 257-D is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- 257-D: Comparable affinity for SI and NSI viruses, in contrast to MAb MN215. [Schutten1995b] (**variant cross-recognition or cross-neutralization**)
- 257-D: Only inhibition of SI phenotype virus, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor. [Schutten1995a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 257-D: In serotyping study using flow-cytometry, bound only to virus with KRIHI. [Zolla-Pazner1995a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • 257-D: Called 257-D-IV – could neutralize MN and closely related JRCSF, but not 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs. [D'Souza1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**) • 257-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 better revealed this V3 epitope on TCLA SF2 and dual tropic (MU3) viruses than on macrophage tropic isolates. [Stamatatos1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • 257-D: Potent MN neutralization, slow dissociation constant. [VanCott1994] (**binding affinity**) • 257-D: Included a multi-lab study for antibody characterization and assay comparison – best NAb against MN, but not IIIB. [D'Souza1994] (**variant cross-recognition or cross-neutralization**) • 257-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG – complement mediated virolysis of MN, but not in the presence of sCD4. [Spear1993] (**complement**) • 257-D: Additive MN or SF2 neutralization when combined with CD4 binding site MAb F105 – does not neutralize RF. [Cavacini1993a] (**antibody interactions**, **variant cross-recognition or cross-neutralization**) • 257-D: Neutralizes MN – binds SF2: epitope KSIYI – specificity: MN, SF2, NY5, RF. [Gorny1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • 257-D: Reacts with MN, NY5, CDC4 and SF2, does not cross-react with RF, WM52, or HXB2. [Karwowska1992b] (**variant cross-recognition or cross-neutralization**) • 257-D: Called 257-2-D-IV – potent neutralizing MAb. [D'Souza1991]				
462	311-11-D (311-11D, 311, 311D, 311-D)	gp160 (305–313)	gp120	KRIHIGP	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1998, Spear1993, Gorny1993, Gorny1991 **Keywords** antibody binding site definition and exposure, antibody generation, complement, inter-clade comparisons, review. • 311-11-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 311-11-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 311-11-D showed weak reactivity. [Nyambi2000] (**inter-clade comparisons**) • 311-11-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 311-11-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 311-11-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG. [Spear1993] (**complement**) • 311-11-D: Neutralizes MN – binds SF2: KSIYIGP. [Gorny1993] (**antibody binding site definition and exposure**, **antibody generation**)				
463	41148D	gp160 (305–313)	gp120 (MN)	KRIHIGP	L	HIV-1 infection	human (IgG1)
		Ab type V3 **References** Gorny2004, Alsmadi1998, Pinter1993b **Keywords** ADCC, review, variant cross-recognition or cross-neutralization.					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 41148D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 4117C and 41148D are anti-V3 MAbs that neutralize TCLA strains. [Gorny2004] (**review**)
- 41148D: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against strains IIIB, MN, SF-2, comparable to 4117C, however 41148D is 10x less efficient at neutralization, showing ADCC and neutralization don't always correlate. [Alsmadi1998] (**ADCC**)
- 41148D: Neutralizes less potently than 4117C, reacts with MN, IIIB, SF2. [Pinter1993b] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
464	391/95-D (391-95D, 391.5, 391/95D)	gp160 (305–318)	gp120 (MN)	KRIHIGPGRAFY	L	HIV-1 infection	human (IgG1κ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Zhang2002, Lawson2002, Guillon2002, Park2000, Ly2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Stamatatos1998, Stamatatos1997, Seligman1996, Stamatatos1995, Fontenot1995, Gorny1993, Gorny1991
Keywords acute infection, antibody binding site definition and exposure, co-receptor, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 391/95-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**)
- 391/95-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 391/95-D: The phenotype and genotype of viral env sequences were studied over a period of seroconversion in one individual – Env trans-complementation demonstrated infectivity of clones derived pre-seroconversion were not influenced by MAb 391/95-D, but post-seroconversion clones were enhanced in the presence of 391/95-D, although the V3 binding region was unchanged – a change in the CD4-binding site was observed (NL43 427 Glu–>Lys) to be present in the post-seroconversion 391/95-D enhanced clone (see [Guillon2002]) [Lawson2002]. [Guillon2002, Lawson2002] (**enhancing activity**, **acute infection**)
- 391/95-D: The affect of Ab binding on infectivity was studied by pseudotyping three related envs with different phenotypes – R5 viruses were preferentially enhanced, not X4 – the V3 region was the main determinant of Ab-mediated enhancement and modulation of the interaction between CCR5 and gp120 is critical – tests with MAbs anti-V3 391/95-D and CD4BS-specific GP68 indicate that Ab specificity did not determine whether or not infectivity was enhanced or neutralized, rather the phenotype was determined by Env conformation. [Guillon2002] (**co-receptor**, **enhancing activity**)
- 391/95-D: Called 391/95D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000] (**antibody binding site definition and exposure**)
- 391/95-D: Called 391-95D – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000] (**antibody binding site definition and exposure**)
- 391/95-D: Called 391.5 – MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**)
- 391/95-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 391/95-D: Called 391-95D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V1 or V2 did not enable neutralization by V3 MAbs 391-95D or 257D. [Stamatatos1998] (**antibody binding site definition and exposure**, **inter-clade comparisons**) • 391/95-D: Called 391-95D – binds more extensively than MAb 257-D on the surface of HIV-1 isolates SF162 and SF128A – neutralizes more potently than 257-D – stronger neutralization of primary macrophage targets than PBMC – binding post-gp120-sCD4 association related to anti-V3 Abs neutralizing capacity. [Stamatatos1997] (**variant cross-recognition or cross-neutralization**) • 391/95-D: Competition ELISAs with serial deletions estimated the epitope to be KRIHIGPGRAFY – unconstrained peptide had higher affinity than cyclic. [Seligman1996] (**antibody binding site definition and exposure**) • 391/95-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 better revealed this V3 epitope on macrophage tropic and dual tropic (MU3) viruses, but not in TCLA SF2. [Stamatatos1995] (**antibody binding site definition and exposure**) • 391/95-D: Neutralizes MN – binds to SF2, not IIIB. [Gorny1993]				
465	Aw	gp160 (305–320)	gp120 (Gun-1wt)	KSITIGPGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Aw: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – Aw gives weak neutralization of both wildtype and v strains. [McKnight1995]					
466	Bw	gp160 (305–320)	gp120 (Gun-1wt)	KSITIGPGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Bw: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – Bw gives weak neutralization of only the wildtype strain, does not bind to variant. [McKnight1995]					
467	DO142-10 (DO 142-10)	gp160 (305–320)	gp120 (MN)	KRIHIGPGRAFYTT	L	HIV-1 infection	human (IgG1)
		Ab type V3 **References** Gorny2004, Kwong2002, Sullivan1998a, Parren1998a, Parren1997a, Parren1997c, Ditzel1997, Seligman1996 **Keywords** antibody binding site definition and exposure, antibody generation, binding affinity, enhancing activity, review, variant cross-recognition or cross-neutralization. • DO124-10: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. DO124-10 neutralizes some TCLA strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D0124-10: Called D0124. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**) • DO124-10: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DO124-10 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism – while DO124-10 enhances YU2 entry 6-fold, it neutralizes HXBc2 under identical conditions. [Sullivan1998a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**) • DO142-10: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different that Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**variant cross-recognition or cross-neutralization**, **binding affinity**) • DO142-10: Binds to gp120 MN and an MN V3 peptide with equal affinity, but binds a consensus B peptide and JRCSF less well, and to IIIB gp120 not at all. [Parren1997a] (**variant cross-recognition or cross-neutralization**, **binding affinity**) • DO142-10: Neutralizes TCLA strains but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**) • DO142-10: Phage expression libraries panned against MN peptide were used to select Fab DO142-10 – Fab binds MN gp120, but not a primary isolate rec gp120. [Ditzel1997] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • DO142-10: Fab fragment – competition ELISAs with serial deletions defined the epitope KRIHIGPGRAFYTT. [Seligman1996] (**antibody binding site definition and exposure**, **antibody generation**)			
468	Dv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Dv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. [McKnight1995]					
469	Fv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Fv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. [McKnight1995]					
470	Gv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V3 **References** McKnight1995 • Gv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. [McKnight1995]					
471	Hv	gp160 (305–320)	gp120 (Gun-1v)	KSITIGSGRAFHAI	L	Vaccine	rat
		Vaccine *Vector/Type:* peptide *Strain:* Gun-1 *HIV component:* V3 **Ab type** V3 **References** McKnight1995 • Hv: Rat antibodies were raised against V3 peptides that represent either the wildtype (wt), or brain-cell tropic variant (v) of the isolate Gun-1 – neutralization of only the variant strain, does not bind to wildtype. [McKnight1995]					
472	polyclonal	gp160 (305–322)	gp140 (SF162)	KSITIGPGRAFYATGD	yes	Vaccine	macaque, rabbit (IgG)
		Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade SF162 *HIV component:* gp140 *Adjuvant:* MF59 **Ab type** V3 **References** Barnett2001 • SF162ΔV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter, delivered by gene gun, SF162Δ2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intactSF162, was used as the immunogen – NAbs titers specific for SF162 increased with multiple immunizations, while titers for non-homologous isolates decreased, but anti-V3 peptide binding Abs were not likely the source of this distinction because anti-V3 titers were much lower than those against the entire envelope, and the second booster immunization did not increase the titer of anti-V3 loop Abs. [Barnett2001]					
473	50.1 (R/V3-50.1, Fab 50.1)	gp160 (306–310)	gp120 (MN)	RIHIG	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 **Ab type** V3 **Research Contact** Mary White-Scharf, Repligen Corporation, Cambridge, MA **References** Zhang2002, York2001, Park2000, Hoffman1999, Stanfield1999, LaCasse1998, Berman1997, Seligman1996, Fontenot1995, VanCott1995, Moore1994b, Robert-Guroff1994, VanCott1994, Bou-Habib1994, Rini1993, Ghiara1993, Potts1993, White-Scharf1993, D'Souza1991 • 50.1: NIH AIDS Research and Reference Reagent Program: 1289. • 50.1: Called R/V3-50.1 – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] • 50.1: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – the dissociation constant, Kd of 50.1 for the cell associated primary and TCLA Envs was equal, 7nM. [York2001] • 50.1: Called R/V3-50.1 – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes – 50.1 could only neutralize the sensitive form. [Park2000]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 50.1: The crystal structure of V3 loop peptides bound to Fabs was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different Fabs were bound. [Stanfield1999] • 50.1: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized. [LaCasse1998] • 50.1: Binds to 6/7 isolates from breakthrough cases from a MN gp120 vaccine trial. [Berman1997] • 50.1: Competition ELISAs with serial deletions produced comparable estimate of epitope length to crystal structure and alanine substitution – KRIHIGP. [Seligman1996] • 50.1: Used to monitor HIV-1 Env expression in infected H9 cells. [VanCott1995] • 50.1: Shows modest cross-reactivity among B clade gp120s, little outside B clade. [Moore1994b] • 50.1: Chimeric MN V3 loop in an HXB2 background allows increased FACS signal, Ab affinity, and viral neutralization. [Robert-Guroff1994] • 50.1: Potent MN neutralization, slow dissociation rate. [VanCott1994] • 50.1: No neutralization of primary isolate JR-CSF – greater affinity for and neutralization of T cell tropic strain T-CSF, derived from JR-CSF. [Bou-Habib1994] • 50.1: Crystal structure of V3 loop bound to 50.1 – light chain binds just to the left of GPG, heavy chain binds further to the left. [Rini1993] • 50.1: Crystal structure of a 24 amino acid peptide from the V3 loop bound to 59.1 and 50.1 Fab fragments – epitope KRIHIGP. [Ghiara1993] • 50.1: No synergistic neutralization of MN when combined with CD4BS MAb F105 – isotype stated to be IgG2a. [Potts1993] • 50.1: Epitope defined by peptide reactivity and changes affinity with amino acid substitutions – epitope RIHIGP. [White-Scharf1993] • 50.1: Called R/V3-50.1 – potent neutralizing of lab strains. [D'Souza1991]			
474	polyclonal	gp160 (306–318)	gp120 (NY5)	KKGIAIGPGRTLY			(IgM)
		Ab type V3 **References** Metlas1999a, Metlas1999b • Auto-Abs that react with the V3 loop of NY5 are present in the sera of HIV- individuals, and are predominantly IgM. [Metlas1999b]					
475	BAT123 (BAT-123, CGP 47 439)	gp160 (306–322)	gp120 (308–322 HXB2)	RIRIQRGPGRAFVTIGK	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1 **Ab type** V3 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY **References** Gauduin1998, Parren1998a, Andrus1998, Poignard1996a, Sattentau1995b, Gauduin1995, Pirofski1993, Thali1993, Safrit1993, Moore1993a, Fung1990, Liou1989, Fung1987 • BAT123: Post-exposure passive transfer of murine BAT123 can confer protection to hu-PBL-SCID mice challenged with HIV-1 LAI – this protection is not elicited by CGP 47 439, a BAT123 chimera that has a human IgG1 Fc domain, suggesting that the protection is mediated by complement – the protective ability of BAT123 is lost when mice were treated with cobra venom factor, which inactivates serum complement – IgG1 does not fix complement efficiently so an IgG2 MAb might perform better. [Gauduin1998] • BAT123: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] • BAT123: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection. [Andrus1998] • BAT123: Epitope described as RGPGRAFVTIGK – V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus (BAT123 less so than the others), mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. [Poignard1996a] • BAT123: Binds with high affinity to monomer and oligomer, rapid association and potent neutralization of lab strain. [Sattentau1995b]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- BAT123: Passive transfer of BAT123 to hu-PBL-SCID mice 1 hour prior to inoculation with HIV-1 LAI, or up to four hours post-exposure, could protect mice from infection – the protection, like the MAb, was specific for the viral strain LAI. [Gauduin1995]
- BAT123: Variable region sequenced – heavy chain: V 3660-SB32, D unknown, J H3 – light chain: V kappa21, J kappa2. [Pirofski1993]
- BAT123: Passive transfer to Hu-PBS-SCID mice confers protection against challenge with homologous cell-free virus. [Safrit1993]
- BAT123: Called BAT-123 – conformational, does not bind well to denatured gp120 – not reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120. [Moore1993a]
- BAT123: Anti-idiotypic MAb, AB19-4i, stimulates anti-anti-ID which neutralizes MN and IIIB. [Fung1990]
- BAT123: CGP 47 439 is a BAT123 chimera that has a human IgG1 Fc domain.

476 838-D (838) gp160 (307–311) Env (RF) KSITK L HIV-1 infection human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

References Gorny2004, Zhang2002, He2002, Nyambi2000, Gorny2000a, Zolla-Pazner1999b, Zolla-Pazner1999a, Nyambi1998, Hioe1997b, Gorny1997

Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 838-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 838-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002]
- 838-D: Called 838 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002]
- 838-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 838-D showed intermediate reactivity. [Nyambi2000] (**inter-clade comparisons**)
- 838-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 838-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**)
- 838-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to many A, B, C and F peptides, poor binding to D and E. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**)
- 838-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 838-D bound B clade virions but had limited cross-reactivity with other clades, with low levels of binding to A and D virions. [Nyambi1998] (**inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 838-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**) • 838-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 838-D was cross-reactive with V3 peptides from clade A and C, and could bind to 5/8 B clade V3 peptides – 50% neutralization of RF was obtained. [Gorny1997] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)				
477	1006-15D (1006)	gp160 (307–312)	gp120 (RF)	KSITKG	no	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, He2002, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1997 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review. • 1006-15D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 1006-15D: Called 1006 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002] • 1006-15D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1006-15D showed strong cross-reactivity. [Nyambi2000] (**inter-clade comparisons**) • 1006-15D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 1006-15D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several B and F peptides, one C peptide, and some reactivity with A peptides – no binding was observed with D and E peptides. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 1006-15D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – was somewhat cross-reactive with V3 peptides from clade A, C and other B clade V3 peptides, but not E clade. [Gorny1997] (**antibody generation**, **inter-clade comparisons**)				
478	782-D (782)	gp160 (307–312)	Env (RF)	KSITKG	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Hioe1997b, Gorny1997 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 782-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 782-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 782-D showed intermediate reactivity. [Nyambi2000] (**inter-clade comparisons**) • 782-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 782-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several B and F peptides, one C peptide, and some reactivity with A and D peptides. [Zolla-Pazner1999a] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**) • 782-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**) • 782-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 782-D was not cross-reactive with V3 peptides from clade A or E, but could bind to 3/8 B clade V3 peptides, and 1/2 C clade V3 peptides – 50% neutralization of RF was obtained. [Gorny1997] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)				
479	908-D (908, 908-12D)	gp160 (307–312)	gp120 (RF)	KSITKG	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1997 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review. • 908-D:This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 908-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross -reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 908-D showed strong cross-reactivity, but achieved only 50% neutralization on 2/5 isolates tested. [Nyambi2000] (**inter-clade comparisons**) • 908-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 908-D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed strong binding to several A, B, C and F peptides, and poor binding to E and D peptides. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 908-D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 908-D was not cross-reactive with V3 peptides from clade E, but could bind to 6/8 B clade V3 peptides, 2/4 A clade, and 1/2 C clade – 50% neutralization of RF was obtained. [Gorny1997] (**antibody binding site definition and exposure**, **antibody generation**, **inter-clade comparisons**)				
480	1027-15D (1027, 1027-D, 1027D)	gp160 (307–313)	Env (RF)	KSITKGP	no	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Zhang2002, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1997 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review. • 1027-15D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 1027-15D: Called 1027-D – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**antibody binding site definition and exposure**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1027-15D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1027-15D showed strong cross-reactivity. [Nyambi2000] (**inter-clade comparisons**) • 1027-15D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 838, 782, 1027, 908, and 1006, all selected with RF V3 peptide – the core amino acids KSITK tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 1027-15D: Review of clade specificity and anti-V3 HIV-1-Abs – this Ab showed moderate binding to several B and F peptides, one C peptide, and was not reactivity with A, D and E peptides. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 1027-15D: Five human MAbs against were derived from HIV-infected North American subjects after selection by the V3 RF peptide – 1027-15D was not cross-reactive with V3 peptides from clade A or E, but could bind to 3/8 B clade V3 peptides, and 1/2 C clade V3 peptides. [Gorny1997] (**antibody binding site definition and exposure**, **antibody generation**, **inter-clade comparisons**)			
481	F19.26-4	gp160 (307–319)	gp120 (312–324 LAI)	IRIQRGPGRAFVT	L	Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Boudet1994 • F19.26-4: Strain specific – used to raise anti-idiotype antibodies. [Boudet1994]					
482	F19.48-3	gp160 (307–319)	gp120 (312–324 LAI)	IRIQRGPGRAFVT	L	Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Boudet1994 • F19.48-3: Strain specific – used to raise anti-idiotype antibodies. [Boudet1994]					
483	F19.57-11	gp160 (307–319)	gp120 (312–324 LAI)	IRIQRGPGRAFVT	L (LAI)	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Boudet1995, Boudet1994, Boudet1991 • F19.57-11: Anti-anti-idiotypic antibodies (Ab3) were raised in BALBc mice that had greater breadth of reactivity than the original F19.57-11 (Ab3 could also recognize 1282 and SF2, with aa TRK(R or S)IYIGPGRA(WY or FH)T) [Boudet1995] • F19.57-11: MAb F19.57-11 is strain specific for LAI – used to raise anti-idiotype rabbit antibodies (called 57-B Ab2) [Boudet1994]					
484	M77	gp160 (307–320)	gp120 (IIIB)	IRIQRGPGRAFVTI	L	HIV-1 infection	human (IgG)
		Ab type V3 **Research Contact** Advanced BioScience Laboratories, Rockville, MD, commercial **References** Gorny2004, Finnegan2002, Denisova2000, Watkins1996, Denisova1996, Denisova1995, DeVico1995, Cook1994, Watkins1993, diMarzo Veronese1993, diMarzo Veronese1992, Pal1992 **Keywords** antibody binding site definition and exposure, escape, review, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization. • M77: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. M77 neutralizes some TCLA strains. [Gorny2004] (**review**) • M77: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. Cluster I and II MAbs bound to gp120/gp41 complexes at the cell-to-cell contact interface, in contrast to M77 which bound to gp120 that was evenly dispersed over the target cell surface. [Finnegan2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• M77: M77 is highly strain specific for IIIB, but anti-idiotypic Abs directed against M77 can in turn elicit an Ab response with expanded HIV cross-reactivity – this mechanism may serve to prolong the primary response and to counter-balance viral immune evasion by mutation. [Denisova2000] (**variant cross-recognition or cross-neutralization**) • M77: Native M77 is highly strain specific, and V3 binding is primarily dependent on its heavy chain – a light chain switched Fab version of M77 could recognize HIV-1 strains that had substitutions on the left side of the V3 loop – R in GPGR is likely to be critical for binding. [Watkins1996] (**variant cross-recognition or cross-neutralization**) • M77: Used M77 bound to gp120 as an immunogen – analysis of polyclonal and monoclonal (62 MAbs were generated) response suggests the M77-gp120 immunogen generated MAbs to more linear epitopes than gp120 alone or gp120 bound to CD4. [Denisova1996] (**vaccine-specific epitope characteristics**) • M77: Stated to be a murine MAb – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – M77 neutralization was only slightly reduced by this mutation. [Watkins1993] (**escape**) • M77: Conformational rearrangements upon binding of M77 to gp120 generates novel epitopes called metatopes. [Denisova1995] • M77: Reacted with both reduced and non-reduced covalently cross-linked gp120-CD4 complex. [DeVico1995] (**antibody binding site definition and exposure**) • M77: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. [Cook1994] • M77: Antibody binding to viral isolates from IIIB infected lab worker followed through time – A to T substitution resulted in the loss of neutralization and native gp120 binding, but not peptide binding. [diMarzo Veronese1993] (**escape**) • M77: IIIB-specific MAb, immunoprecipitates deglycosylated form. [diMarzo Veronese1992] (**variant cross-recognition or cross-neutralization**)					
485	polyclonal	gp160 (307–321)	gp120 (307–321)	IRIQRGPGRAFVTIG	L	HIV-1 infection	chimpanzee
		Ab type V3 **References** Goudsmit1988 **Keywords** antibody binding site definition and exposure, autologous responses, variant cross-recognition or cross-neutralization. • By three months post infection, chimpanzees infected with four strains of HIV-1 developed perisistant Ab responses. The V3 loop was a critical binding domain for strain-specific NAbs in sera from the infected chimpanzees. [Goudsmit1988] (**antibody binding site definition and exposure**, **autologous responses**, **variant cross-recognition or cross-neutralization**)					
486	SP.BAL114	gp160 (308–317)	gp120 (BAL)	SIHIGPGRAF	L		mouse (IgG2aκ)
		Ab type V3 **References** Arendrup1995 • Authors suggest that during *in vivo* immunoselection of escape virus, the V3 domain gains increasing resemblance to that of lab strains. [Arendrup1995]					
487	SP.SF2:104	gp160 (308–317)	gp120 (SF2)	SIYIGPGRAF	L	HIV-1 infection	(IgG2aκ)
		Ab type V3 **References** Arendrup1995, Arendrup1993 • SP.SF2:104: Authors suggest that during *in vivo* immunoselection of escape virus, the V3 domain gains increasing resemblance to lab strains. [Arendrup1995] • SP.SF2:104: Anti-V3 antibody that could neutralize primary virus isolated from a time point of neutralization resistance of autologous virus. [Arendrup1993]					
488	polyclonal	gp160 (308–319)	gp120 (304–318 LAI)	RIHIGPGRAFYT		HIV-1 infection	human (IgG, IgM)
		Ab type V3 **References** Langedijk1995 • Polylconal sera from six individuals tested for reactivity against a panel of peptides based on autologous sequences provide evidence for immunological escape mutations in the tip of the V3 loop. [Langedijk1995]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
489	19b	gp160 (308–320)	gp120	-I----G--FY-T	L	HIV-1 infection	human (IgG1)

Ab type V3 **Research Contact** James Robinson, University of Connecticut, Storrs

References Gorny2004, Pantophlet2003b, Zwick2003, Poignard2003, Kwong2002, Zhang2002, Schulke2002, Kolchinsky2001, Park2000, Binley1999, Trkola1998, Parren1998a, Mondor1998, Parren1997c, Boots1997, Ugolini1997, Fouts1997, Binley1997a, D'Souza1997, Trkola1996a, Wu1996, Gauduin1996, Sattentau1995c, Moore1995b, Moore1995a, Moore1995c, Sattentau1995a, Moore1994a, Moore1994b, Scott1990

Keywords antibody binding site definition and exposure, antibody interactions, review, vaccine antigen design.

- 19b: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset also neutralize some primary isolates. [Gorny2004] (**review**)
- 19b: This paper attempts to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Adding a glycosylation sequon (P313N) to the V3 loop knocked out binding to anti-V3 MAbs loop 2, 19b and 447-52-D. [Pantophlet2003b] (**vaccine antigen design**)
- 19b: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. [Zwick2003] (**antibody interactions**)
- 19b: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- 19b: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, A DA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers. [Poignard2003]
- 19b: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002]
- 19b: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. [Schulke2002]
- 19b: Mutations in two glycosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 19b. [Kolchinsky2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 19b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form but 19b was an exception and required around 950 ng/ml to neutralize either form. [Park2000]
- 19b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999]
- 19b: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains. [Trkola1998]
- 19b: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- 19b: Used as a control in this Hx10 binding and neutralizing MAb study because 19b does not bind to Hx10. [Mondor1998]
- 19b: Neutralizes TCLA strains but not primary isolates. [Parren1997c]
- 19b: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 19b has an epitope involving the tip of the V3 loop, with 5 or 6 essential amino acids distributed within a 12 amino acid stretch – the previously determined binding site was confirmed -I—-G–FY-T and some tolerated variants described, the I can be I, V, or L, the Y can be Y, F, or W – probably a beta-turn is required for FY or FF binding, but WY in can bind with out the context of the turn. [Boots1997]
- 19b: Viral binding inhibition by 19b was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 19b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 19b bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997]
- 19b: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – there were four sequences with variations in the defined epitope among the 9 isolates tested. [D'Souza1997]
- 19b: Inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a]
- 19b: MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of 19b blocks this inhibition. [Wu1996]
- 19b: Not as effective as IgG1b12 at neutralization *ex vivo* of virus direct from plasma of HIV-1 infected individuals. [Gauduin1996]
- 19b: Review: more broadly cross-reactive than anti-V3 tip MAb 447-D. [Moore1995b]
- 19b: Despite broad gp120 binding reactivity, not broadly neutralizing. [Moore1995a]
- 19b: Binds to some gp120s from clades A,B,C,E, and F – weakly neutralized some B and one C clade virus. [Moore1995c]
- 19b: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. [Sattentau1995c]
- 19b: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies. [Moore1994a]
- 19b: V3 loop binding MAb that is more broadly clade cross-reactive than most (binds to 19/29 clade B and 10/12 clade E gp120s) [Moore1994b]

490	4G10	gp160 (308–322)	gp120 (308–322 LAI)	RIQRGPGRAFVTGK		Vaccine	mouse

Vaccine *Vector/Type:* HBcAg fusion *HIV component:* V3
Ab type V3 **Research Contact** Dr. Albrecht von Brunn, Max-von-Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany
References vonBrunn1993

- 4G10: NIH AIDS Research and Reference Reagent Program: 2534.

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 4G10: A 25 amino acid V3-loop sequence fused to HBcAg enhanced V3 immunogenicity. [vonBrunn1993]					
491	5F7	gp160 (308–322)	gp120 (308–322 LAI)	RIQRGPGRAFVTGK		Vaccine	mouse
		Vaccine *Vector/Type:* HBcAg fusion *HIV component:* V3					
		Ab type V3 **Research Contact** Dr. Albrecht von Brunn, Max-von-Pettenkofer-Institut, Ludwig-Maximilians-Universitat Munchen, Germany					
		References vonBrunn1993					
		• 5F7: NIH AIDS Research and Reference Reagent Program: 2533.					
		• 5F7: A 25 amino acid V3-loop sequence fused to HBcAg enhanced V3 immunogenicity. [vonBrunn1993]					
492	G3-523	gp160 (308–322)	gp120 (308–322)	RIQRGPGRAFVTIGK			mouse
		Ab type V3					
		References Jagodzinski1996, Matsushita1988					
		• G3-523: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits G3-523 binding. [Jagodzinski1996]					
493	MN215	gp160 (308–322)	gp120 (MN)	RIHIGPGRAFYTTKN	L	HIV-1 infection	human (IgG1)
		Ab type V3					
		References Gorny2004, Schutten1995b					
		Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization.					
		• MN215: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. MN215 neutralizes some TCLA strains. [Gorny2004] (**review**)					
		• MN215: Minimum epitope for MAB using the Dutch consensus is AFYTTGE, different than defined for MN – generated by EBV transformation of PBMC – displayed higher affinity for NSI than for SI glycoproteins – amino acids HIGP were essential for binding. [Schutten1995b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)					
494	Nea 9301	gp160 (308–323)	gp120 (IIIB)	RIQRGPGRAFVTIGKI			mouse
		Ab type V3 **Research Contact** Dupont, commercial					
		References Wagner1996					
495	4117C	gp160 (309–315)	gp120	IXIGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3					
		References Gorny2004, He2002, Alsmadi1998, Pinter1993b, Pinter1993a, diMarzo Veronese1993, Tilley1992, Tilley1991a					
		Keywords ADCC, antibody binding site definition and exposure, antibody interactions, review, variant cross-recognition or cross-neutralization.					
		• 4117c: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 4117C and 4118D are anti-V3 MAbs that neutralize TCLA strains. [Gorny2004] (**review**)					
		• 4117C: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002]					
		• 4117C: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against MN and SF2, but not IIIB and RF. [Alsmadi1998] (**ADCC**, **variant cross-recognition or cross-neutralization**)					
		• 4117C: Binds V3 loop – does not immunoprecipitate soluble gp120, does react with gp120 on intact virions. [Pinter1993b] (**antibody binding site definition and exposure**)					
		• 4117C: Neutralizes SF2 and MN synergistically combined with anti-CD4 binding site discontinuous MAb. [Pinter1993a, Tilley1992] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 4117C: Potent neutralizing activity against MN, SF-2, and NY-5 – synergy with CD4BS MAb 1125H. [Tilley1991a] (**antibody binding site definition and exposure**, **antibody interactions**, **variant cross-recognition or cross-neutralization**)					
496	419-D (419, 419D)	gp160 (309–315)	gp120 (MN)	IHIGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, He2002, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Nyambi1998, Hioe1997b, Fontenot1995, Spear1993, Gorny1993, Karwowska1992b **Keywords** antibody binding site definition and exposure, complement, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 419-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 419-D: Called 419 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002] • 419-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 419-D showed intermediate reactivity, and no neutralization when tested against five strains – discrepancy between the epitope as described in earlier papers and as described here, KRIHIGP. [Nyambi2000] (**inter-clade comparisons**) • 419-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 419-D: Review of clade specificity and anti-V3 HIV-1-Abs – epitope is described as KRIHIGP. [Zolla-Pazner1999a] (**antibody binding site definition and exposure**, **review**) • 419-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 419-D bound to 3/4 B clade virions, and to D clade MAL. [Nyambi1998] (**inter-clade comparisons**) • 419-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**) • 419-D: Mediated deposition of complement component C3 on HIV infected cells, enhanced by second Ab binding, rabbit anti-human IgG. [Spear1993] (**complement**) • 419-D: Neutralizes MN – binds SF2: IYIGPGR. [Gorny1993] (**variant cross-recognition or cross-neutralization**) • 419-D: MN, NY5 and SF2 strain specific, does not cross-react with RF, CDC4, WM52 or HXB2. [Karwowska1992b] (**variant cross-recognition or cross-neutralization**)					
497	453-D (453)	gp160 (309–315)	gp120 (MN)	IHIGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Fontenot1995, VanCott1994, Gorny1993, Gorny1991 **Keywords** antibody binding site definition and exposure, binding affinity, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization. • 453-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**variant cross-recognition or cross-neutralization**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 453-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 453-D showed intermediate reactivity. [Nyambi2000] (**inter-clade comparisons**)
- 453-D : MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group – MAb 268, with a previously defined core epitope identical to 453 (HIGPGR), was not part of this reactivity group, illustrating that context can be critical. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**)
- 453-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**)
- 453-D : Called 453, epitope described as KRIHIGPGR – the tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant. [Fontenot1995] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 453-D: Moderate homologous neutralization, moderately slow dissociation rate. [VanCott1994] (**binding affinity**)
- 453-D: Neutralizes MN – binds SF2: IYIGPGR – specificity: MN, SF2, NY5, RF. [Gorny1993] (**antibody binding site definition and exposure**)

498 504-D (504, 504-10D) gp160 (309–315) gp120 (MN) IHIGPGR L HIV-1 infection human (IgG1κ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1993
Keywords antibody binding site definition and exposure, inter-clade comparisons, review.

- 504-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**)
- 504-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 504-D showed weak reactivity. [Nyambi2000] (**inter-clade comparisons**)
- 504-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**)
- 504-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**)
- 504-D – Neutralizes MN – binds SF2: IYIGPGR. [Gorny1993] (**antibody binding site definition and exposure**)

499 83.1 (MAb 83.1) gp160 (309–315) gp120 (SF2) IYIGPGR L Vaccine mouse (IgG1)

Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3
Ab type V3 **Research Contact** Mary White-Scharf, Repligen Corporation, Cambridge, MA
References Binley1999, Keller1999, Jelonek1999, Potts1993, White-Scharf1993

- 83.1: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999]
- 83.1: 19 day old mice injected with 83.1 have a shift in IgG1 response away from the V3 loop upon vaccination, without decreasing the total IgG anti-gp120 response, suggesting that prior treatment with a MAb can mask immunogenic sites and shift the immune response to vaccination. [Keller1999]
- 83.1: Maternally transferred anti-V3 loop MAb selectively inhibits the anti-V3 loop Ab component of the IgG response to rgp120 SF2 in 21 day old BALBc mice. [Jelonek1999]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 83.1: Study of synergism of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (e. g. V3 loop MAbs) due to conformational changes. [Potts1993] • 83.1: Neutralizes SF2. [White-Scharf1993]					
500	5023B	gp160 (309–316)	gp120 (309–316 BH10)	IQRGPGra	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5023B: Generation and fine mapping of murine MAbs. [Langedijk1991]					
501	F58/D1 (F58)	gp160 (309–316)	gp120 (IIIB)	IxxGPGRA	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* virus derived protein *HIV component:* gp120 **Ab type** V3 **References** Jackson1999, Millar1998, Moore1993c, Broliden1991, Akerblom1990 • F58/D1: A 17 amino acid MicroAB was made from the third complementarity-determining region of the heavy chain of MAb – F58 neutralized 5x's more efficiently in terms of mass than the original MAb, 32-fold less on a molar basis – neutralization does not involve initial attachment, but fusion and events in early infection. [Jackson1999] • F58/D1: The interaction of a 17-amino-acid neutralizing microantibody (MicroAB) based on F58 and HIV-1 env was studied by electrospray ionization mass spectrometry. [Millar1998] • F58/D1: Binding to native gp120 1-3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. [Moore1993c]					
502	P1/D12	gp160 (309–316)	gp120	IxxGPGRA	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Moore1993c, Akerblom1990 • P1/D12: Binding to native gp120 1-3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. [Moore1993c]					
503	P4/D10 (P4D10)	gp160 (309–316)	gp120	IxxGPGRA	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Schonning1999, Schonning1998, Jacobson1998, Hinkula1994, Arendrup1993, Moore1993c, Marks1992, Broliden1991, Broliden1990, Akerblom1990 • P4/D10: Called P4D10 – the stoichiometry of MAb neutralization was tested and the data indicated that binding for neutralization was was incremental not all or none, i.e., each envelope oligomer binds a single MAb and each Env oligomer bound reduces the chances of infection – MAb BC1071 was used for virion quantification – P4D10 binds only to Env with a glycosylation site mutation at the base of the V3 loop A308T. [Schonning1999] • P4/D10: Called P4D10 – In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU – Ab binding site was suggested to be 314-323 of BRU. [Schonning1998] • P4/D10: Review of passive immunotherapy, summarizing [Hinkula1994] in relation to other studies [Jacobson1998]. [Hinkula1994, Jacobson1998] • P4/D10: Used for passive immunotherapy in four late-stage HIV-infected patients – the serum level of p24 did not decrease in any of these four – see also MAb F58/H3. [Hinkula1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• P4/D10: Primary isolates from different time points from one individual were not susceptible to neutralization by P4/D10. [Arendrup1993] • P4/D10: Binding to native gp120 3 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. [Moore1993c] • P4/D10: Variable domain sequenced and is identical to F58/H3. [Marks1992] • P4/D10: Neutralizing and ADCC activity. [Broliden1990]					
504	IIIB-13 V3 (1044-13 IIIB-V3-13 1727)	gp160 (309–317)	gp120 (308–316 IIIB)	IQRGPGRAF	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Ab type** V3 **References** Zhang2002, Chakrabarti2002, Watkins1993, D'Souza1994, Laman1993, Laman1992 • IIIB-13 V3: NIH AIDS Research and Reference Reagent Program: 1727. • IIIB-13 V3: UK Medical Research Council AIDS reagent: ARP3046. • IIIB-13 V3: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] • IIIB-13 V3: Called 1727: Used as a standard for comparing immune responses to modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation – experiment showed enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. [Chakrabarti2002] • IIIB-13 V3: Called IIIB-V3-13 – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – IIIB-V3-13 neutralization was only slightly reduced by this mutation. [Watkins1993] • IIIB-13 V3: Included in a panel of antibodies used in a multi-lab study for antibody characterization and assay comparison, some neutralization of strains other than IIIB. [D'Souza1994] • IIIB-13 V3: Neutralizes IIIB but not MN. [Laman1992] • IIIB-13 V3: Also known as 1044-13 and as IIIB-V3-13 (J. P. Moore, per. comm.)					
505	IIIB-34 V3 (IIIB-V3-34)	gp160 (309–317)	gp120 (308–316 IIIB)	IQRGPGRAF	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB **Ab type** V3 **References** Laman1993, Laman1992 • IIIB-34 V3: UK Medical Research Council AIDS reagent: ARP3047. • IIIB-34 V3: Called IIIB-V3-34 – IIIB strain specific neutralization – binding is reduced somewhat by DTT or SDS-DTT, enhanced by NP40, but binds to native and denatured gp120. [Laman1993] • IIIB-34 V3: Neutralizes IIIB but not MN – QXGPG are critical amino acids for binding by Pepscan analysis. [Laman1992]					
506	A47/B1	gp160 (309–318)	gp120 (307–316 IIIB)	IQRGPGRAFV	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990					
507	D59/A2	gp160 (309–318)	gp120 (307–316 IIIB)	IQRGPGRAFV	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Akerblom1990					
508	G44/H7	gp160 (309–318)	gp120 (307–316 IIIB)	IQRGPGRAFV	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V3 **References** Akerblom1990					
509	MO96/V3 (M096, M096/V3)	gp160 (309–318 + 329–338)	gp120 (309–318)	IQRGPGRAFV+AHCNISRAKW		in vitro stimulation or selectio	human (IgM)
		Ab type V3 **References** Gorny2004, Ohlin1992 **Keywords** antibody binding site definition and exposure, antibody generation, review. • M093/V3: Review. provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains; a subset can also neutralize some primary isolates. The three IgMs, M096, M097, and M099, are non-neutralizing. [Gorny2004] (**review**) • M096/V3: Generated in response to IIIB Env 286-467 upon *in vitro* stimulation of uninfected-donor lymphocytes, and binds to two peptides: 309-318 + 329-338. [Ohlin1992] (**antibody binding site definition and exposure**, **antibody generation**)					
510	μ5.5 (5.5, mu5.5, Rmu5.5)	gp160 (309–319)	gp120 (MN)	IHIGPGRAFYT	L P		mouse (IgG1κ)
		Ab type V3 **References** Okamoto1998, Maeda1992 • mu5.5: Rmu5.5 is a humanized antibody of mouse MAb m5.5 – neutralized primary isolates with similar V3 loops – passive transfer of MAb to SCID-hu or hu-PBL-SCID mice conferred protection. [Okamoto1998] • mu5.5: sCD4 causes loss of IIIB type-specificity for MAb 0.5beta, allowing binding and neutralization of MN, in contrast to MAb mu5.5. [Maeda1992]					
511	loop 2 (Loop 2, IgG1 Loop 2, loop2)	gp160 (309–320)	gp120	SISGPGRAFYTG	L	HIV-1 infection	human
		Ab type V3 **Research Contact** D. Burton, Scripps Research Institute, La Jolla, CA **References** Gorny2004, Pantophlet2003b, Zwick2003, Sullivan1998a, Parren1998a, Mondor1998, Parren1997a, Parren1997c, Ugolini1997, Ditzel1997, Wu1996, Moore1994b, Barbas III1993 **Keywords** antibody generation, antibody interactions, antibody sequence, variable domain, binding affinity, co-receptor, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization. • loop 2: Called loop2. This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. loop 2 neutralizes some TCLA strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • loop 2: This paper attempts to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Adding a glycosylation sequon (P313N) to the V3 loop knocked out binding to anti-V3 MAbs loop 2, 19b and 447-52-D. [Pantophlet2003b] (**vaccine antigen design**) • loop 2: Called loop2. scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. [Zwick2003] (**antibody interactions**) • loop 2: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – loop 2 enhances YU2 at concentrations up to 20 ug/ml. [Sullivan1998a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- loop 2: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1 loop 2 is only 2-fold greater than monovalent Fab loop 2, suggesting the IgG1 form may bind with only one arm. [Parren1998a] (**binding affinity**)
- loop 2: Neutralizes TCLA strains but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- loop 2: Epitope is suggested to be GPGRAF – binds to 10/17 US clade B monomeric gp120s – IgG1 form can neutralize MN and 2 primary isolates tested. [Parren1997a]
- loop 2: Viral binding inhibition by loop 2 MAb or Fab was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- loop 2: Binds to gp120 from MN and SF2 but not LAI. [Ditzel1997] (**variant cross-recognition or cross-neutralization**)
- loop 2: MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 – binding of loop 2 blocks this inhibition. [Wu1996] (**co-receptor**)
- loop 2: Called Loop 2 – shows modest cross-reactivity among B clade gp120s, little outside B clade. [Moore1994b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- loop 2: Sequences of the heavy and light chain Fab variable regions were generated. [Barbas III1993] (**antibody sequence, variable domain**)
- loop 2: Also known as Loop 2, IgG1 Loop 2 was a obtained by engineering Fab loop2 into an IgG1 molecule. (**antibody generation**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
512	268-D (268-11-D-IV, 268D, 268, 268-11D, 268-10D, MAb 268, 268-10-D, ARP3024)	gp160 (310–315)	gp120 (MN)	HIGPGR	L	HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Zhang2002, Vella2002, York2001, Park2000, Nyambi2000, Hioe2000, Laisney1999, Oggioni1999, Beddows1999, Zolla-Pazner1999b, Zolla-Pazner1999a, LaCasse1998, Stamatatos1997, Hioe1997b, Wisnewski1996, McKeating1996b, Fontenot1995, Zolla-Pazner1995a, Stamatatos1995, VanCott1994, Spear1993, Gorny1993, Karwowska1992b, D'Souza1991, Gorny1991
Keywords review.

- 268-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, a subset can also neutralize some primary isolates. [Gorny2004] (**review**)
- 268-D: NIH AIDS Research and Reference Reagent Program: 1511.
- 268-D: UK Medical Research Council AIDS reagent: ARP3024.
- 268-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera—2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5—thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002]
- 268-D: Called ARP3024: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. [Vella2002]
- 268-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – one of the TCLA V3 viruses 320SI-C3.3 shows reduced binding with this MAb, the sequence of the epitope in 320SI is HIGPGR and in 320SI-C3.3 is RIGPGR. [York2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
				• 268-D: Called 268D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000] • 268-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 268-D showed weak reactivity. [Nyambi2000] • 268-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V3 MAbs 447-52-D and 268-10-D did not effect proliferation. [Hioe2000] • 268-D: Called MAb 268 – To identify potential mimotopes of V3, a hexapeptide phage library was screened with MAb 268 – two hexamers were identified, HLGPGR or KAIHRI that bind to 268 with the same binding site as the V3 loop and inhibit 268 MN gp120 – KLH conjugated hexamer KAIHRI stimulates Abs in rabbits that cross-react with ML gp120. [Laisney1999] • 268-D: Called 268-11D – Study of a live-vector mucosal vaccine that expresses HIV-1 V3 domains using the bacterium Streptococcus gordonii which can express heterologous Ag and can colonize the oral cavity and vagina of mice – 268-D and 257-D recognized S. gordonii expressing the V3 domain of MN – the vaccine stimulated V3-specific IgG2a in mice. [Oggioni1999] • 268-D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 268-D bound rgp120 W61D but could only neutralize the W61D isolate following T-cell line adaptation. [Beddows1999] • 268-D: Peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group – MAb 453, with an identical core epitope to 268 based on prior experiments (HIGPGR), was not part of this reactivity group, illustrating that context can be critical. [Zolla-Pazner1999b] • 268-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] • 268-D: A T-cell line-adapted (TCLA) derivative of SI primary isolate 168P acquired the ability to be neutralized by anti-V3 MAbs – the primary isolate could use either CCR5 or CXCR4, and was not neutralized when infection was directed via either pathway, however the TCLA derivative uses CXCR4 only and is neutralized. [LaCasse1998] • 268-D: Poor reactivity against HIV-1 isolates SF162 and SF128A and no neutralization, in contrast to MAbs 391/95-D and 257-D. [Stamatatos1997] • 268-D: 268-D is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] • 268-D: Failed to neutralize HXB2 and chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b] • 268-D: The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – V3 loop epitopes were less accessible to Ab binding on the virion surface than in the gp120 monomer, particularly for macrophage-tropic isolates SF162 and SF128a, relative to T-cell tropic SF2 – sCD4 association with gp120 did not influence the binding of 268-D to virion-associated gp120, although sCD4 binding did alter epitope exposure for other anti-V3 MAbs. [Stamatatos1995] • 268-D: Serotyping study using flow-cytometry, if H of HIGPGR was substituted in virus, 268-D did not bind. [Zolla-Pazner1995a] • 268-D: Moderate dissociation rate and homologous neutralization titer. [VanCott1994] • 268-D: Mediated deposition of complement component C3 on HIV infected cells, but not in the presence of sCD4. [Spear1993] • 268-D: Neutralizes MN – binds SF2: YIGPGR – specificity: MN, SF2, NY5, RF, CDC4. [Gorny1993] • 268-D: Reacts with MN, NY5, CDC4, RF and SF2, does not cross-react with WM52 or HXB2. [Karwowska1992b] • 268-D: Called 268-11-D-IV – strain specific weakly neutralizing. [D'Souza1991]			
513	386-D (386, 386-10D, 386D)	gp160 (310–315)	gp120 (MN)	HIGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Gorny2004, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Fontenot1995, VanCott1994, Gorny1993, Karwowska1992b **Keywords** antibody binding site definition and exposure, binding affinity, inter-clade comparisons, isotype switch, review. • 386-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 386-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 386-D showed intermediate reactivity. [Nyambi2000] (**isotype switch**, **inter-clade comparisons**) • 386-D: Peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 386-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 386-D: Slow dissociation rate, potent homologous neutralization. [VanCott1994] (**binding affinity**) • 386-D: Neutralizes MN – binds SF2: YIGPGR – specificity: MN, SF2, NY5, RF, CDC4. [Gorny1993] (**antibody binding site definition and exposure**)			
514	5042A	gp160 (310–315)	gp120 (310–315 BH10)	QrGPGR	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **References** Gorny1991, Langedijk1991 • 5042A: Generation and fine mapping of murine MAbs. [Langedijk1991]					
515	5042B	gp160 (310–315)	gp120 (310–315 BH10)	QRGPGr	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5042B: Generation and fine mapping of murine MAbs. [Langedijk1991]					
516	418-D (418, 418D)	gp160 (310–316)	gp120 (MN)	HIGPGRA	L	HIV-1 infection	human (IgG1κ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Zhang2002, Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Gorny1993, Karwowska1992b **Keywords** antibody binding site definition and exposure, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 418-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 418-D: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] • 418-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 418-D showed intermediate reactivity. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**) • 418-D: Called 418 – MAb peptide-reactivity pattern clustered with immunological related MAbs: 391.5, 412 and 418, all selected with MN V3 peptide – the core amino acids HIGPGR tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 418-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**) • 418-D: Neutralizes MN, does not bind to SF2 or HXB2. [Gorny1993] (**variant cross-recognition or cross-neutralization**)			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 418-D: MN strain specific, does not cross-react with SF2, NY5, RF, CDC4 WM52 or HXB2. [Karwowska1992b] (**variant cross-recognition or cross-neutralization**)					
517	5021	gp160 (310–316)	gp120	QrGPGRa	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **References** Moore1993c, Langedijk1991, Durda1990, Durda1988 • 5021: Binding to native gp120 100-300 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. [Moore1993c] • 5021: Generation and fine mapping of murine MAbs. [Langedijk1991]					
518	5025B	gp160 (310–316)	gp120 (310–316 BH10)	QRGPGra	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5025B: Generation and fine mapping of murine MAbs. [Langedijk1991]					
519	5042	gp160 (310–316)	gp120	QRGPGRA	L	Vaccine	mouse
		Vaccine *Vector/Type:* peptide **Ab type** V3 **References** Moore1993c, Durda1990, Durda1988 • 5042: Binding to native gp120 100-300 fold greater than to denatured – 314G/W substitution abolishes binding, changes outside the loop have little effect. [Moore1993c]					
520	110.3	gp160 (310–317)	gp120 (308–328 BRU)	QRGPGRAF	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1 **Ab type** V3 **References** Connelly1994, Pirofski1993, Langedijk1992, Evans1989, Thomas1988 • 110.3: An anti-idiotypic MAb generated against 110.3 both mimics and binds to V3, suggesting that the V3 loop may associated with itself. [Connelly1994] • 110.3: MAb variable region sequenced – heavy chain: V 7138(40), D deletion, J H4 – light chain: V kappa21(47), J kappa2. [Pirofski1993] • 110.3: Included as a control. [Evans1989]					
521	110.4	gp160 (310–317)	gp120 (308–328 BRU)	QRGPGRAF	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1 **Ab type** V3 **Research Contact** Genetic Systems Corp, Seattle WA, E. Kinney-Thomas **References** Guillerm1998, Cao1997b, Valenzuela1998, McDougal1996, Connelly1994, Boudet1994, Thali1994, Arendrup1993, Pirofski1993, Thali1993, Langedijk1992, Thali1992b, Thomas1988 • 110.4: Used for flow cytometry in a study of the anti-CD4, CDR3 loop MAb called 13B8.2, in a study of HIV-1 induced programmed cell death. [Guillerm1998] • 110.4: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4. [Cao1997b] • 110.4: Neutralization of LAI in CEM cells by anti-V3 MAbs 110.4 and N11-20 is through inhibition of viral binding to the cell. [Valenzuela1998] • 110.4: Neutralizes HIV-1 LAI. [McDougal1996] • 110.4: An anti-idiotypic MAb generated against 110.3 also blocks binding of 110.4. [Connelly1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 110.4: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb. [Thali1994]
- 110.4: Primary isolates from different time points from one individual were not susceptible to neutralization by 110.4. [Arendrup1993]
- 110.4: MAb variable region sequenced – heavy chain: V 3660-SB32, D closest to DSP2.3, 2.4 and .6, J H2 – light chain: V kappa21, J kappa2. [Pirofski1993]
- 110.4: 313 P/S substitution in the V3 region disrupts binding. [Thali1992b]

522 110.5 gp160 (310–317) gp120 (308–328 BRU) QRGPGRAF L Vaccine mouse (IgG1κ)

Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1
Ab type V3 **Research Contact** E. Kinney-Thomas or Genetic Systems, Seattle WA
References Parren1998a, Ugolini1997, Binley1997a, Jeffs1996, McDougal1996, Poignard1996a, Moore1996, Sattentau1995b, Sattentau1995c, Klasse1993a, Thali1993, Moore1993c, Pirofski1993, McKeating1992a, Langedijk1992, Sattentau1991, Cordell1991, Moore1990b, Thomas1988, Reitz1988

- 110.5: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- 110.5: Viral binding inhibition by 110.5 was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 110.5: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. [Jeffs1996]
- 110.5: Neutralizes HIV-1 LAI. [McDougal1996]
- 110.5: V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. [Poignard1996a]
- 110.5: Reciprocal binding inhibition with other anti-V3 MAbs – enhances binding of some anti-V2 MAbs – binding enhanced by some CD4 binding site MAbs. [Moore1996]
- 110.5: Binds with high affinity to monomer and oligomer, rapid association and potent neutralization of lab strains – neutralizes cell-free Hx10. [Sattentau1995b]
- 110.5: Pretreatment of HX10-infected H9 cells with sCD4 decreases signal from 110.5 at 37 degrees due to dissociation of gp120-gp41. [Sattentau1995c]
- 110.5: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 110.5 is not affected. [Klasse1993a, Reitz1988]
- 110.5: Thrombin cleavage of V3 loop between R-315 and A-316 abrogates binding – can inhibit C4 region antibody which has conformational requirements (G3-299) – binding to native gp120 100-300 fold greater than to denatured. [Moore1993c]
- 110.5: Variable region sequenced – heavy chain: V 3660-SB32, D closest to DSP2.3, 2.4 and .6, J H2 – light chain: V kappa21, J kappa2. [Pirofski1993]
- 110.5: Two fold increase in binding to gp120 in the presence of bound sCD4. [Sattentau1991]
- 110.5: Binding insensitive to gp120 reduction. [Cordell1991]
- 110.5: Did not induce dissociation of gp120, as sCD4 did – discrepancy with [Poignard1996a], that was suggested to be due to MAb interference with detection, as the gp120-MAb complex was denatured in the Poignard study [Moore1990b]. [Moore1990b, Poignard1996a]

523 58.2 gp160 (310–317) gp120 (MN) HIGPGRAF L Vaccine mouse (IgG1κ)

Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3
Ab type V3 **Research Contact** Repligen Corp.
References York2001, Stanfield1999, Seligman1996, Moore1994b, Potts1993, White-Scharf1993

- 58.2: 58.2's epitope was noted to be IGPGRAF – Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 58.2: The crystal structure of Fab 58.2 bound to V3 loop peptides was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different MAbs were bound – 58.2's epitope was defined as KRKRIHIGPGRAFY. [Stanfield1999] • 58.2: Competition ELISAs with serial deletions produced longer estimates of epitope length, RIHIGPGRAFY, than Alanine substitution, suggesting significance of non-contact residues. [Seligman1996] • 58.2: Modest cross-reactivity among B clade gp120s, little outside B clade – core epitope as I-IHIG. [Moore1994b] • 58.2: Did not synergistically neutralize MN in combination with MAb F105 – there was synergistic neutralization when combined with sCD4. [Potts1993] • 58.2: Epitope defined by peptide reactivity and changes in affinity with amino acid substitutions – 4/7 primarily isolates were neutralized. [White-Scharf1993]					
524	polyclonal	gp160 (310–318)	gp120	QRGPGRAFV?	L	Vaccine	mouse (IgA, IgG1, IgG2a)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate, peptide Brucella abortus (Ba) conjugate, peptide lipopolysaccharide (LPS) conjugate *Strain:* B clade MN *HIV component:* V3 **References** Golding2002a • Internasal (i.n.) immunization with V3-Ba induced mucosal anti-V3 NAbs and IFN-gamma secreting T cells – V3-Ba, V3-KLH and V3-LPS could each induce serum and mucosal IgA and IgG in BALB/c mice – i.n. plus i.p. immunizations gave higher titers than i.n. alone – the response to V3-KLH was mainly restricted to IgG1, and to V3-Ba, IgG2a – class II KO mice (CD4+-deficient) did not respond to V3-KLH, but did respond to V3-Ba, suggesting that V3-Ba may be effective in eliciting Ab responses in HIV-1 infected individuals that have impaired CD4+ T cell function. [Golding2002a]					
525	537-D (537)	gp160 (311–315)	gp120 (MN)	IGPGR	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi2000, Zolla-Pazner1999b, Zolla-Pazner1999a, Fontenot1995, VanCott1994, Gorny1993, Gorny1992, Karwowska1992b • 537-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 537-D showed weak reactivity. [Nyambi2000] • 537-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. [Zolla-Pazner1999b] • 537-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] • 537-D: Moderate homologous neutralization, relatively rapid dissociation constant. [VanCott1994] • 537-D: MN type specific neutralization observed – binds SF2, also IGPGR. [Gorny1992, Gorny1993] • 537-D: Reacts with MN, NY5, CDC4, RF, WM52 and SF2, but does not cross-react with HXB2. [Karwowska1992b]					
526	5020	gp160 (311–316)	gp120 (311–316 BH10)	RGPGRA	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **References** Langedijk1991 • 5020: Generation and fine mapping of murine MAbs. [Langedijk1991]					
527	RC25	gp160 (311–316)	gp120 (JRFL)	IGPGRA	L		humanized mouse
		Ab type V3 **References** Kaizu2003, Kimura2002 **Keywords** co-receptor, HAART.					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• RC25: MD14 is a R5X4 SHIV with a B clade Env; the V3 loop of an E-clade Env was inserted in to MD14 to create SHIV-TH09V3, an R5 virus. SHIV-TH09V3 could infect both cynomolgous and pig-tailed macaques, and the R5 co-receptor usage was maintained after passage through macaques. The MAb RC25 recognized B clade V3 loops, and reacted with SHIV-MD14. Rabbit anti-sera raised against a NSI Clade E consensus preferentially recognized SHIV-TH09V3. [Kaizu2003] (**co-receptor**) • RC25: RC25 is a humanized MAb that recognizes the epitope IGPGRA – it has strong neutralizing activity against JRFL (R5 virus) and weak against NL4-3 (X4 virus) and is used as a control in a study of NAb activity in patients undergoing HAART. [Kimura2002] (**HAART**)					
528	5023A (5023, NEA-9205, NEA 9205)	gp160 (311–317)	gp120 (311–317 BH10)	RgPGRAF	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **Research Contact** Paul Durda, Du Pont de Nemours and Co **References** Schonning1998, Rovinski1995, Back1993, D'Souza1991, Langedijk1991 • 5023A: Called NEA-9205 – The N306 glycan of the V3 loop makes the tip of the V3 loop inaccessible to this MAb in oligomeric Env, loss of this glycan enhances neutralization sensitivity. [Schonning1998] • 5023A: Called 5023 in this paper – Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen. [Rovinski1995] • 5023A: Called 5023 – Langedijk also has an MAb called 5023B – gp41 amino acid substitutions 668 (N/S) and 675 (I/M) in gp41 interfere with 5023s neutralization potency, region 662-675 is ELDKWANLWNWFNI. [Back1993] • 5023A: Called 5023 – Langedijk also has an MAb called 5023B – strong cross-reactive neutralizing MAb. [D'Souza1991] • 5023A: Generation and Fine mapping of murine MAbs. [Langedijk1991]					
529	110.6	gp160 (311–318)	gp120 (BRU)	RGPGRAFV	L (weak)	Vaccine	mouse (IgG1λ)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1 **Ab type** V3 **References** Langedijk1992, Pirofski1993, Thomas1988 • 110.6: Variable region sequenced – heavy chain: V J558-146b.1alpha, D closest to DSP16.2, J H3 – light chain: V lambda1, J lambda1. [Pirofski1993]					
530	polyclonal	gp160 (311–318)	gp120 (MN)	IGPGRAFY	L	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* B. abortus complex *Strain:* B clade MN, B clade SF2 *HIV component:* gp120 **Ab type** V3 **References** Golding1995 • Ab is evoked even in mice depleted of CD4+ cells.					
531	10/36e	gp160 (311–321)	gp120 (311–321 HXB10)	RGPGRAFVTIG	L (HXB10)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V3 **References** Peet1998, McKeating1993b, McKeating1992a • 10/36e: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 10/36e binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998] • 10/36e: Binding to virion gp120 enhanced by sCD4. [McKeating1992a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
532	10/54 (10/54ow/6i/6i)	gp160 (311–321)	gp120 (311–321 HXB10)	RGPGRAFVTIG	L (HXB10)	Vaccine	rat (IgG1)

Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120
Ab type V3
References Peet1998, McKeating1993b, McKeating1993a, McKeating1992a

- 10/54: Called 10/54ow/6i/6i: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 10/54 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]
- 10/54: Studied in the context of a neutralization escape mutant. [McKeating1993a]
- 10/54: Binding to virion gp120 enhanced by sCD4. [McKeating1992a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
533	11/85b (11/85b/14I/14I)	gp160 (311–321)	gp120 (311–321 HXB10)	RGPGRAFVTIG	L (HXB2)	Vaccine	rat (IgG2b)

Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120
Ab type V3
References McKeating1993b, McKeating1992a

- 11/85b: Binding to virion gp120 enhanced by sCD4. [McKeating1992a]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
534	polyclonal	gp160 (311–322)	gp120 (MN)	IGPGRAFYTTKN	L (MN ALA-1)	Vaccine	guinea pig

Vaccine *Vector/Type:* human rhinovirus 14 *Strain:* B clade MN *HIV component:* V3
Ab type V3
References Smith1998

- The tip of the MN V3 loop (IGPGRAFYTTKN) was inserted into cold-causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies – chimeric viruses elicited potent NAbs against ALA-1 and MN. [Smith1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
535	0.5β (0.5 beta, 0.5beta)	gp160 (311–324)	gp120 (316–330 HXB2)	RGPGRAFVTIGKIG	L (IIIB)	Vaccine	mouse (IgG1κ)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Env
Ab type V3 **Research Contact** Shuzo Matsushita or Toshio Hattori of Kumamoto University
References Kawai2003, Zvi2000, Tugarinov2000, Jagodzinski2000, Fortin2000, Tugarinov1999, Faiman1997, Wyatt1997, Zvi1997, Huang1997, Faiman1996, Jeffs1996, McDougal1996, Warrier1996, Jagodzinski1996, Zvi1995a, Zvi1995b, Broder1994, Boudet1994, Okada1994, Thali1994, Cook1994, Watkins1993, Klasse1993a, Moore1993c, diMarzo Veronese1993, Sperlagh1993, McKeating1992a, Maeda1992, Emini1992, Matsushita1992, D'Souza1991, Nara1990, Reitz1988, Skinner1988a, Skinner1988b, Matsushita1988
Keywords anti-idiotype, antibody binding site definition and exposure, antibody generation, antibody interactions, brain/CSF, complement, escape, structure, variant cross-recognition or cross-neutralization.

- 0.5beta: For Fv fragment of 0.5beta, the combined variable regions of the heavy and light chain residues, were purified. Binding of the V3 peptide epitope TRKSIRIQRGPGRAFVTIGK was studied through mutagenesis of arginines and the free energy of binding in various salt concentrations. R4A, R8A, and R11A all reduce the free energy; R8 is embedded in the peptide-Fv fragment, while R11 is more solvent exposed. [Faiman1996] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 0.5beta: 0.5beta was used as a control for gp120 expression relative to Nef expression soon after infection of cultures. The goal of this study was to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Human heavy chain, mouse light chain anti-Nef IgM were obtained. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. [Kawai2003] (**complement**)
- 0.5beta: NIH AIDS Research and Reference Reagent Program: 1591.
- 0.5beta: UK Medical Research Council AIDS reagent: ARP3025.
- 0.5beta: NMR and mutation cycles were employed to generate a model of the peptide-antibody complex, showing aa residues that interact or do not contribute to the binding of MAb 0.5beta Fv with the peptide – F96(L) of 0.5beta binds to Pro13, H52(H) interacts with Ile7, Ile9, Gln10, and D56(H) interacts with Arg11 of the V3 loop peptide – RGPG retains hairpin conformation binds in the center of a groove. [Zvi2000] (**structure**)
- 0.5beta: 14/18 residues of peptide P1053, RKSIRIQRGPGRAFVTIG, were shown to be involved in the Ab recognition site using NMR – QRGPGR forms a beta-hairpin turn at the center of the binding pocket. [Tugarinov2000] (**antibody binding site definition and exposure**)
- 0.5beta: MAbs 0.5beta and G3-42 were used to study synthesis of oligomeric and monomeric forms of Env – inhibition of glycosylation by tunicamycin results in reduction of oligomeric gp120 at the cell surface and of monomer in the cytoplasm – neither MAb recognized non-glycosylated Env precursor. [Jagodzinski2000]
- 0.5beta: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab. [Fortin2000] (**antibody interactions**)
- 0.5beta: NMR structure reveals that Ab bound IIIB-V3 peptide adopts an unexpected type VI cis proline beta-turn. [Tugarinov1999] (**structure**)
- 0.5beta: The Fv fragment was purified and the temperature dependence and effect of mutations was studied. [Faiman1997]
- 0.5beta: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997] (**antibody binding site definition and exposure**)
- 0.5beta: The structure of a 17 amino acid V3 peptide bound to the Fab was studied using NMR. [Zvi1997] (**structure**)
- 0.5beta: Relative to the native peptide, an O-linked alpha-galactosamine modified V3 peptide enhanced binding to 0.5 beta, while an N-linked beta-glucosamine modified peptide showed reduced binding. [Huang1997] (**antibody binding site definition and exposure**)
- 0.5beta: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. [Jeffs1996] (**antibody binding site definition and exposure**)
- 0.5beta: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. [Warrier1996] (**antibody interactions**)
- 0.5beta: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits 0.5beta binding – 0.5beta epitope described as GPGRAFVTIG. [Jagodzinski1996]
- 0.5beta: NMR of 0.5beta bound NNTRKSIRIQRGPGRAFVTIGKIG suggests that the bound amino acids are in the region SIRIQRGPGRAFVT. [Zvi1995a] (**antibody binding site definition and exposure**)
- 0.5beta: The interactions of the peptide RKSIRIQRGPGRAFVT 0.5beta were studied by NMR, and hydrophobic interactions between the two Is and the V form the base of a 12 amino acid loop with GPGR at the apex. [Zvi1995b] (**antibody binding site definition and exposure**)
- 0.5beta: Type-specific neutralization of IIIB – does not neutralize SF2. [Broder1994] (**variant cross-recognition or cross-neutralization**)
- 0.5beta: Binding domain aa 310-319: RGPGRAFVTIGKIG – mutations in the V3 loop from basic residues can destroy virus infectivity and syncytium formation: R306T, R309T and R313G can also reduce binding of V3 MAbs with two different binding sites: 9284 and 0.5beta. [Okada1994] (**antibody binding site definition and exposure**)
- 0.5beta: gp41 mutation that confers resistance to neutralization by anti-CD4 binding site antibodies does not reduce neutralizing efficiency of this V3 region MAb. [Thali1994]
- 0.5beta: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – this MAb can inhibit gp120 binding to GalCer *in vitro*. [Cook1994] (**brain/CSF**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 0.5beta: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – of the MAbs tested , 0.5beta neutralization was the most profoundly affected by this mutation. [Watkins1993] (**escape**)
- 0.5beta: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to some antiserum and conformationally sensitive neutralizing MAbs – neutralization efficiency of 0.5beta is not affected. [Klasse1993a, Reitz1988] (**antibody binding site definition and exposure**)
- 0.5beta: Binding to native gp120 100-300 fold greater than to denatured. [Moore1993c] (**antibody binding site definition and exposure**)
- 0.5beta: Neutralization of virus carrying an A to T substitution (contrast with MAb M77) [diMarzo Veronese1993]
- 0.5beta: Monoclonal anti-idiotype antibodies that mimic the 0.5beta epitope were generated. [Sperlagh1993] (**anti-idiotype**)
- 0.5beta: sCD4 causes loss of IIIB type-specificity, allowing binding and neutralization of MN, in contrast to MAb mu5.5. [Maeda1992]
- 0.5beta: Chimeric mouse-human MAb Cbeta1 was constructed by combining the human Cgamma1 and Ckappa constant regions with the 0.5beta murine MAb – ADCC and neutralizing activity. [Matsushita1992] (**complement**)
- 0.5beta: Potent neutralizing activity. [D'Souza1991]
- 0.5beta: Emergence of virus resistant to MAb 0.5beta and autologous sera neutralization in IIIB infected chimps. [Nara1990] (**escape**)
- 0.5beta: Type-specific neutralization of IIIB – does not neutralize MN or RF. [Matsushita1988, Skinner1988b] (**antibody generation**)

536 Cβ1, 0.5β gp160 (311–324) gp120 (316–330 HXB2) RGPGRAFVTIGKIG L Vaccine humanized mouse (IgG1)

Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Env
Ab type V3
References Ferrantelli2002, Kimura2002, Matsushita1992, Emini1992

- Cbeta1: Review of passive immunoprophylaxis with human NAbs that also includes this chimeric mouse-human MAb, noting it protected 2/2 Chimpanzees from HIV-1 IIIB infection in the Emini *et al.*study published in 1992. [Ferrantelli2002]
- Cbeta1: Defines epitope as IQRGPGRA – strong neutralizing activity against NL4-3 (X4 virus) and none against JRFL (R5 virus) – used as a control in a study of NAb activity in patients undergoing HAART. [Kimura2002]
- Cbeta1: Chimeric mouse-human MAb Cbeta1 was constructed by combining the human Cgamma1 and Ckappa constant regions with the 0.5beta murine MAb – ADCC and neutralizing activity. [Matsushita1992]
- Cbeta1: passive transfer to chimpanzees confers protection against challenge with homologous cell-free virus – mouse 0.5beta human IgG1 chimera. [Emini1992]

537 NM-01 (hNM01, hNM-01) gp160 (312–315) gp120 (MN) GPGR L Vaccine mouse (IgG)

Vaccine *Vector/Type:* human rhinovirus 14 *Strain:* B clade MN *HIV component:* V3
Ab type V3 **Research Contact** M. Terada, Jason Grabely
References Zwick2003, Nakamura2000, Smith1998, Yoshida1997, Ohno1991
Keywords antibody interactions, complement, immunotherapy.

- NM-01: Called hNM01. scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. The humanized version of this MAb was one of the V3 MAbs used. [Zwick2003] (**antibody interactions**)
- NM-01: Called hNM01. The CDR region of the murine MAb NM-01 was put into a human IgG frame. The epitope recognition was preserved, but the neutralizing potency of the humanized form was enhanced. It could activate complement. [Nakamura2000] (**complement**, **immunotherapy**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• NM-01: The tip of the MN V3 loop was inserted into cold-causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and NM-01 was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. [Smith1998] • NM-01: Resistance mutation selected by propagation of molecular cloned isolate in the presence of NM-01. [Yoshida1997]					
538	1026	gp160 (312–317)	gp120 (MN)	GPGRAF	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp120 **Ab type** V3 **References** Bou-Habib1994, Nakamura1993 • 1026: Greater affinity for T cell-tropic strain T-CSF, derived from JR-CSF, than to the primary isolate JR-CSF. [Bou-Habib1994] • 1026: Bound diverse strains, neutralizing activity against MN, close to GPGRAF. [Nakamura1993]					
539	1034	gp160 (312–317)	gp120 (MN)	GPGRAF	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp120 **Ab type** V3 **References** Berman1997, Bou-Habib1994 • 1034: Binds to 5/7 isolates from breakthrough cases from a MN gp120 vaccine trial. [Berman1997] • 1034: Greater affinity for T cell tropic T-CSF, derived from JR-CSF, than to the primary isolate JR-CSF, close to GPGRAF. [Bou-Habib1994]					
540	59.1 (R/V3-59.1)	gp160 (312–317)	gp120 (308–313 MN)	GPGRAF	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* V3 **Ab type** V3 **Research Contact** Mary White-Scharf and A. Profy, Repligen Corporation **References** York2001, Stanfield1999, Smith1998, Ghiara1997, Seligman1996, D'Souza1994, Bou-Habib1994, Ghiara1993, Potts1993, White-Scharf1993, D'Souza1991 • 59.1: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001] • 59.1: The crystal structure of V3 loop peptides bound to Fabs was obtained – conformational changes in the tip of the V3 loop (GPGR) were observed when different MAbs were bound. [Stanfield1999] • 59.1: The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 59.1 was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. [Smith1998] • 59.1: A conformationally restricted analog of the tip of the V3 loop was constructed and bound with Fab 59.1 – crystal structure shows interactions between 59.1 and an MN peptide and 59.1 and the modified peptide are similar, but NMR studies reveal that the modified peptide is more ordered in solution, retaining the Fab bound form. [Ghiara1997] • 59.1: Competition ELISAs with serial deletions produced longer estimate of epitope length than x-ray crystallography or Alanine substitution, RIHIGP-GRAFYTT, suggesting significance of non-contact residues. [Seligman1996] • 59.1: Multi-lab study for antibody characterization and assay comparison – neutralizes MN and IIIB. [D'Souza1994] • 59.1: Greater affinity for T-cell tropic strain T-CSF than the primary isolate JR-CSF, from which T-CSF was derived. [Bou-Habib1994] • 59.1: Crystal structure of a 24 amino acid peptide from the V3 loop bound to 59.1 Fab fragment – contact residues IGPGRAF. [Ghiara1993] • 59.1: Synergistic neutralization of MN when combined with sCD4 or the CD4BS MAb F105. [Potts1993] • 59.1: Epitope defined by peptide reactivity and binding affinity with amino acid substitutions – GPGRAF. [White-Scharf1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 59.1: Called R/V3-59.1 – potent neutralizing MAb. [D'Souza1991]					
541	polyclonal	gp160 (312–317)	gp120 (316–321)	GPGRAF		Vaccine	rabbit
		Vaccine *Vector/Type:* protein, polyepitope *HIV component:* gp160 *Adjuvant:* BSA **Ab type** V3 **References** Lu2000b, Lu2000c • High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to ELDKWA, weak to GPGRAF – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here. [Lu2000c, Lu2000b]					
542	10E3	gp160 (312–318)	gp120 (317–323 IIIB)	GPGRAFY		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade IIIB *HIV component:* V3 **Ab type** V3 **References** Li2002, Tian2001 **Keywords** vaccine antigen design. • 10E3: A polyepitope vaccine was designed based on a recombinant GST fusion protein containing three repeats of the 2F5 core epitope ELDKWA combined with the V3 region peptide GPGRAFY. Abs raised in mice could recognize the peptides, sgp41, and CHO-WT cells that expressed HIV-1 Env on their surface. [Li2002] (**vaccine antigen design**) • 10E3: Peptides GPGRAFY and ELDKWAG were conjugated to KLH and used to raise mouse monoclonal Ab – MAb hybridomas were generated with defined specificity – 10E3 binds to the peptide GPGRAFY and to rgp160. [Tian2001]					
543	polyclonal	gp160 (312–318)	gp120 (317–323)	GPGRAFY		Vaccine	rabbit, mouse
		Vaccine *Vector/Type:* peptide *HIV component:* V3 *Adjuvant:* BSA **Ab type** V3 **References** Yu2000 • High levels of epitope-specific Abs were induced by the peptide-BSA conjugates C-(GPGRAF)_4-BSA or C-(TRPNNNTRKSIRIQRGPGRAFYTIG KI)-BSA but not by rgp160 vaccine. [Yu2000]					
544	N11-20 (110-H)	gp160 (312–320)	gp120 (317–325)	GPGRAFVTI	L (LAI)		mouse (IgG1κ)
		Ab type V3 **Research Contact** J. C. Mazie, Hybridolab, Institut Pasteur **References** Valenzuela1998 • N11-20: Neutralization of LAI in CEM cells by anti-V3 MAbs 110.4 and N11-20 is through inhibition of virus binding to the cell. [Valenzuela1998]					
545	5025A (5025)	gp160 (313–317)	gp120 (313–317 BH10)	pgRAF	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* B clade BH10 *HIV component:* V3 **Ab type** V3 **Research Contact** Paul Durda, Du Pont de Nemours and Co **References** D'Souza1991, Langedijk1991 • 5025: Called 5025 – strain specific weakly neutralizing. [D'Souza1991] • 5025A: Generation and fine mapping of murine MAbs. [Langedijk1991]					
546	N70-1.9b	gp160 (313–318)	gp120 (316–322)	PGRAFY	L	HIV-1 infection	human (IgG1)
		Ab type V3 **References** Gorny2004, Scott1990, Robinson1990a **Keywords** ADCC, review, variant cross-recognition or cross-neutralization.					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• N70-1.9b: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, while many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • N70-1.9b: Type specific neutralization, ADCC directed against MN infected cells. [Scott1990] (**ADCC**, **variant cross-recognition or cross-neutralization**) • N70-1.9b: Type specificity. [Robinson1990a] (**variant cross-recognition or cross-neutralization**)					
547	902	gp160 (313–324)	gp120 (IIIB)	PGRAFVTIGKIG	L	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp160 **Ab type** V3 **Research Contact** Bruce Chesebro, Rocky Mountain National Laboratory, Montana **References** Sakaida1997, Earl1994, Broder1994, Laman1993, Chesebro1988 • 902: NIH AIDS Research and Reference Reagent Program: 522. • 902: V3-BH10 peptide with loop-structure inhibits IL-2 induced T-cell proliferation, thought to be due to altering intracellular signaling, and MAb 908 can block the peptide inhibition. [Sakaida1997] • 902: Used as a control in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] • 902: Epitope may be partially masked or altered in the oligomeric molecule. [Broder1994] • 902: Strain specific neutralization of HIV. [Chesebro1988]					
548	694/98-D (694/98, 694.8, 694/98D)	gp160 (314–317)	gp120 (IIIB)	GRAF	L	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Drs. S. Zolla-Pazner and M. Gorny, NYU Med Center NY, NY **References** Gorny2004, Zwick2003, Zhang2002, He2002, Edwards2002, Park2000, Nyambi2000, Altmeyer1999, Zolla-Pazner1999b, Zolla-Pazner1999a, Schonning1998, Nyambi1998, Andrus1998, Li1998, Smith1998, Zolla-Pazner1997, Li1997, Forthal1995, Zolla-Pazner1995a, VanCott1995, Cook1994, VanCott1994, Laal1994, Gorny1994, Spear1993, Cavacini1993a, Gorny1993, Gorny1992, Gorny1991, Skinner1988b **Keywords** antibody interactions, review, variant cross-recognition or cross-neutralization. • 694/98D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • 694/98D: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. [Zwick2003] (**antibody interactions**) • 694/98-D: Called 694 – Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002] • 694/98-D: Called 694/98D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] • 694/98-D: Called 694/98D – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000] • 694/98-D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 694/98-D showed intermediate reactivity. [Nyambi2000]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 694/98-D: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not linear V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. [Altmeyer1999] • 694/98-D: MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. [Zolla-Pazner1999b] • 694/98-D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] • 694/98-D: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, anti-V3 MAbs were found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan more efficiently than HIV-BRU. [Schonning1998] • 694/98-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 694/98-D bound only to B and D clade virions and had limited cross reactivity. [Nyambi1998] • 694/98-D: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998] • 694/98-D: The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 694/98-D was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. [Smith1998] • 694/98-D: Used to study pre- and post-exposure prophylaxis Hu-PBL-SCID mice infected by an intraperitoneal injection of HIV-1 LAI – MAb half-life in plasma in mice is 9 days – 2 hours post-694/98-D mice were challenged with LAI, and at an Ab concentration of 1.32 mg/Kg, 50% of the mice were infected – one of the infected mice carried the resistant form GRTF rather than GRAF (critical amino acids for binding are GRA) – post-exposure prophylaxis was effective if delivered 15 min post-exposure, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection. [Andrus1998] • 694/98-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – 694/98-D has synergistic response with MAbs F105, 15e, b12, 2F5, 17b, 2G12, and 48d, and with HIVIG. [Li1997] • 694/98-D: ADCC activity, and no viral enhancing activity. [Forthal1995] • 694/98-D: Serotyping study using flow-cytometry – bound GRAX bearing virus in 10/11 cases – somewhat conformation dependent. [Zolla-Pazner1995a] • 694/98-D: Human HIV-1 infected sera and MAb 694/98 have high reactivity to MN and RF infected H9 cells, but Genentech rec gp120 IIIB vaccine recipients do not. [VanCott1995] • 694/98-D: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – V3 MAbs can inhibit gp120 binding to GalCer *in vitro* – binding of GalCer to gp120 inhibited but did not completely block MAb binding. [Cook1994] • 694/98-D: GRVY did not alter peptide binding – GRVI and GQAW enhanced dissociation – GQVF and GQAL did not bind. [VanCott1994] • 694/98-D: Potent neutralization of IIIB – no neutralization synergy in combination with CD4 binding domain MAbs. [Laal1994] • 694/98-D: 50% neutralization of HIV-IIIB at a concentration of 0.15mug/ml. [Gorny1994] • 694/98-D: Called 694-D – complement mediated virolysis of IIIB, but not in the presence of sCD4. [Spear1993] • 694/98-D: Neutralizes MN and IIIB (GRAF) – binds SF2 (GRAF) – binding reactivity: MN, IIIB, SF2, NY5, RF, CDC4, WM52. [Gorny1993] • 694/98-D: Type-specific lab isolate neutralization was observed – binds with 1-3 fold greater affinity to gp120 than to peptides. [Gorny1992] • 694/98-D: This MAb was first described here. [Skinner1988b]					
549	MO101/V3,C4	gp160 (314–323 + 494–503) **Ab type** V3-C4 **References** Ohlin1992	gp120 (314–323)	GRAFVTIGKI+LGVAPTKAKR		in vitro stimulation or selectio	human (IgM)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• MO101: Generated in response to IIIB Env 286-467 upon *in vitro* stimulation of uninfected-donor lymphocytes – reacts with peptides 314-323 + 494-503 from the V3 and C4 regions. [Ohlin1992]					
550	MO101/V3,C4	gp160 (314–323 + 494–503) **Ab type** V3-C5 **References** Ohlin1992	gp120 (314–323)	GRAFVTIGKI+LGVAPTKAKR		in vitro stimulation or selectio	human (IgM)
		• MO101: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286-467 – reacts with peptides from the V3 and C4 regions, positions 314-323 + 494-503, peptides GRAFVTIGKI + LGVAPTKAKR. [Ohlin1992]					
551	MO101/V3,C4	gp160 (314–323 + 494–503) **Ab type** V3-C5 **References** Ohlin1992	gp120 (494–503)	GRAFVTIGKI+LGVAPTKAKR		in vitro stimulation or selectio	human (IgM)
		• MO101: Generated through *in vitro* stimulation of uninfected-donor lymphocytes with pB1 containing IIIB Env 286-467 – reacts with peptides from the V3 and C4 regions, positions 314-323 + 494-503, peptides GRAFVTIGKI + LGVAPTKAKR. [Ohlin1992]					
552	9205 (NEA-9205 NEA9205)	gp160 (315–317) **Vaccine** *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 **Ab type** V3 **Research Contact** NEN, Boston MA, commercial **References** Gram2002, Schonning1999, Schonning1998, Fontenot1995, VanCott1994, Allaway1993, Trujillo1993, Durda1990	gp120 (IIIB)	RAF(corereactivity)	L	Vaccine	mouse (IgG1)
		• 9205: Called NEA9205 – gp120 capture ELISAs with MAbs D7324 (anti-C-term) or 9205 (anti-V3) were compared in a study of orientation of glycosylation sites – CD4 binding could only inhibit deglycosylation when gp120 was bound to the plate by D7324, not by 9205, while Abs from HIV-1 infected people inhibited deglycosylation most effectively when gp120 was caught by 9205. [Gram2002] • 9205: Called NEA-9205 – the stoichiometry of MAb neutralization was tested and the data indicated that binding for neutralization was was incremental not all or none, i.e., each envelope oligomer binds a single MAb and each Env oligomer bound reduces the chances of infection – 9205 binds only to Env with a glycosylation site mutation in the V3 loop, A308T. [Schonning1999] • 9205: Called NEA-9205 – The N306 glycan of the V3 loop makes the tip of the V3 loop inaccessible to this MAb in oligomeric Env, loss of this glycan enhances neutralization sensitivity. [Schonning1998] • 9205: Neutralizes IIIB but not MN – significantly slower dissociation constant for IIIB than MN. [VanCott1994] • 9205: Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion. [Allaway1993] • 9205: Called NEA-9205, epitope RIQRGPGRAFVTIGK – reacts with three human brain proteins of 35, 55, 110 kd molecular weight – similar to 9284 – RAF is the core reactivity. [Trujillo1993] • 9205: Also see MAb called 5023A.					
553	110.I	gp160 (316–322) **Vaccine** *Vector/Type:* protein *HIV component:* gp120 **Ab type** V3 **Research Contact** F. Traincard, Pasteur Institute, France **References** Parren1998a, Wyatt1997, Poignard1996a, Moore1996, Sattentau1995b, Moore1994c, Moore1993c	gp120 (316–322)	AFVTIGK	L	Vaccine	mouse
		• 110.I: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] • 110.I: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997] • 110.I: Epitope suggested to be RAFVTIGK – V3 MAbs 9284, BAT123, 110.5, and 110.I could each significantly increase gp120 dissociation from virus, mimicking sCD4, and expose the gp41 epitope for MAb 50-69, in contrast to anti-V2 MAbs. [Poignard1996a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 110.I: Reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and enhances binding of some anti-V2 MAbs – binding enhanced by some anti-CD4 binding site MAbs. [Moore1996] • 110.I: Binds equally well to monomer and oligomer, rapid association and potent neutralization of lab strains. [Sattentau1995b] • 110.I: Binds to carboxy-terminal side of the V3 loop – inhibits binding of C4 region MAb G3-299. [Moore1993c]					
554	anti-HIV-2 polyclonal	gp160 (317–320 + 333–225)	gp120 (315–318 SBL6669 HIV-2)	FHSQ+WCR		Vaccine	guinea pig (IgG)
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 SBL6669-ISY *HIV component:* V3 **Ab type** V3 **References** Morner1999 • Neutralizing Abs against HIV-2 V3 are produced when peptides spanning two non-contiguous parts of the V3 loop are used for vaccination including amino acids 315-318 near the tip (FHSQ) and 329-331 (WCR) at the C-term Cys. [Morner1999]					
555	IIIB-V3-01	gp160 (320–328)	gp120 (IIIB)	IGKIGNMRQ	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* V3 **Ab type** V3 **Research Contact** Jon Laman **References** Laman1993 • IIIB-V3-01: NIH AIDS Research and Reference Reagent Program: 1726. • IIIB-V3-01: UK Medical Research Council AIDS reagent: ARP3046. • IIIB-V3-01: Specific for carboxy-terminal flank of the IIIB V3 loop – epitope is hidden native gp120, exposed on denaturation. [Laman1993]					
556	D/6D1	gp160 (346–377)	gp120 (351–382 LAI)	ASKLREQFGNNKTIIFKQSSGGDPE-IVTHSFN	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp120 **Ab type** V4 **References** Bristow1994 • D/6D1: V4 MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp120 and rgp160. [Bristow1994]					
557	4D7/4	gp160 (360–380)	gp120 (361–380 LAI)	IFKQSSGGDPEIVTHSFNCGG		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** V4 **Research Contact** S. Ranjbar, NIBSC, UK **References** Moore1994c • 4D7/4: UK Medical Research Council AIDS reagent: ARP3051. • 4D7/4: C3 region – the relative affinity for denatured/native gp120 is >10. [Moore1994c]					
558	36.1(ARP 329)	gp160 (361–381)	gp120 (362–381 LAI)	FKQSSGGDPEIVTHSFNCGGE		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** V4 **References** Moore1994c, Thiriart1989 • 36.1: UK Medical Research Council AIDS reagent: ARP329. • 36.1: The relative affinity for denatured/native gp120 is >30 – mutations 380 G/F, 381 E/P impair binding. [Moore1994c]					
559	C12	gp160 (361–381)	gp120 (362–381 LAI)	FKQSSGGDPEIVTHSFNCGGE		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V4 **Research Contact** George Lewis **References** Moore1994d, Abacioglu1994, Moore1994c, Moore1993a • C12: C3 region – epitope boundaries mapped by peptide scanning, core FNCGG. [Abacioglu1994] • C12: The relative affinity for denatured/native gp120 is >30 – mutations 380 G/F, 381 E/P, and 384 Y/E impair binding – also binds GEFFYCNSTQLFNS, gp120(380-393 LAI) [Moore1994c] • C12: Bound preferentially to denatured IIIB gp120. [Moore1993a]					
560	110.D	gp160 (380–393)	gp120 (380–393 LAI)	GEFFYCNSTQLFNS	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** C3 **Research Contact** F. Traincard, Pasteur Institute, France **References** Valenzuela1998, Moore1994c • 110.D: The relative affinity for denatured/native gp120 is >50. [Moore1994c]					
561	B32	gp160 (380–393)	gp120 (380–393 LAI)	GEFFYCNSTQLFNS		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** C3 **References** Abacioglu1994, Moore1994c • B32: C3 region – epitope boundaries mapped by peptide scanning – FFY(core) [Abacioglu1994] • B32: The relative affinity for denatured/native gp120 is >100 – mutations 380 G/F, 381 G/P, 382 F/L, 384 Y/E, and 386 N/R impair binding. [Moore1994c]					
562	polyclonal (VEI4)	gp160 (391–413)	Env	FNSTWFNSTWSTEGSNNTEGSDT		HIV-1 infection	human
		Ab type V4 **References** Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. [Carlos1999]					
563	B15	gp160 (395–400)	gp120 (395–400 BH10)	WFNSTW		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** V4 **Research Contact** George Lewis **References** Abacioglu1994, Moore1993c, Moore1993a • B15: V4 region – epitope boundaries mapped by peptide scanning. [Abacioglu1994] • B15: Binds native BH10 gp120 with 5 fold less affinity than denatured – does not bind native or denatured MN gp120. [Moore1993c] • B15: Bound preferentially to denatured IIIB gp120. [Moore1993a]					
564	B34	gp160 (395–400)	gp120 (395–400 BH10)	WFNSTW		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** V4 **References** Abacioglu1994 • B34: V4 region – epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
565	7F11	gp160 (397–439)	gp120 (IIIB)			Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp120 **References** Nilsen1996, Lasky1987					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 7F11: There is another MAb with this name that binds to integrase. [Nilsen1996]					
566	E51	gp160 (420–423)	gp120 (420–423 HXB2)	IKQI	P		human
		Ab type CD4i **Research Contact** Joseph Sodroski, joseph_sodroski@dfci.harvard.edu **References** Xiang2003 **Keywords** antibody binding site definition and exposure, antibody generation, co-receptor, inter-clade comparisons, variant cross-recognition or cross-neutralization. • E51: E51 recognizes a highly conserved epitope localized in the basic β19-strand (gp120 aa420-423), a region involved in CCR5 binding. The MAb was isolated from a EBV transformed B-cell line established from an HIV+ individual undergoing early STI. Fab fragments were also produced. E51, like CD4i MAb 17b, blocks CCR5 binding to sCD4-bound gp120. The presence sCD4 induces a conformational change in gp120, which enhances ligand recognition. The substitutions E381R, F383S, R419D I420R, K421D, Q422L, I423S, and Y435S (HXB2 numbering) all severely reduce 17b and E51 binding. All but I423S also diminish CCR5 binding by more than 50%. The mutation F383S also inhibits sCD4 binding and CD4BS MAb F105 binding, and K421D inhibits F105 binding, but not sCD4. E51 has more cross-neutralizing potency than other prototype CD4i MAbs (17b) for B and C clade isolates. E51 and 17b both neutralized HIV-1 clade B strains HXBc2 and ADA, while JR-FL and 89.6 were only neutralized by E51, not 17b. Clade C strains MCGP1.3 and SA32 were both inhibited by 17b and E51, but E51 was more potent against SA32. [Xiang2003] (**antibody binding site definition and exposure**, **antibody generation**, **co-receptor**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)			
567	5C2E5	gp160 (422–431)	gp120 (406–415 IIIB)	QFINMWQEVK		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp120 **Ab type** C4 **Research Contact** T. Gregory and R. Ward, Genentech, San Francisco **References** Cordell1991, Lasky1987 • 5C2E5: Cross-competition with MAbs 5C2E5, ICR38.8f and ICR38.1a. [Cordell1991] • 5C2E5: Blocks the gp120-CD4 interaction. [Lasky1987]						
568	G3-211	gp160 (423–437)	gp120 (423–437 IIIB)	IINMWQKVGKAMYAP	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C4 **References** Sun1989 • G3-211, 42, 299, 508, 519, 536, 537: Cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – different neutralization efficiencies. [Sun1989]					
569	G3-537	gp160 (423–437)	gp120 (423–437 IIIB)	IINMWQKVGKAMYAP	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C4 **References** Zwick2003, McKeating1992b, Ho1991b, Sun1989 **Keywords** antibody interactions. • G3-537: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4 MAbs used. [Zwick2003] (**antibody interactions**) • G3-537: Weakly neutralizing – binds to a linear binding domain of gp120, NMWQEVGKAMYAPPISG. [McKeating1992b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G3-537, 211, 299, 508, 519, 536, 42: Cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – different neutralization efficiencies. [Sun1989]					
570	polyclonal	gp160 (425–436)	gp120	NMWQEVGKAMYA	L	Vaccine	mouse (IgA)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *Adjuvant:* Cholera toxin (CT) **Ab type** CD4BS **References** Bukawa1995 • Polyclonal secretory IgA antibody raised by mucosal immunization is able to neutralize IIIB, SF2, and MN – HIV-1 neutralization may be due to the V3, CD4 or HPG30 component of the multicomponent peptide immunogen. [Bukawa1995]					
571	1795	gp160 (425–441)	gp120 (425–441 IIIB)	NMWQEVGKAMYAPPISG	L	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** CD4BS **References** McKeating1992b • 1795: CD4 binding site – weakly neutralizing – binding inhibited by WQEVGKAMYA, GKAM may be involved. [McKeating1992b]					
572	ICR38.1a (38.1a, 388/389, ARP388/389)	gp160 (429–438)	gp120 (427–436 BRU)	EVGKAMYAPP	L	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** C3, C4 **References** Vella2002, Kropelin1998, Peet1998, Jeffs1996, Moore1993c, McKeating1993a, McKeating1993b, McKeating1992c, McKeating1992a, McKeating1992b, Cordell1991 • ICR38.1a: UK Medical Research Council AIDS reagent: ARP388/ARP389. • ICR38.1a: Called ARP388/ARP389: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs – lists epitope as WQEVGKAMYA. [Vella2002] • ICR38.1a: Called 388/389 – anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998] • ICR38.1a: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR38.1a was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998] • ICR38.1a: Called 38.1a – 10 to 20 fold increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. [Jeffs1996] • ICR38.1a: Unreactive with solid-phase decapeptide, competed in solution phase assay – ICR 38.1a and ICR 38.8f were initially reported to be independent MAbs, but are actually subclones of the same MAb. [Moore1993c] • ICR38.1a: Studied in the context of a neutralization escape mutant. [McKeating1993a] • ICR38.1a: Unable to exert a synergistic effect in combination with V3 directed MAbs, in contrast to MAb 39.13g, that binds to a conformational epitope involved in CD4 binding. [McKeating1992a] • ICR38.1a: Weakly neutralizing – binds linear determinant in the CD4 binding domain – cross-competition with MAbs G3-536, 5C2E5, and ICR38.8f. [Cordell1991, McKeating1992b]					
573	G3-299	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* virus derived protein *HIV component:* gp120 **Ab type** C4 **Research Contact** M. Fung and Tanox Biosystems Inc and David Ho, ADARC, NY **References** Zwick2003, Kwong2002, Parren1998a, Wyatt1997, Ditzel1997, Binley1997a, Poignard1996a, Moore1996, Sattentau1995b, Moore1993c, Sun1989					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

Keywords antibody binding site definition and exposure, antibody interactions.

- G3-299: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4-V3 MAbs used. [Zwick2003] (**antibody interactions**)
- G3-299: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the G3-299 epitope as V3 loop/outer domain. [Kwong2002] (**antibody binding site definition and exposure**)
- G3-299: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- G3-299: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997]
- G3-299: Epitope described as KQIINMWQKVGKAMYAPPIS – binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69. [Poignard1996a]
- G3-299: Discontinuous V3-C4 epitope, binding enhanced by a few anti-C1, anti-CD4 binding site, and V2 MAbs – binding reciprocally inhibited by anti-V3 MAbs – G3-229 enhances the binding of some anti-V2 MAbs. [Moore1996]
- G3-299: Binds with higher affinity to monomer than to oligomer, slow association rate, although faster than other C4 MAbs tested, with more potent neutralization of lab strain. [Sattentau1995b]
- G3-299: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – G3-42, G3-299 lower affinity than G3-508, G3-519, and G3-536 – bound native gp120, not denatured – poor peptide binding, epitope spans V3-C4 regions – 433A/L, 435Y/H and 430V/S substitutions impaired binding, V3 loop cleavage or insertion abolished binding. [Moore1993c]
- G3-299: Best neutralization of IIIB in panel of 7 MAbs that bind overlapping epitope. [Sun1989]

574	G3-42 (G3 42)	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type C4 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY
References Zwick2003, Jagodzinski2000, Binley1999, Binley1997a, Trkola1996a, Poignard1996a, Moore1996, Jagodzinski1996, Sattentau1995b, Thali1993, Moore1993c, Sun1989
Keywords antibody interactions.

- G3-42: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4-V3 MAbs used. [Zwick2003] (**antibody interactions**)

B Cell

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 0.5beta: MAbs 0.5beta and G3-42 were used to study synthesis of oligomeric and monomeric forms of Env – inhibition of glycosylation by tunicamycin results in reduction of oligomeric gp120 at the cell surface and of monomer in the cytoplasm – neither MAb recognized non-glycosylated Env precursor. [Jagodzinski2000]
- G3-42: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999]
- G3-42: Called G3 42 – Does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study – described as V3-C4 discontinuous epitope. [Trkola1996a]
- G3-42: Epitope described as KQIINMWQKVGKAMYAPPIS – binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69. [Poignard1996a]
- G3-42: Inhibits binding of many anti-V3, -CD4 binding site, and -C4 region MAbs – enhances binding of some anti-V2 region MAbs. [Moore1996]
- G3-42: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS potently inhibits G3-42 binding – G3-42 epitope described as KVGKAMYAPP. [Jagodzinski1996]
- G3-42: Binds with higher affinity to monomer than to oligomer, slow association rate. [Sattentau1995b]
- G3-42: Inhibits binding of CD4 inducible MAb 48d. [Thali1993]
- G3-42: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – G3-42, G3-299 have lower affinity than G3-508, G3-519, and G3-536 – bound native gp120, not denatured – poor peptide binding, epitope spans V3-C4 regions – 433A/L, 435Y/H and 430V/S substitutions impaired binding, V3 loop insertion abolished binding. [Moore1993c]
- G3-42: Neutralization of IIIB but not RF. [Sun1989]

575	G3-508 (G3 508)	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type C4 **Research Contact** M. Fung and Tanox Biosystems Inc and David Ho, ADARC, NY
References Binley1998, Parren1998a, Binley1997a, Trkola1996a, Poignard1996a, Moore1996, Sattentau1995b, Moore1993c, Thali1993, Sun1989

- G3-508: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998]
- G3-508: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- G3-508: Called G3 508 – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a]
- G3-508: Binding resulted in slight gp120 dissociation from virus and exposure of the gp41 epitope for MAb 50-69. [Poignard1996a]
- G3-508: Inhibits binding of some V3, C4 and CD4 binding site MAbs, enhances binding of V2 region MAbs. [Moore1996]
- G3-508: Binds with higher affinity to monomer than to oligomer, slow association rate. [Sattentau1995b]
- G3-508: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 10 fold greater affinity than native – 433A/L, 435Y/H and 430V/S substitutions impaired binding. [Moore1993c]
- G3-508: Inhibits binding of CD4 inducible MAb 48d. [Thali1993]
- G3-508: Neutralization of IIIB and RF. [Sun1989]

576	G3-519	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

Ab type C4 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY
References Zwick2003, Binley1999, Parren1998a, Wyatt1997, Binley1997a, Poignard1996a, Moore1996, Sattentau1995b, D'Souza1994, Moore1993c, Moore1993a, Sun1989
Keywords antibody interactions.

- G3-519: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the C4 MAbs used. [Zwick2003] (**antibody interactions**)
- G3-519: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999]
- G3-519: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- G3-519: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997]
- G3-519: Epitope described as KVGKAMYAPP – binding resulted in slight gp120 dissociation from virus but no significant exposure of the gp41 epitope for MAb 50-69. [Poignard1996a]
- G3-519: Non-reciprocal enhanced binding in the presence of the C5 MAb 1C1 and the C1 MAb 135/9 – reciprocal enhanced binding with some V2 MAbs. Inhibited binding the presence of some C4, V3 and CD4 binding site MAbs. [Moore1996]
- G3-519: Binds with higher affinity to monomer than to oligomer, slow association rate. [Sattentau1995b]
- G3-519: Included in a multi-lab study for antibody characterization, and binding and neutralization assay comparison, also binds IIIB: IIN-MWQKVGKAMYAPP. [D'Souza1994]
- G3-519: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 5 fold greater affinity than native – 433A/L, 435Y/H, 438P/R and 430V/S substitutions impaired binding. [Moore1993c]
- G3-519: Neutralizes IIIB, is reactive with SF-2 gp120, mild inhibition of HIV-1+ sera binding to IIIB gp120. [Moore1993a]
- G3-519: Best neutralization of RF in panel of 7 MAbs that bind overlapping epitope. [Sun1989]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
577	G3-536	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120
Ab type C4 **Research Contact** Tanox Biosystems Inc and David Ho, ADARC, NY
References Parren1998a, Poignard1996a, Moore1996, Sattentau1995b, Gorny1994, Moore1993c, Moore1993a, McKeating1992b, Cordell1991, Ho1991b, Sun1989

- G3-536: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- G3-536: Epitope described as KVGKAMYAPP. [Poignard1996a]
- G3-536: Inhibits binding of some V3, C4 and CD4 binding site MAbs, enhances binding of V2 region MAbs. [Moore1996]
- G3-536: Binds with higher affinity to monomer than to oligomer, slow association rate. [Sattentau1995b]
- G3-536: Enhances binding of anti-V2 MAb 697-D. [Gorny1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G3-536: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPIS, and SF-2 and MN gp120s – bound denatured with 15 fold greater affinity than native – 433A/L, 435Y/H, 438P/R, and 430V/S substitutions impaired binding. [Moore1993c] • G3-536: Neutralizes IIIB, is reactive with SF-2 gp120, mild inhibition of HIV-1+ sera binding to IIIB gp120. [Moore1993a] • G3-536: Weakly neutralizing – binds to a linear determinant in the CD4 binding domain of gp120. [McKeating1992b] • G3-536: Cross-competition with MAbs 5C2E5, ICR38.8f and ICR38.1a. [Cordell1991] • G3-536: Weak neutralization of IIIB and RF – cross-react with diverse strains by immunofluorescence – blocks HIV binding to CD4+ cells – epitope:IINMWQKVGKAMYAP. [Sun1989]					
578	ICR38.8f	gp160 (429–438)	gp120 (429–438 BRU)	EVGKAMYAPP	L	Vaccine	rat (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** C4 **References** Moore1993c, Cordell1991 • ICR38.8f:ICR 38.1a and ICR 38.8f were initially reported to be independent MAbs, but are actually subclones of the same MAb. [Moore1993c] • ICR38.8f: Weakly neutralizing – binds linear determinant in the CD4 binding domain – cross-competition with ICR38.1a, 5C2E5, and G3-536. [Cordell1991]					
579	MO86/C3	gp160 (429–443)	gp120 (429–443)	EVGKAMYAPPISGQI		in vitro stimulation or selectio	human (IgM)
		Ab type C4 **References** Ohlin1992 • MO86: Generated in response to IIIB Env 286-467 upon *in vitro* stimulation of uninfected-donor lymphocytes. [Ohlin1992]					
580	13H8	gp160 (431–440)	gp120 (412–453)	GKAMYAPPIS	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade MN **Ab type** C4 **References** Jeffs1996, Nakamura1993, Nakamura1992 • 13H8: 3 and 4.5 fold increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120, respectively. [Jeffs1996] • 13H8: Binds V3 and C4 peptides (J. P. Moore, per. comm.) • 13H8: Bound diverse strains, neutralizing activity against MN. [Nakamura1993] • 13H8: Cross blocks 5C2 in IIIB-rsgp160 ELISA – reactive with diverse strains in rgp120 ELISA. [Nakamura1992]					
581	G45-60	gp160 (431–440)	gp120 (429–438 BRU)	GKAMYAPPIS	L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* virus derived protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** C4 **References** Jagodzinski1996, Moore1996, Gorny1994, Moore1993c, Sun1989 • G45-60: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus CRDS inhibits G45-60 binding. [Jagodzinski1996] • G45-60: Non-reciprocal enhancement of G45-60 binding by some C1 and C5 antibodies – reciprocal enhancement of some V2 region MAbs – reciprocal inhibition with many MAbs that bind to the V3, C4 and CD4 binding site regions. [Moore1996] • G45-60: Enhances binding of anti-V2 MAb 697-D. [Gorny1994] • G45-60: C4 region – binds HXB2 20mer KQIINMWQKVGKAMYAPPI, decapeptide flanking peptides also bound – bound equivalently to native and denatured gp120 – 433A/L and 435Y/H (not 430V/S) substitutions impaired binding. [Moore1993c]					
582	polyclonal	gp160 (432–451)	gp120 (42–61 LAI)	KAMYAPPISGQIRCSSNITG	no	Vaccine	mouse
		Vaccine *Vector/Type:* vaccinia *HIV component:* Env					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C4 **References** Collado2000 • Vaccinia p14 can elicit NAbs and p39 tends to be immunodominant, so these two proteins were fused to regions of HIV-1 Env – reduced glycosylation was noted when p14 or p39 was placed in the N-term region of the fusion protein – chimeric proteins shifted the Env Ab response from V3 to either a C1 or C4 domain, depending on the construct – all chimeric Env proteins: 14kEnv, 39kEnv, and Env39k elicited a strong Ab response to the C1 region of gp120 (LFCASDAKAYDTEVHNVWAT), and Env39k mounted a strong response to the C4 region (KAMYAPPISGQIRCSSNITG) [Collado2000]					
583	1662	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1662: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
584	1663	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1663: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
585	1664	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1664: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
586	1697	gp160 (433–439)	gp120 (IIIB)	AMYAPPI	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1697: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
587	1794	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1794: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
588	1804	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1804: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
589	1807	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C4 **References** McKeating1992b • 1807: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
590	1808	gp160 (433–442)	gp120 (IIIB)	AMYAPPISGQ	no	Vaccine	
		Vaccine *Vector/Type:* poliovirus *HIV component:* Env **Ab type** C4 **References** McKeating1992b • 1808: Did not bind to native gp120, epitope not exposed. [McKeating1992b]					
591	polyclonal (VEI5)	gp160 (454–474)	Env	LTRDGGNNNNESEIFRPGGGD		HIV-1 infection	human
		Ab type V1, V2, V3, V4, V5 **References** Carlos1999 • Antibody response to the epitopes in a vaccine construct (VEI) containing peptides from 5 hypervariable regions of gp120 was detected in the sera of HIV-1 positive subjects, including sera from 6 non-subtype B infections – serum samples from San Francisco, Canada and Puerto Rico cohort showed presence of antibodies against all five VEI hypervariable regions, but most consistently against the V3 region peptide NNNTRKSIRIGPGRAFYTTGDIGNIRQ. [Carlos1999]					
592	polyclonal	gp160 (460–467)	gp120 (LAI)	NNNNGSEI		HIV-1 infection, Vaccine	human
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **Ab type** V5 **References** Loomis-Price1997 • HIV-1+ positive individuals were given a gp160 vaccine as immunotherapy, and this region was the most reactive new epitope as measured by a modified Pepscan technique which improved sensitivity – 4/14 showed vaccine-induced reactivity. [Loomis-Price1997]					
593	CRA1(ARP 323) (CRA-1)	gp160 (461–470)	gp120 (451–470 LAI)	SNNESEIFRL	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** V5-C5 **Research Contact** M. Page, NIBSC, UK **References** Yang2000, Trkola1996a, Moore1996, Moore1994c, Moore1994d, Moore1993a • CRA1: UK Medical Research Council AIDS reagent: ARP323. • CRA1: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] • CRA1: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] • CRA1: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – reciprocal binding inhibition with anti-C5 antibodies 1C1 and M91 – non-reciprocal binding enhancement some C1 and V2 antibodies – non-reciprocal binding inhibition of some CD4 binding site antibodies. [Moore1996] • CRA1: The relative affinity for denatured/native gp120 is 24 – C5 mutations 470 P/L or G, 475 M/S impairs binding to the native gp120 – only mutation 470 P/L impairs binding to denatured. [Moore1994c] • CRA1: Some C5 mutations abrogate binding 470 P/L or G, 475 M/S, some C2 mutations enhance binding. [Moore1994d] • CRA1: Bound preferentially to denatured IIIB and SF2 gp120. [Moore1993a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
594	M91	gp160 (461–470)	gp120 (451–470 LAI)	SNNESEIFRL	no	Vaccine	rat (IgG2a)

Vaccine *Vector/Type:* protein *HIV component:* Env
Ab type V5-C5 **Research Contact** Fulvia di Marzo Veronese
References Zwick2003, Yang2000, Binley1998, Ditzel1997, Moore1996, Moore1994d, Moore1994c, diMarzo Veronese1992
Keywords antibody interactions.

- M91: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- M91: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000]
- M91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998]
- M91: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – M91 binding was enhanced by 1C1, but 1C1 binding was inhibited by M91 – non-reciprocal binding enhancement of C1 and V2 antibodies – non-reciprocal binding inhibition of CD4 binding site antibodies. [Moore1996]
- M91: 470 P/L impairs binding, but not 475 D/V, in contrast to CRA1 – some C2 mutations can enhance binding. [Moore1994d]
- M91: The relative affinity for denatured/native gp120 is 24 – mutation in position 470 P/L impairs binding. [Moore1994c]
- M91: Immunoblot reactive, RIP negative, but precipitates deglycosylated gp120 – reacts with strains IIIB, 451, MN, RF, and RUTZ. [diMarzo Veronese1992]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
595	9201	gp160 (471–482)	gp120 (475–486 LAI)	GGGDMRDNWRSE	no		mouse

Ab type C5 **Research Contact** Du Pont
References McDougal1996

- 9201: Does not neutralize LAI. [McDougal1996]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
596	1C1	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse (IgG)

Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env
Ab type C5 **Research Contact** Repligen Inc, Cambridge, MA, commercial
References Zwick2003, Moore1996, VanCott1995, Moore1994d, Moore1994c
Keywords antibody interactions.

- 1C1: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- 1C1: C5 region linear epitope, binds weakly to nondenatured monomeric gp120 – M91 binding was enhanced by 1C1, but 1C1 binding was inhibited by M91 – non-reciprocal binding enhancement of some C1 and V2 antibodies – non-reciprocal binding inhibition of some CD4 binding site antibodies. [Moore1996]
- 1C1: Linear epitope not exposed on conformationally intact gp120. [VanCott1995]
- 1C1: C2 and V3 regions substitutions can influence binding. [Moore1994d]
- 1C1: The relative affinity for denatured/native gp120 is 15. [Moore1994c]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
597	3F5	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env **Ab type** C5 **Research Contact** S. Nigida, NCI, USA **References** Moore1994c • 3F5: The relative affinity for denatured/native gp120 is 100. [Moore1994c]					
598	5F4/1	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C5 **Research Contact** S. Ranjbar, NIBSC, UK **References** Moore1994c • 5F4/1: V5-C5 region – preferentially binds SDS-DTT denatured gp120 (>10 fold) – mutation 485 K/V impairs binding. [Moore1994c]					
599	660-178	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** C5 **Research Contact** G. Robey, Abbott Labs **References** Moore1994d, Moore1994c • 660-178: DeltaV1/V2 and DeltaV1/V2/V3 reduce binding – C2 and C5 mutations enhance binding. [Moore1994d] • 660-178: The relative affinity for denatured/native gp120 is >100. [Moore1994c]					
600	9301	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* Env **Ab type** C5 **Research Contact** Dupont, commercial **References** Wagner1996, Moore1994d, Moore1994c, Moore1993a, Skinner1988b • 9301: Wagner *et al.* claim that Nea 9301 is anti-V3 – might they have meant MAb 9305? [Wagner1996] • 9301: The relative affinity for denatured/native gp120 is 19. [Moore1994d] • 9301: Bound preferentially to denatured IIIB gp120. [Moore1993a]					
601	B221 (221)	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp160 **Ab type** C5 **Research Contact** Rod Daniels **References** Moore1994d, Moore1994c, Bristow1994, Moore1993a • B221: UK Medical Research Council AIDS reagent: ARP301. • B221: Called 221 – C2 and V3 substitutions influence binding. [Moore1994d] • B221: The relative affinity for denatured/native gp120 is 12 – mutation 477 D/V impairs binding. [Moore1994c] • B221: MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. [Bristow1994] • B221: Called 221 – bound preferentially to denatured IIIB gp120. [Moore1993a]					
602	8C6/1	gp160 (471–490)	gp120 (471–490 LAI)	GGGDMRDNWRSELYKYKVVK		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI **Ab type** V5-C5 **Research Contact** S. Ranjbar, NIBSC, UK **References** Moore1994c • 8C6/1: UK Medical Research Council AIDS reagent: ARP3052. • 8C6/1: V5-C5 region – preferentially binds SDS-DTT denatured gp120 (>30 fold) – mutation 485 K/V impairs binding. [Moore1994c]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
603	H11	gp160 (472–477)	gp120 (472–477 HXB2)	GGDMRD			mouse
		Ab type C5					
		References Pincus1996, Pincus1993a					
		• H11: Binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. [Pincus1993a, Pincus1996]					
604	W2	gp160 (472–491)	gp120 (472–491 LAI)	GGDMRDNWRSELYKYKVVKI		Vaccine	mouse (IgG)
		Vaccine *Strain:* B clade LAI *HIV component:* Env					
		Ab type C5 **Research Contact** D. Weiner, U. Penn., USA					
		References Moore1994c					
		• W2: The relative affinity for denatured/native gp120 is 30 – mutation 485 K/V impairs binding. [Moore1994c]					
605	M38	gp160 (485–504)	gp120 (490–508)	KYKVVKEIPLGVAPTKAKRR	no	Vaccine	mouse
		Vaccine *Vector/Type:* virus *Strain:* B clade IIIB *HIV component:* HIV-1					
		Ab type C5					
		References Maksiutov2002, Beretta1994, DeSantis1994, Lopalco1993, Grassi1991, Beretta1987					
		• M38: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV, as well as to a fragment of IFN-related IFRD2 (PC4-B) protein, ARTKARSRVRDKRA. [Maksiutov2002]					
		• M38: Infected individuals have HLA class I-gp120 cross-reactive antibodies. [DeSantis1994]					
		• M38: Binds to the carboxy terminus of gp120, in a gp41 binding region, and also to denatured human HLAs (antigenic homology) [Lopalco1993]					
		• M38: Binds to gp120 and to a 80 kd human protein expressed on a small fraction of mononuclear cells in the lymph nodes. [Beretta1987]					
606	Chim 1 (C-1)	gp160 (487–493)	gp120 (492–498 HXB2)	KVVKEIP			humanized chimpanzee
		References Pincus1996, Pincus1993a					
		• Chim 1: Binds to gp120 but not to infected cells – when linked to ricin A, the immunotoxin did not mediate cell killing – sCD4 has no effect. [Pincus1993a, Pincus1996]					
607	polyclonal	gp160 (490–511)	gp120 (495–516 BRU)	KIEPLGVAPTKAKRRVVQREKR	no	HIV-1 infection	human
		References Maksiutov2002, Hernandez2000					
		• This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV, as well as to a fragment of IFN-related IFRD2 (PC4-B) protein, ARTKARSRVRDKRA. [Maksiutov2002]					
		• Chimeric peptide combining two peptides gp160(495-516 and 584-612) served as a specific and broadly reactive antigen for diagnostic detection of HIV-1. [Hernandez2000]					
608	110.1	gp160 (491–500)	gp120 (491–500 LAI)	IEPLGVAPTK	no	Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1					
		Ab type C5 **Research Contact** Genetic Systems Corp, Seattle WA, E. Kinney-Thomas					
		References Maksiutov2002, Valenzuela1998, Binley1997a, McDougal1996, Cook1994, Moore1994c, Pincus1991, Thomas1988, Linsley1988, Gosting1987					
		• 110.1: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. [Maksiutov2002]					
		• 110.1: Does effect LAI viral binding or entry into CEM cells. [Valenzuela1998]					
		• 110.1: Does not neutralize HIV-1 LAI. [McDougal1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 110.1: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the carboxy-terminus of gp120 inhibit gp120 binding to GalCer but not as potently as anti-V3 MAbs – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994] • 110.1: The relative affinity for denatured/native gp120 is 0.7. [Moore1994c] • 110.1: Difference in the epitope: mapped to aa 421-429 (KQIINMWQE), the T1 sequence – poor efficacy as an immunotoxin when linked to RAC. [Pincus1991] • 110.1: Referred to as 110-1 – does not inhibit CD4-gp120 binding or neutralize HIV-1 strains. [Linsley1988] • 110.1: There is another antibody with this ID that binds to gp120, but at aa 200-217.					
609	42F	gp160 (491–500)	gp120 (491–500 HXB2)	IEPLGVAPTK	no	HIV-1 infection	human (IgG1λ)
		Ab type C5 **References** Maksiutov2002, Alsmadi1998, Alsmadi1997 • 42F: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. [Maksiutov2002] • 42F: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against strains IIIB, MN, SF-2, and RF, but not a clone of MN. [Alsmadi1998] • 42F: 42F and 43F were isolated from a long term non-progressor by EBV transformation of PBMC – samples were taken 14 months apart – both MAbs stained diverse strains of infected cells and directed ADCC – were more potent for ADCC if the cell was infected with HIV-1, rather than just presenting absorbed gp120. [Alsmadi1997]					
610	43F	gp160 (491–500)	gp120 (491–500 HXB2)	IEPLGVAPTK	no	HIV-1 infection	human (IgG1λ)
		Ab type C5 **References** Maksiutov2002, Alsmadi1997 • 43F: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. [Maksiutov2002] • 43F: 42F and 43F were isolated from a long term non-progressor by EBV transformation of PBMC – samples were taken 14 months apart – both MAbs stained diverse strains of infected cells and directed ADCC – were more potent for ADCC if the cell was infected with HIV-1, rather than just presenting absorbed gp120. [Alsmadi1997]					
611	RV110026	gp160 (491–500)	gp120 (491–500 LAI)	IEPLGVAPTK		Vaccine	human
		Vaccine *Vector/Type:* peptide *Strain:* B clade LAI **Ab type** C5 **Research Contact** Commercial, Olympus Inc **References** Maksiutov2002, Moore1994d, Moore1994c • RV110026: This epitope is similar to a fragment of the human protein mast/stem cell growth factor receptor precursor, VVPTKADKRRSV. [Maksiutov2002] • RV110026: Preferentially binds SDS-DTT denatured gp120 (15 fold using R1/87 as capture reagent) [Moore1994c]					
612	105-306	gp160 (492–500)	gp120 (498–505 HAM112, O group)	KPFSVAPTP		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160 **Ab type** C-term **References** Scheffel1999 • 105-306: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 105-306 bound to two overlapping peptides. [Scheffel1999]					
613	GV1G2	gp160 (494–499)	gp120 (494–499 IIIB)	LGVAPT		Vaccine	mouse
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120-Mab complex **Ab type** C5					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Denisova1996 • GV1G2: When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes – MAbs GV12F6 and GV3H1 are homologous to GV1G2 and were generated in the same experiment. [Denisova1996]					
614	750-D	gp160 (498–504)	gp120 (503–509)	PTKAKRR	no	HIV-1 infection	human (IgG3λ)
		Ab type C-term **References** Hioe2000, Forthal1995 • 750-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C5 MAbs 450-D and 750-D did not effect proliferation. [Hioe2000] • 750-D: Not neutralizing, positive ADCC activity, and no viral enhancing activity. [Forthal1995]					
615	450-D (450-D-3, 450D)	gp160 (498–504)	gp120 (475–486 BH10)	PTKAKRR(orRRVVQRE,orMRDNW-RSELYKYdependingonreferen-ce)	no	HIV-1 infection	human (IgG1λ)
		Ab type C5 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Verrier2001, Hioe2001, Hioe2000, Hioe1997b, Li1997, Manca1995a, Forthal1995, Cook1994, Gorny1994, Laal1994, Spear1993, Karwowska1992b, Karwowska1992a, Durda1988 • 450-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] • 450-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN gamma production – 450-D does not have this effect and was used as a control in this study. [Hioe2001] • 450-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – C5 MAbs 450-D and 750-D did not effect proliferation. [Hioe2000] • 450-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] • 450-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 6 mug/ml. [Li1997] • 450-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells. [Manca1995a] • 450-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. [Forthal1995] • 450-D: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the carboxy-terminus of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994] • 450-D: Epitope is defined as PTKAKRR. [Gorny1994] • 450-D: Not neutralizing alone, could synergize anti-CD4 binding site antibody neutralization. [Laal1994] • 450-D: Did not mediate deposition of complement component C3 on HIV infected cells. [Spear1993] • 450-D: Bound to MN, SF-2 and IIIB, but was not neutralizing. [Karwowska1992a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
616	670-D (670)	gp160 (498–504)	gp120 (503–509)	PTKAKRR	no	HIV-1 infection	human (IgG1λ)

Ab type C5 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Zwick2003, Verrier2001, Nyambi2000, Gorny2000b, Altmeyer1999, Nyambi1998, Gorny1998, Hioe1997b, Gorny1997, Hill1997, Forthal1995, Zolla-Pazner1995a
Keywords antibody interactions.

- 670-D: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- 670-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001]
- 670-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 670-D bound 21/26, and was the most cross-reactive C5 MAb. [Nyambi2000]
- 670-D: A gp120 C5 MAb used as a negative control in a study of anti-gp41 MAbs. [Gorny2000b]
- 670-D: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. [Altmeyer1999]
- 670-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-C5 Abs 670-D and 1331A bound to 3/4 B clade viruses (they didn't bind to IIIB), and to subtype D MAL – 670-D also reacted with subtype A. [Nyambi1998]
- 670-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b]
- 670-D: gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect. [Hill1997]
- 670-D: Not neutralizing, positive ADCC activity, and no viral enhancing activity, numbering provided suggests epitope is RRVVQRE. [Forthal1995]
- 670-D: Group specific cross-clade binding in serotyping study using flow-cytometry. [Zolla-Pazner1995a]

617	polyclonal	gp160 (503–509)	gp120 (471–477)	RRVVQRE		Vaccine	mouse (IgG)

Vaccine *Vector/Type:* peptide *HIV component:* gp120
References Jeyarajah1998

- Mice were immunized with peptide APTKAKRRVVQREKR – epitope excision and extraction combined with mass spectrometry was used to map the fine structure of epitopes recognized by polyclonal Ab to HIV-1 Env – a major epitope was identified between positions 472 and 478. [Jeyarajah1998]

618	722-D	gp160 (503–509)	gp120 (503–509)	RRVVQRE	no	HIV-1 infection	human (IgG1κ)

Ab type C-term

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Forthal1995, Laal1994 • 722-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. [Forthal1995] • 722-D: Not neutralizing alone, could synergize anti-CD4 binding site antibody neutralization. [Laal1994]					
619	polyclonal	gp160 (503–511)	gp120 (508–516)	RRVVQREKR		HIV-1 infection	human
		Ab type C-term **References** Loomis-Price1997, Palker1987 • Most HIV-1+ individuals have an antibody response to this epitope – in this study, reactivity to RRVVQREKR was used as a positive control for HIV-1+ gp160 vaccine recipients. [Loomis-Price1997]					
620	1131-A	gp160 (505–511)	gp120 (510–516 LAI)	VVQREKR	no	HIV-1 infection	human (IgG3λ)
		Ab type C-term **References** Bandres1998 • 1131-A: A very high affinity antibody used in studies that demonstrate that CXCR4 can bind to gp120 in the absence of CD4-gp120 interactions, and that this binding can be enhanced by Env deglycosylation. [Bandres1998]					
621	858-D	gp160 (505–511)	gp120 (510–516 LAI)	VVQREKR	no	HIV-1 infection	human (IgG)
		Ab type C-term **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi2000, Gorny2000a, Forthal1995, Zolla-Pazner1995a • 858-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 858-D bound only 4/26, the worst of all anti-C5 MAbs tested, while MAb 1331A, which shares the same core epitope (positions 495-516), bound to 18/26 isolates. [Nyambi2000] • 858-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer. [Gorny2000a] • 858-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. [Forthal1995] • 858-D: Group specific cross-clade binding in serotyping study using flow-cytometry. [Zolla-Pazner1995a]					
622	989-D	gp160 (505–511)	gp120 (LAI)	VVQREKR		HIV-1 infection	human (IgG)
		Ab type C-term **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Nyambi2000, Gorny2000a, Zolla-Pazner1995a • 989-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 989-D bound to 6/26 isolates. [Nyambi2000] • 989-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer. [Gorny2000a] • 989-D: In serotyping study using flow-cytometry, showed B clade specificity, but only reacted with 7/11 B clade virus. [Zolla-Pazner1995a]					
623	1331A	gp160 (505–511)	gp120 (510–516)	dwVVQREKR		HIV-1 infection	human (IgG3λ)
		Ab type C5 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Zwick2003, Edwards2002, Gorny2002, Nyambi2000, Hochleitner2000b, Gorny2000a, Nyambi1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1331A: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding MAb that had no impact on 4KG5 binding. [Zwick2003] • 1331A: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] • 1331A: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control as binding was not diminished by treating gp120 with DTT or sodium metaperiodate to reduce disulfide bonds), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) [Gorny2002] • 1331A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 4 C5 MAbs, 2 bound well, 2 bound weakly – MAb 858-D bound only 4/26, the worst of all anti-C5 MAbs tested, while MAb 1331A, which shares the same core epitope (positions 495-516), bound to 18/26. [Nyambi2000] • 1331A: The Ab binding site was studied with epitope excision (protein is bound in native conformation to immobilized MAb, then digested with proteolytic enzymes) and extraction (protein is digested then allowed to react with Ab), followed by mass spectroscopy – two non-contiguous aa in C5 were protected, E-507 and I-487, which are thought to be located on opposite sides of hydrophobic pocket involved in gp120/gp41 interaction. [Hochleitner2000b] • 1331A: Core epitope dwVVQREKR maps to gp120(510-516) – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – C5 MAbs 858-D, 989-D and 1331A bound with a 5-10 fold preference for the monomer. [Gorny2000a] • 1331A: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-C5 Abs 670-D and 1331A bound to 3/4 B clade viruses (they don't bind to IIIB), and to subtype D MAL. [Nyambi1998]				
624	1A1	gp160 (525–543)	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
		Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Maksiutov2002, Buchacher1994 • 1A1: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. [Maksiutov2002] • 1A1: Human MAb generated using EBV transformation of PBL from HIV-1+ volunteers. [Buchacher1994]					
625	24G3	gp160 (525–543)	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
		Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Maksiutov2002, Buchacher1994, Buchacher1992 • 24G3: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. [Maksiutov2002] • 24G3: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells. [Buchacher1994]					
626	25C2 (IAM 41-25C2)	gp160 (525–543)	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
		Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX **References** Maksiutov2002, Sattentau1995c, Buchacher1994, Buchacher1992 • 25C2: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. [Maksiutov2002]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 25C2: Called IAM 41-25C2 – Binding domain overlaps sites that are critical for gp120-gp41 association – binding is enhanced by sCD4 – binding region defined as: gp41(21-38 BH10) [Sattentau1995c] • 25C2: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells – binds oligomeric and monomeric gp41, and gp160. [Buchacher1994]					
627	5F3	gp160 (525–543)	gp41 (526–543 BH10)	AAGSTMGAASMTLTVQARQ	no	HIV-1 infection	human (IgG1κ)
		Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Maksiutov2002, Buchacher1994 • 5F3: This epitope is similar to a fragment of the HLA class II histocompatibility antigen, GGSCMAALTVTLTV. [Maksiutov2002] • 5F3: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells. [Buchacher1994]					
628	α(566-586)	gp160 (561–581)	gp41 (566–586 BRU)	AQQHLLQLTVWGIKQLQARIL		HIV-1 infection	human
		References Poumbourios1992					
629	PC5009	gp160 (572–591)	gp41 (577–596 BRU)	GIKQLQARILAVERYLKDQQ		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **References** Poumbourios1992 • PC5009: Recognized only monomeric gp41. [Poumbourios1992]					
630	polyclonal α577-596	gp160 (572–591)	gp41 (577–596 BRU)	GIKQLQARILAVERYLKDQQ		HIV-1 infection	human
		References Poumbourios1992 • alpha(577-596): Affinity purified from HIV-1+ plasma – preferentially bind oligomer. [Poumbourios1992]					
631	polyclonal	gp160 (576–592)	gp41 (583–599)	LQARILAVERYLKDQQL		HIV-1 infection	human
		References Klasse1993b • 42 HIV-1 positive human sera were tested against wildtype peptide, and peptide with substitution 589 A to T: 11/42 reacted strongly with wildtype, weakly with A589T – 31 reacted weakly with parental, even more weakly with substituted. [Klasse1993b]					
632		gp160 (577–583)	gp41 (582–589)	QARILAV	yes	HIV-1 exposed seronegative	human (IgA)
		Ab type Leucine zipper motif **References** Clerici2002a • Six sera from HIV-exposed uninfected individuals(EU), HIV-infected individuals and healthy controls were analyzed for IgA Abs – neutralizing activity was observed with total IgA from both EU and HIV+ – the EU IgA exclusively bound to a distinctive epitope within gp41, QARILAV, in the coiled coil pocket important for gp120-gp41 interactions – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5. [Clerici2002a]					
633		gp160 (577–583)	gp41 (582–589)	QARILAV	yes	Vaccine	mouse (IgA)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 *Adjuvant:* Keyhole Limpit Haemocyanin (KLH) **Ab type** Leucine zipper motif **References** Clerici2002a • Six sera from HIV-exposed uninfected individuals(EU), HIV-infected individuals and healthy controls were analyzed for IgA Abs – neutralizing activity was observed with total IgA from both EU and HIV+ – the EU IgA exclusively bound to a distinctive epitope within gp41, QARILAV – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5. [Clerici2002a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
634	1F11	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)

Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny2004, Buchacher1994, Buchacher1992
Keywords antibody generation, review.

- 1F11: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 1F11: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
635	1H5	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)

References Gorny2004, Buchacher1994, Buchacher1992
Keywords antibody generation, review.

- 1H5: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 1H5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
636	3D9	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)

Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny2004, Buchacher1994, Buchacher1992
Keywords antibody generation, review.

- 3D9: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 3D9: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
637	4B3	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1λ)

Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria
References Gorny2004, Chen1994b, Buchacher1994, Buchacher1992
Keywords antibody generation, review.

- 4B3: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 4B3: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
638	4D4	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1λ)

Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX
References Gorny2004, Binley1999, Sattentau1995c, Chen1994b, Buchacher1994, Buchacher1992
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design.

- 4D4: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 4D4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**antibody binding site definition and exposure**, **vaccine antigen design**) • 4D4: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)			
639	4G2	gp160 (578–612)	gp41 (579–613 BH10)	ARILAVERYLKDQQLLGIWGCSGKL-ICTTAVPWNA	no	HIV-1 infection	human (IgG1κ)
		Research Contact H. Katinger, Inst. Appl. Microbiol., Vienna, Austria **References** Gorny2004, Buchacher1994, Buchacher1992 **Keywords** antibody generation, review. • 4G2: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**) • 4G2: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)					
640	polyclonal	gp160 (579–589)	gp41 (586–596 IIIB)	RILAVERYLKD		Vaccine	rabbit, mouse
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 *Adjuvant:* BSA **Ab type** C-domain **References** Xiao2000b • Strong epitope-specific neutralizing antibody responses were induced using the peptide C(RILAVERYLKD)_2-BSA, but not full gp160. [Xiao2000b]					
641	polyclonal	gp160 (579–589)	gp41 (586–596)	RILAVERYLKD		Vaccine	rabbit
		Vaccine *Vector/Type:* protein, polyepitope *HIV component:* gp160 *Adjuvant:* BSA **Ab type** N-term **References** Lu2000b, Lu2000c • High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to both ELDKWA and GPGRAFY – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here. [Lu2000c, Lu2000b]					
642	polyclonal	gp160 (579–599)	gp41 (583–604)	RILAVERYLKDQQLLGIWGCS	no	Vaccine	rabbit
		Vaccine *Vector/Type:* protein *HIV component:* desialylated gp160 **References** Benjouad1993 • MAbs raised against desialylated HIV-1 gp160 cross-react with HIV-2 gp140 due to immunodominant conserved epitope in gp41. [Benjouad1993]					
643	2A2/26	gp160 (579–601)	gp41 (584–606 BRU)	RILAVERYLKDQQLLGIWGCSGK		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* gp41 **References** Poumbourios1995, Poumbourios1992 • 2A2/26: Delta 550-561 (Delta LLRAIEAQQHLL), a region important for oligomer formation diminishes binding, Delta (550-561 +571-581) abrogates binding. [Poumbourios1995]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2A2/26: Immunodominant region, binds both oligomer and monomer. [Poumbourios1992]					
644	50-69 (SZ-50.69, 50-69D)	gp160 (579–603)	gp41 (579–603 BH10)	RILAVERYLKDQQLLGIWGCSGKLI	no	HIV-1 infection	human (IgG2κ)

Ab type cluster I **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY

References Gorny2004, Finnegan2002, Follis2002, Verrier2001, Zwick2001b, Nyambi2000, Gorny2000a, Gorny2000b, Mitchell1998, Hioe1997b, Boots1997, Stamatatos1997, Klasse1996, Binley1996, Poignard1996a, McDougal1996, Manca1995a, Sattentau1995c, Chen1995, Laal1994, Spear1993, Eddleston1993, Sattentau1991, Robinson1991, Xu1991, Gorny1989, Pinter1989, Till1989

Keywords antibody binding site definition and exposure, antibody interactions, complement, enhancing activity, immunotoxin, inter-clade comparisons, kinetics, mimotopes, review, variant cross-recognition or cross-neutralization.

- 50-69: This is one of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 50-69: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**)
- 50-69: Called 50-69D. Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**)
- 50-69: NIH AIDS Research and Reference Reagent Program: 531.
- 50-69: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**)
- 50-69: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – MAb 50-69 binding to infected cells is enhanced by sCD4, while 4E10 and Z13 binding is essentially unaltered. [Zwick2001b] (**antibody binding site definition and exposure**)
- 50-69: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 50-69 bound the majority of isolates although binding was moderate to weak – specifies discontinuous binding site range as aa 579-613. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 50-69: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**)
- 50-69: A cluster I epitope that binds to rgp41 567-647, recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn't react with either of the peptides N51 or C43 individually – MAbs 50-69 and 1367 had similar properties – MAb 50-69 bound the fusogenic form of the protein in liquid phase. [Gorny2000b] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 50-69: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613 – identifies non-contiguous W596-G597-C598 and C604-T605 as minimal epitope. [Mitchell1998] (**antibody binding site definition and exposure**) • 50-69: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 50-69 maps to an immunodominant domain in gp41 – three groups of peptides were selected, one which seems most closely related to gp41 sequence peptide consensus is WGCxx(RK)(x n)LxC – the analogous gp41 sequence WGCSGKLIC is present in most M group clades, except D with a common L to H substitution. [Boots1997] (**mimotopes**) • 50-69: Binding of anti-gp120 MAbs IgG1b12 or 654-30D does not mediate significant exposure of the gp41 epitopes for MAbs 2F5 and 50-69. [Stamatatos1997] (**antibody interactions**) • 50-69: Used to test exposure of gp41 upon sCD4 binding. [Klasse1996] • 50-69: Binds to a linear epitope located in the cluster I region – binding of 50-69 and 240-D inhibited by Fabs A1, A4, M8B, M26B, M12B and T2. [Binley1996] (**antibody binding site definition and exposure**) • 50-69: Prebinding of anti-V3, and CD4i MAbs 48d and 17b, but not anti-V2 neutralizing MAbs, expose the 50-69 epitope. [Poignard1996a] (**antibody interactions**) • 50-69: Does not neutralize HIV-1 LAI. [McDougal1996] (**variant cross-recognition or cross-neutralization**) • 50-69: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. [Manca1995a] • 50-69: Preferentially binds oligomer – binding increased after pretreatment of infected cells with sCD4 – binding domain overlaps site that is critical for gp120-gp41 association. [Sattentau1995c] (**antibody binding site definition and exposure**) • 50-69: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. [Chen1995] (**antibody binding site definition and exposure**) • 50-69: Epitope described as cluster I, 601-604, conformational – does not neutralize IIIB or synergize neutralization by anti-V3 MAb 447-52D or by CD4 BS MAbs. [Laal1994] (**antibody binding site definition and exposure**, **antibody interactions**) • 50-69: Did not mediate deposition of complement component C3 on HIV infected cells unless cells were pre-incubated with sCD4 – complement mediated virolysis of MN and IIIB in the presence of sCD4. [Spear1993] (**complement**) • 50-69: Called SZ-50.69 – binds to an epitope within aa 579-613. [Eddleston1993] (**antibody binding site definition and exposure**) • 50-69: Two fold increase in binding to gp120 in the presence of bound sCD4. [Sattentau1991] (**antibody binding site definition and exposure**) • 50-69: Enhances HIV-1 infection *in vitro* – synergizes with huMAb 120-16 *in vitro* to enhance HIV-1 infection to level approaching that found in polyclonal anti-HIV serum. [Robinson1991] (**antibody interactions**, **enhancing activity**) • 50-69: The epitope is affected by the conformation conferred by the two cysteines at amino acids 598 and 604. [Xu1991] (**antibody binding site definition and exposure**) • 50-69: Kills HIV-infected cells when coupled to deglycosylated ricin A chain. [Gorny1989] (**immunotoxin**) • 50-69: Reacts preferentially with gp160 oligomer, compared to gp41 monomer. [Pinter1989] (**antibody binding site definition and exposure**) • 50-69: Combined with deglycosylated A chain of ricin is toxic to lines of HIV-infected T cells (H9) and monocytes (U937) [Till1989] (**immunotoxin**)				
645	9-11	gp160 (579–604)	gp41 (584–609)	RILAVERYLKDQQLLGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **References** Mani1994 • 9-11: required the C-C disulfide bridge and loop formation, can bind simultaneously with 41-1. [Mani1994]					
646	98-43	gp160 (579–604)	gp41 (579–604 HXB2)	RILAVERYLKDQQLLGIWGCSGKLIC	no	HIV-1 infection	human (IgG2κ)
		References Xu1991, Tyler1990, Gorny1989, Pinter1989 • 98-43: NIH AIDS Research and Reference Reagent Program: 1241. • 98-43: 579-604 binds in the immunodominant region. [Xu1991] • 98-43: Poor ADCC (in contrast to MAb 120-16, gp41(644-663)) [Tyler1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 98-43: Reacts equally well with oligomer and monomer. [Pinter1989]					
647	41-1 (41.1)	gp160 (579–608)	gp41 (584–609)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV		Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **References** Pincus1998, Pincus1996, Mani1994, Pincus1993a, Pincus1991, Dalgleish1988, Gosting1987 • 41-1: Called 41.1, and described as a human MAb, binding 579-604 – a panel of immunotoxins was generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] • 41-1: Did not require the C-C disulfide bridge and loop formation, can bind simultaneously with 9-11. [Mani1994] • 41-1: Called 41.1, and described as a human MAb – cross-competes with 41.4 – sCD4 enhances the efficacy of immunotoxins *in vitro* 30-fold – MAb was coupled to ricin A chain (RAC) [Pincus1993a] • 41-1: Efficacious as an immunotoxin when coupled to RAC – gave linear epitope as gp160 579-603. [Pincus1991] • 41-1: This antibody seems to have been named the same as a different MAb to gp41(735-752) [Dalgleish1988] • 41-1: Broadly reactive. [Gosting1987] • 41-1: Also called 41.1, although possibly not, the literature is confusing because two gp41 MAbs that bind to this region with similar names (dash versus period) are listed as murine and human. • 41-1: This antibody to gp41(584-609) [Mani1994] seems to have been named the same as a different MAb to gp41(735-752 IIIB) [Dalgleish1988]. [Dalgleish1988, Mani1994]				
648	41.4	gp160 (579–608)	gp41 (584–609)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV			
		Research Contact Jan McClure, Bristol-Myers Squibb Pharmaceutical Res Inst, Seattle, WA **References** Pincus1993a • 41.4: Binds to peptide weakly, but to gp160 with higher affinity than 41.1, and cross-competes with 41.1 – probably conformational – MAb was coupled to ricin A chain (RAC) – sCD4 enhances the efficacy of immunotoxins *in vitro* 30-fold. [Pincus1993a]					
649	Fab A1 (A1)	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Gorny2004, Binley1996 **Keywords** anti-idiotype, antibody generation, antibody sequence, variable domain, review. • Fab A1: Called A1. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**) • Fab A1: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. [Binley1996] (**anti-idiotype**, **antibody generation**, **antibody sequence, variable domain**)					
650	Fab A4 (A4)	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)
		References Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review. • Fab A4: Called A4. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**) • Fab A4: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
651	Fab M12B (M12B)	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)

References Gorny2004, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.
- Fab M12B: Called M12B. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- Fab M12B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

652	Fab M26B (M26B)	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)

References Gorny2004, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.
- Fab M26B: Called M26B. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- Fab M26B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

653	Fab M8B (M8B)	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)

References Gorny2004, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.
- Fab M8B: Called M8B. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- Fab M8B: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

654	Fab T2 (T2)	gp160 (579–608)	gp41 (584–609 LAI)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAV	no	HIV-1 infection	human (IgG1κ)

References Gorny2004, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.
- Fab T2: Called T2. One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- Fab T2: Binds to cluster I region – competes with MAbs 240-D and 50-69 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

655	86 (No. 86)	gp160 (579–613)	gp41 (586–620 IIIB)	RILAVERYLKDQQLLGIWGCSGKLI-CTTAVPWNAS	no	HIV-1 infection	human (IgG1κ)

Research Contact Evan Hersh and Yoh-Ichi Matsumoto
References Gorny2004, Mitchell1998, Wisnewski1996, Moran1993, Pincus1991, Robinson1990c, Robinson1990b, Sugano1988
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, complement, enhancing activity, immunotoxin, review, variant cross-recognition or cross-neutralization.
- 86: This is one of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 86: NIH AIDS Research and Reference Reagent Program: 380. • 86: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613. [Mitchell1998] (**enhancing activity**, **variant cross-recognition or cross-neutralization**) • 86: 86 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**) • 86: Heavy (V HI) and light (V kappaI) chain sequenced – enhancing activity – similar germline sequence to MAb S1-1, but very different activity. [Moran1993] (**enhancing activity**, **antibody sequence, variable domain**) • 86: Poor immunotoxin activity when coupled to RAC – peptide binding stated to be aa 579-603. [Pincus1991] (**antibody binding site definition and exposure**, **immunotoxin**) • 86: Peptide 586-620 blocks complement mediated ADE. [Robinson1990c] (**enhancing activity**) • 86: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity in the presence of complement. [Robinson1990b] (**complement**, **enhancing activity**) • 86: Reacts with gp41 and also reacted weakly with gp120. [Sugano1988] (**antibody binding site definition and exposure**)			
656	polyclonal	gp160 (580–597)	gp41 (584–602)	ILAVERYLKDQQLLGIWG	no	HIV-1 infection	human
		References Petrov1990 • Immunodominant and broadly reactive peptide. [Petrov1990]					
657	V10-9	gp160 (580–613)	gp41 (586–620 IIIB)	ILAVERYLKDQQLLGIWGCSGKLIC-TTAVPWNAS	no	HIV-1 infection	human (IgG1κ)
		References Gorny2004, Robinson1990c, Robinson1990b **Keywords** antibody interactions, enhancing activity, review. • V10-9: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**) • V10-9: Peptide 586-620 blocks complement mediated ADE. [Robinson1990c] (**enhancing activity**) • V10-9: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity, synergistically enhanced by MAb 120-16. [Robinson1990b] (**antibody interactions**, **enhancing activity**)					
658	polyclonal	gp160 (582–589)	gp41 (589–596)	AVERYLKD		HIV-1 infection	human
		References Klasse1991 • Substitutions and deletions in peptide 583-599 were systematically studied – alterations in AVERYLKD abrogated the antigenicity of peptides with most of 14 human sera. [Klasse1991]					
659	polyclonal	gp160 (584–604)	gp41 (74–94)	ERYLKDQLLGIWGCSGKLIC		HIV-1 infection	human
		References Shafferman1989 • Immunogenic domain useful for diagnostics. [Shafferman1989]					
660	polyclonal	gp160 (584–612)	gp41 (587–617 BRU)	ERYLKDQQLLGIWGCSGKLICTTAV-PWNA	no	HIV-1 infection	human
		References Hernandez2000 • Chimeric peptide combining two peptides gp160(495-516 and 584-612) served as a specific and broadly reactive antigen for diagnostic detection of HIV-1. [Hernandez2000]					
661	2F11	gp160 (589–600)	gp41 (589–600 HXB2)	DQQLLGIWGCSG	no	HIV-1 infection	human (IgG1)
		References Gorny2004, Enshell-Seijffers2001, Eaton1994					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

Keywords ADCC, enhancing activity, review.

- 2F11: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 2F11: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. [Enshell-Seijffers2001] (**enhancing activity**)
- 2F11: Enhances infectivity even in the absence of complement – does not mediate ADCC or neutralize virus. [Eaton1994] (**ADCC**, **enhancing activity**)

662	246-D (SZ-246.D, 246, 246D)	gp160 (590–597)	gp41 (579–604 HXB2)	qqLLGIWg	no	HIV-1 infection	human (IgG1κ)

Ab type cluster I **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY

References Gorny2004, Finnegan2002, Follis2002, Edwards2002, Gorny2002, Verrier2001, Nyambi2000, Gorny2000b, Mitchell1998, Hioe1997b, Earl1997, Saarloos1995, Manca1995a, Forthal1995, Eddleston1993, Spear1993, Robinson1991, Xu1991

Keywords antibody binding site definition and exposure, antibody interactions, complement, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization.

- 246-D: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 246-D: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**)
- 246-D: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**)
- 246-D: NIH AIDS Research and Reference Reagent Program: 1245.
- 246-D: Called 246D – Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] (**antibody binding site definition and exposure**)
- 246-D: Called 246 – Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades tested, A, B, C, D, F and CRF01 (clade E) [Gorny2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 246-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**) • 246-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 246-D bound strongly or moderately to all 26 HIV-1 group M clades viruses tested and showed the strongest binding of all anti-Env MAbs tested, including the V3 and C5 region MAbs – notes core epitope as LLGI – no neutralizing activity was observed when 246-D was tested with five isolates. [Nyambi2000] (**inter-clade comparisons**) • 246-D: Core epitope aa 591 to 597, a cluster I epitope that does not bind to either a peptide complex that approximates the core of the fusogenic form of gp41 or the individual peptides N51 and C43 that form this structure – MAbs 181-D and 246-D had similar properties. [Gorny2000b] (**antibody binding site definition and exposure**) • 246-D: This antibody, along with murine MAb D61, can be blocked by any of a group of 8 conformational MAbs (M10, D41, D54, T4, T6, T9, T10 and T35) [Earl1997] (**antibody interactions**) • 246-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations and 246-D neutralized 91US056 – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**) • 246-D: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613. [Mitchell1998] (**antibody binding site definition and exposure**) • 246-D: Ab-mediated activation of complement on HIV+ cells is higher than Ab independent activation—what has been termed "Ab independent" in fact results in part from IgM in normal human serum that is HIV-cross-reactive. [Saarloos1995] (**complement**) • 246-D: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. [Manca1995a] • 246-D: No neutralizing activity, both ADCC and viral enhancing activity. [Forthal1995] (**complement**, **enhancing activity**) • 246-D: Called SZ-246.D. [Eddleston1993] • 246-D: No neutralizing activity, some enhancing activity. [Robinson1991] (**enhancing activity**) • 246-D: Did not mediate deposition of complement component C3 on HIV infected cells unless cells were pre-incubated with sCD4. [Spear1993] (**complement**) • 246-D: Fine mapping indicates core is LLGI. [Xu1991] (**antibody binding site definition and exposure**)					
663	polyclonal	gp160 (590–607)	gp41	QQLLGIWGCSGKLICTTA	no	HIV-1 infection	human (IgG)
		References Parekh2002 • A simple enzyme immunoassay (EIA) that detects increasing levels of anti-HIV IgG after seroconversion can be used for detecting recent HIV-1 infection – longitudinal specimens from 139 incident infections in the US and Thailand were used in the study – the method was generally applicable for HIV-1 subtypes A, B, C, D and E(CRF01) [Parekh2002]					
664	9G5A	gp160 (591–594)	gp41 (596–599 IIIB)	QLLG		anti-idiotype	mouse (IgM)
		References Beretta1994, Lopalco1993 • 9G5A: Anti-idiotype to gp120 C terminus (C5 region) MAb M38. [Lopalco1993]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
665	181-D (SZ-181.D)	gp160 (591–597)	gp41 (591–597 HXB2)	qLLGIWg	no	HIV-1 infection	human (IgG2κ)

Ab type cluster I **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Gorny2004, Nyambi2000, Gorny2000b, Fontenot1995, Forthal1995, Eddleston1993, Robinson1991, Xu1991
Keywords ADCC, antibody binding site definition and exposure, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 181-D: This is one of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 181-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 181-D bound the majority of isolates although binding was moderate to weak. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 181-D: Core epitope aa 591 to 597, a cluster I epitope that does not bind to either a peptide complex that approximates the core of the fusogenic form of gp41 or the individual peptides N51 and C43 that form this structure – MAbs 181-D and 246-D had similar properties. [Gorny2000b] (**antibody binding site definition and exposure**)
- 181-D: No neutralizing, no ADCC, and no viral enhancing activity. [Forthal1995] (**ADCC**, **enhancing activity**)
- 181-D: Called SZ-181.D. [Eddleston1993]
- 181-D: No enhancing or neutralization activity. [Robinson1991] (**enhancing activity**)
- 181-D: Fine mapping indicates core is LLGIW. [Xu1991] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
666	240-D (F240)	gp160 (592–600)	gp41 (592–600 HXB2)	LLGIWGCSG	no	HIV-1 infection	human

Ab type cluster I **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY
References Gorny2004, Finnegan2002, Nyambi2000, Mitchell1998, Wisnewski1996, Wisnewski1995, Binley1996, Spear1993, Robinson1991, Xu1991
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, complement, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization.

- 240-D: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- 240-D: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**)
- 240-D: NIH AIDS Research and Reference Reagent Program: 1242.
- 240-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 246-D bound strongly or moderately to 24/26 HIV-1 group M clades viruses tested. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 240-D: Mutations in BH10 gp160, W596Y and T605A, as well as deletions of 605-609 (TTAVP) and 597-609 (GCSGKLICTTAVP), abrogate binding of enhancing MAbs 86, 240D, 50-69, and 246-D – 5/6 enhancing MAbs identified to date bind to the immunodominant region 579-613. [Mitchell1998] (**enhancing activity**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 240-D: V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- 240-D: Binds to a linear epitope located in the cluster I region – binding of 50-69 and 240-D inhibited by Fabs A1, A4, M8B, M26B, M12B and T2. [Binley1996] (**antibody binding site definition and exposure**)
- 240-D: Did not mediate deposition of complement component C3 on HIV infected cells. [Spear1993] (**complement**)
- 240-D: No neutralizing activity, some enhancing activity. [Robinson1991] (**enhancing activity**)
- 240-D: Fine mapping indicates core is IWG. [Xu1991] (**antibody binding site definition and exposure**)

667 F240 gp160 (592–606) gp41 (592–606 BH10) LLGIWGCSGKLICTT no HIV-1 infection human (IgG1κ)

Ab type cluster I **Research Contact** L. Cavacina or M. Posner, Dept. of Med. Harvard Med. School, Boston MA, USA

References Gorny2004, Finnegan2002, Follis2002, Cavacini2003, Cavacini2002, York2001, Cavacini1998a

Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, co-receptor, enhancing activity, review, variant cross-recognition or cross-neutralization.

- F240: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)
- F240: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**)
- F240: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**)
- F240: The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. Anti-gp41 MAb F240 could inhibit B4e8 neutralization. [Cavacini2003] (**antibody interactions**)
- F240: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate, with the exception of F240 which bound both equally well, which captured more virus than any other human MAb tested, and didn't neutralize either isolate.F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 and the gp41 MAb 2F5 for both R5X4 and R5 isolates. F240 binding to gp41 was not affected by the binding of the V3 loop MAb B4a1, but preincubation with F240 could enhance B4a1 binding of the R5 isolate. Synergistic neutralization between F240 and CD4i MAbs 17b and 48d was noted for the R5X4 but not the R5 isolate, and F240 also enhanced neutralization of the R5X4 isolate by 2F5, but had no effect on R5 virus. In contrast, F240 combined with 2G12 demonstrated enhanced neutralization of R5 virus at low Ab concentrations. [Cavacini2002] (**antibody interactions**, **co-receptor**)
- F240: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• F240: Distinct from MAb 240-D, an antibody with a similar epitope in the immunodominant region of gp41 – dose-dependent reactivity with HIV isolates RF, SF2, IIIB, and MN was observed – F240 had no neutralizing activity and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105 – heavy and light chain variable domains were sequenced, and a strong homology to hu MAb 3D6 was observed, as 3D6 binds to the same epitope, these MAbs may define a human Ab clonotype. [Cavacini1998a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**, **antibody sequence, variable domain**)					
668	D49	gp160 (592–608)	gp41 (597–613)	LLGIWGCSGKLICTTAV		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Ab type** cluster I **References** Earl1997, Earl1994 • D49: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues. [Earl1997] • D49: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
669	D61	gp160 (592–608)	gp41 (592–608 HXB2)	LLGIWGCSGKLICTTAV		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Ab type** cluster I **Research Contact** Patricia Earl and Christopher Broder, NIH **References** Golding2002b, Earl1997, Weissenhorn1996, Richardson1996, Earl1994 **Keywords** antibody binding site definition and exposure, antibody generation. • D61: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b – nor did it alter two gp41 MAbs, T9 and D61, inability to inhibit fusion. [Golding2002b] (**antibody binding site definition and exposure**) • D61: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues – this antibody, along with human MAb 246-D, can be blocked by any of a group of 8 conformational MAbs (M10, D41, D54, T4, T6, T9, T10 and T35) – members of this competition group are blocked by sera from HIV-1+ individuals. [Earl1997] (**antibody binding site definition and exposure**) • D61: Does not precipitate gp41(21-166), but due to a structural difference in the disulfide bonding region near the two cysteines – the authors propose that this region may change conformation during the activation of the membrane fusion state of the HIV-1 glycoprotein. [Weissenhorn1996] (**antibody binding site definition and exposure**) • D61: Linear gp41 epitope in the cluster I region – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4. [Richardson1996] (**antibody binding site definition and exposure**) • D61: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)					
670	T32	gp160 (592–608)	gp41 (597–613)	LLGIWGCSGKLICTTAV		Vaccine	mouse
		Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env **Ab type** cluster I **Research Contact** Patricia Earl and Christopher Broder, NIH **References** Earl1997, Earl1994 • T32: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues. [Earl1997] • T32: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
671	T34	gp160 (592–608)	gp41 (597–613)	LLGIWGCSGKLICTTAV		Vaccine	mouse
		Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env **Ab type** cluster I **Research Contact** Patricia Earl and Christopher Broder, NIH					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Earl1997, Earl1994 • T34: Binding maps to region 597-613: WGCSGKLICTTAVPWNA – immunodominant region containing two Cys residues. [Earl1997] • T34: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response – an oligomer with no gp120/gp41 cleavage site was used as the immunogen. [Earl1994]					
672	115.8	gp160 (593–604)	gp41 (598–609)	LGLIWGCSGKLIC		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 115.8: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor reactivity with CSGKLIC – reacts well with longer HIV-2 peptide NSWGCAFRQVC as well as CAFRQVC – disulfide bond between cysteines required. [Oldstone1991]					
673	M-1	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1, IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-1: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. [Yamada1991]					
674	M-11	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-11: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. [Yamada1991]					
675	M-13	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-13: Reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. [Yamada1991]					
676	M-2	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-2: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. [Yamada1991]					
677	M-22	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-22: Strongest reaction of 12 anti-HIV-1 gp41 MAbs to a cellular 43-kd protein found in rat and human astrocytes. [Yamada1991]					
678	M-24	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991 • M-24: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. [Yamada1991]					
679	M-25	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Yamada1991					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• M-25: Reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. [Yamada1991]					
680	M-28	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41					
		References Yamada1991					
		• M-28: Strongly reacted with a cellular 43-kd protein found in rat and human astrocytes as well as with gp41. [Yamada1991]					
681	M-29	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41					
		References Yamada1991					
		• M-29: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. [Yamada1991]					
682	M-36	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41					
		References Yamada1991					
		• M-36: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. [Yamada1991]					
683	M-4	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41					
		References Yamada1991					
		• M-4: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. [Yamada1991]					
684	M-6	gp160 (593–604)	gp41 (598–609)	LGIWGCSGKLIC		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41					
		References Yamada1991					
		• M-6: Unlike M-22, did not react to 43-kd protein found in rat and human astrocytes. [Yamada1991]					
685	polyclonal α598-609	gp160 (594–601)	gp41 (598–609)	GIWGCSGK		HIV-1 infection	human
		References Poumbourios1992					
		• alpha(598-609): Affinity purified from HIV-1+ plasma – immunodominant region, binds oligomer and monomer. [Poumbourios1992]					
686	1B8.env (1B8)	gp160 (594–604)	gp41 (594–605 HXB2)	GIWGCSGKLIC	no	HIV-1 infection	human (IgG2λ)
		References Gorny2004, Enshell-Seijffers2001, Banapour1987					
		Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization.					
		• 1B8B.env: Called 1B8. There are 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)					
		• 1B8.env: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. [Enshell-Seijffers2001]					
		• 1B8.env: Highly conserved epitope recognized by the majority of HIV-1 infected people – MAb does not neutralize. [Banapour1987] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)					
687	polyclonal	gp160 (594–609)	gp41 (601–616)	GIWGCSGKLICTTAVP	no	HIV-1 infection	human
		References Petrov1990					
		• Immunodominant and broadly reactive peptide. [Petrov1990]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
688	polyclonal	gp160 (595–607)	gp41 (600–612)	IWGCSGKLICTTA		HIV-1 infection	human (IgG)

References Belliard2003
Keywords rate of progression.
Country France.

- Sera from 101 slow progressors and 42 fast progressors were tested for responses to Tat peptides, and compared to responses to gp41 peptide 600-612, as anti-Tat antibodies had been shown by others to be elevated in slow progressors. Most patient sera react with this peptide, it is used in diagnostics. In this study, overall levels of Tat antibodies were not different in the two groups, however relative levels of antibodies to different Tat peptides and to this gp41 peptide were observed. [Belliard2003] (**rate of progression**)

689	clone 3	gp160 (597–606)	gp41 (597–606)	GCSGKLICTT	L	HIV-1 infection	human (IgG1)

References Gorny2004, Enshell-Seijffers2001, Cotropia1996, Cotropia1992, Broliden1989
Keywords antibody binding site definition and exposure, inter-clade comparisons, rate of progression, responses in children, review, variant cross-recognition or cross-neutralization.

- clone 3: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. clone 3 neutralized 3 diverse B clade TCLA strains and 3 primary O group strains. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- clone 3: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. [Enshell-Seijffers2001] (**variant cross-recognition or cross-neutralization**)
- clone 3: Inhibits replication of three diverse HIV-1 laboratory strains, as well as an AZT-resistant isolate. [Cotropia1996] (**variant cross-recognition or cross-neutralization**)
- clone 3: Core binding domain gcsgkLIC – lack of serological activity to this region correlates with rapid progression in infants ([Broliden1989]) [Cotropia1992]. [Broliden1989, Cotropia1992] (**antibody binding site definition and exposure**, **responses in children**, **rate of progression**)

690	4	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	mouse (IgG2b)

Vaccine *Vector/Type:* peptide *HIV component:* gp41
References Bizub-Bender1994, Oldstone1991

- 4: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – slightly more reactive with longer HIV-2 peptide NSWGCAFRQVC. [Oldstone1991]
- There is another MAb with this ID that reacts with integrase. [Bizub-Bender1994, Oldstone1991]

691	41-6	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	mouse (IgG2b)

Vaccine *Vector/Type:* peptide *HIV component:* gp41
References Oldstone1991

- 41-6: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – slightly more reactive with LGLIWGCSGKLIC and HIV-2 form NSWGCAFRQVC – disulfide bond between cysteines required. [Oldstone1991]

692	41-7	gp160 (598–604)	gp41 (605–611)	CSGKLIC	no	HIV-1 infection	human (IgG1κ)

References Enshell-Seijffers2001, Bugge1990

- 41-7: Monoclonal antibodies to this epitope have distinct phenotypes—41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial. [Enshell-Seijffers2001]
- 41-7: Sera from 6/6 HIV-1 positive, but no HIV-2 positive individuals, interfered with 41-7 binding – Ab does not neutralize. [Bugge1990]

693	68.1	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	mouse (IgM)

Vaccine *Vector/Type:* peptide *HIV component:* gp41

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Oldstone1991 • 68.1: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – cross-reactive with HIV-2 peptide CAFRQVC – more reactive with longer HIV-1 peptide LGLIWGCSGKLIC and HIV-2 peptide NSWGCAFRQVC. [Oldstone1991]					
694	68.11	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 68.11: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – cross-reactive with HIV-2 peptide CAFRQVC – more reactive with longer HIV-1 peptide LGLIWGCSGKLIC and HIV-2 peptide NSWGCAFRQVC. [Oldstone1991]					
695	75	gp160 (598–604)	gp41 (598–609)	CSGKLIC		Vaccine	rat (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **References** Oldstone1991 • 75: Stimulated by immunization with the peptide: LGLIWGCSGKLIC (aa 598-609) – poor cross-reactivity with HIV-2 peptide CAFRQVC – more reactive with longer HIV-2 peptide NSWGCAFRQVC. [Oldstone1991]					
696	polyclonal	gp160 (598–604)	gp41 (603–609)	CSGKLIC		HIV-1 infection	human
		References Enshell-Seijffers2001 • Monoclonal antibodies to this epitope have distinct phenotypes – 41-7 and 1B8.env were found to be not neutralizing, 2F11 possibly enhancing, and clone 3 beneficial – isolated mimotope-presenting phages corresponding to the immunodominant gp41 epitope CSGKLIC were used to study the diversity of polyclonal responses in 30 HIV+ sera, and all but one of the patients reacted showing distinctive variable polyclonal recognition patterns. [Enshell-Seijffers2001]					
697	105-732	gp160 (599–606)	gp41 (601–608 HAM112, O group)	KGRLICYT		Vaccine	mouse (IgG2bκ)
		Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160 **References** Scheffel1999 • 105-732: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – MAb 105-732 bound to two overlapping peptides. [Scheffel1999]					
698	3D6 (IAM 41-3D6)	gp160 (599–613)	gp41 (604–617 BH10)	SGKLICTTAVPWNAS	no	HIV-1 infection	human (IgG1κ)
		Ab type cluster I, immunodominant region **Research Contact** H. Katinger, Inst. Appl. Microbiol., Vienna, Austria and Viral Testing Systems, Houston, TX **References** Gorny2004, Finnegan2002, Cavacini1999, Cavacini1998a, Cavacini1998b, Kunert1998, Wisnewski1996, Stigler1995, Sattentau1995c, Chen1994b, He1992, Felgenhauer1990 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, kinetics, review, structure. • 3D6: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 3D6: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**)
- 3D6: Cavacini *et al.* note that both MAbs F223 and 3D6 are anti-HIV-1 Env MAbs that have an autoimmune response and that both use uses VH3 germline genes. [Cavacini1999]
- 3D6: Binds to the immunodominant region of gp41 – a strong homology between heavy variable domains of hu MAb 3D6 and MAb F20 was observed, these MAbs may define a human Ab clonotype. [Cavacini1998a] (**antibody sequence, variable domain**)
- 3D6: The complete V, J and D(H) domain was sequenced – in contrast the sequences of five neutralizing MAbs, 3D6 had very little somatic mutation, with homologies of 97-98% relative to germline genes. [Kunert1998] (**antibody sequence, variable domain**)
- 3D6: 3D6 is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- 3D6: Optimum peptide for binding 3D6 Fab was CSGKLICTTAVPW. [Stigler1995] (**antibody binding site definition and exposure**)
- 3D6: Called IAM 41-3D6: binding increased after pretreatment of infected cells with sCD4 – binding domain overlaps site that is critical for gp120-gp41 association. [Sattentau1995c] (**antibody binding site definition and exposure**)
- 3D6: This MAb binds to HIV gp41, and to a 43 kd protein found in human T, B and monocyte cell lines, proposed molecular mimicry. [Chen1994b]
- 3D6: Fab fragment crystal structure. [He1992] (**structure**)
- 3D6: Sequence of cDNA encoding V-regions. [Felgenhauer1990] (**antibody sequence, variable domain**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
699	F172-D8 (F172-D8, scFvD8)	gp160 (604–615)	gp41 (609–620)	CTTAVPWNASWS?			human

References Legastelois2000

- F172-D8: As an approach to intercellular immunization using a single-chain variable fragment, scFvD8 was constructed based on the MAb F172-D8, directed at a loop in gp41 between the two heptad repeat regions – intracellular scFvD8 expression decreased gp160 expression and a scFvD8 transfected cell line did not support infection by HIV-1 Ba-L or primary isolates. [Legastelois2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
700	D50	gp160 (632–655)	gp41 (642–665)			Vaccine	mouse

Vaccine *Vector/Type:* protein *HIV component:* dimeric Env
Ab type cluster II **Research Contact** Patricia Earl and Christopher Broder, NIH
References deRosny2004, Srivastava2002, Yang2000, Earl1997, Richardson1996, Binley1996, Earl1994
Keywords antibody binding site definition and exposure, antibody generation.

- D50: The MAb 2F5 binds to the C-heptad and is neutralizing, but the MAb D50 binds to the C-heptad and is not neutralizing. 2F5 binds preferentially to native gp41 prior to receptor activation. D50 prefers the triggered form after receptor activation. Trapped fusion-intermediates suggest 2F5 remains present shortly after gp120 triggering by CD4, but may be lost by the time the six-helix bundle is formed. D50 binds equally to the fusion-intermediate and six-helix bundle. 2F5 neutralization seems to block a later step of the fusion process. [deRosny2004] (**antibody binding site definition and exposure**)
- D50: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – D50 was used to capture the o-gp140 for ELISA to test the antigencity of o-gp140 using a panel of well characterized MAbs. [Srivastava2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D50: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000] (**antibody binding site definition and exposure**) • D50: Found to bind to a linear peptide, between Env amino acids 642-655 – can be blocked by the conformation dependent MAbs D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45 – the region is in the immunogenic cluster two region – reactive with 9/10 HIV-1 strains tested, all except HIV-1 ADA, in which the change E659D and E662A may result in the loss of binding (ELLE to DLLA) [Earl1997] (**antibody binding site definition and exposure**) • D50: Richardson suggests this is a linear gp41 epitope. [Richardson1996] (**antibody binding site definition and exposure**) • D50: Thought to be a discontinuous epitope recognizing residues between 649-668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding. [Binley1996] (**antibody binding site definition and exposure**) • D50: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)				
701	5-21-3	gp160 (642–665)	gp41 (642–665 HXB2)	IHSLIEESQNQQEKNEQELLELDK		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp41 **References** Scheffel1999, Hunt1990 • 5-21-3: Binds group M gp41, used as a control in a study of group O MAbs. [Scheffel1999] • 5-21-3: Recognizes a contiguous, conformation-dependent epitope in a hydrophilic region. [Hunt1990]					
702	120-16 (SZ-120.16)	gp160 (644–663)	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL	no	HIV-1 infection	human (IgG2κ)
		References Wisnewski1996, Forthal1995, Eddleston1993, Robinson1991, Xu1991, Tyler1990, Robinson1990b, Andris1992 • 120-16: 120-16 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] • 120-16: No neutralizing activity, both ADCC and viral enhancing activity. [Forthal1995] • 120-16: Called SZ-120.16. [Eddleston1993] • 120-16: Synergizes with huMAb 50-69 *in vitro* to enhance HIV-1 infection. [Robinson1991] • 120-16: Less reactive region than AVERY region – most Abs involving this region bound conformational epitopes, this was the only linear one. [Xu1991] • 120-16: Potent ADCC (in contrast to MAb 98-43, gp41(579-604)) [Tyler1990] • 120-16: Antibody dependent enhancement (ADE) of HIV-1 IIIB infectivity, synergistically enhanced by MAb V10-9. [Robinson1990b]					
703	98-6 (SZ-98.6, 98.6, 98-6D)	gp160 (644–663)	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL	no	HIV-1 infection	human (IgG2κ)
		Ab type alpha-helical hairpin intermediate, cluster II **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Gorny2004, Finnegan2002, Follis2002, Golding2002b, Verrier2001, Taniguchi2000, Nyambi2000, Gorny2000a, Gorny2000b, Nyambi1998, Hioe1997b, Wisnewski1996, Sattentau1995c, Manca1995a, Forthal1995, Chen1995, Laal1994, Tani1994, Spear1993, Eddleston1993, Xu1991, Robinson1991, Sattentau1991, Andris1992, Tyler1990, Robinson1990b, Till1989, Gorny1989, Pinter1989 **Keywords** ADCC, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, binding affinity, complement, enhancing activity, immunotoxin, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization. • 98-6: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have any neutralizing activity. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 98-6: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**)
- 98-6: Called 98-6D. Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**)
- 98-6: NIH AIDS Research and Reference Reagent Program: 1240.
- 98-6: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation. [Golding2002b] (**antibody binding site definition and exposure**)
- 98-6: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6—six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D, while six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 98-6: The fusogenic form of gp41 is recognized by 98-6, and the epitope is a conformational epitope formed by the interaction of two regions of gp41 which form an alpha-helical bundle. [Taniguchi2000] (**antibody binding site definition and exposure**)
- 98-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested against 5 isolates, but 98-6 did not bind to these isolates. [Nyambi2000] (**inter-clade comparisons**)
- 98-6: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**)
- 98-6: 98-6 and 2F5 both bind to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, and to C43 alone but not to N51 alone – 98-6 and 2F5 have comparable affinities for C43, but 98-6 has a higher affinity for the complex and the binding of 98-6 is not inhibited by N51. [Gorny2000b] (**antibody binding site definition and exposure**, **binding affinity**)
- 98-6: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade. [Nyambi1998] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 98-6: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**) • 98-6: 98-6 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**) • 98-6: Preferentially recognizes oligomeric form of gp41 – enhanced binding to HIV-1 infected cells at 37 degrees relative to 4 degrees – addition of sCD4 enhances binding. [Sattentau1995c] (**antibody binding site definition and exposure**) • 98-6: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. [Manca1995a] • 98-6: No neutralizing activity, positive ADCC activity, and no viral enhancing activity. [Forthal1995] (**ADCC**, **enhancing activity**) • 98-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. [Chen1995] (**antibody binding site definition and exposure**) • 98-6: Epitope described as cluster II, 644-663, conformational – does not neutralize IIIB or synergize neutralization by anti-V3 MAb 447-52D or by CD4 BS MAbs. [Laal1994] (**antibody binding site definition and exposure**, **antibody interactions**, **variant cross-recognition or cross-neutralization**) • 98-6: This MAb was expressed as a surface anti-gp41 monoclonal antibody receptor for gp41 on a CD4-negative B-cell line. Transfected cells could bind HIV Envelope, but could not be infected by HIV-1. When CD4 delivered by retroviral constructs was expressed on these cells, they acquired the ability to replicate HIV-1, and sIg/gp41 specifically enhanced viral replication. [Tani1994] • 98-6: Did not mediate deposition of complement component C3 on HIV infected cells, binding enhanced by sCD4. [Spear1993] (**complement**) • 98-6: Called SZ-98.6 – binds to a conformational domain within aa 644-663 of gp41, and reacts with astrocytes, as do 167-7 and ND-15G1. [Eddleston1993] (**antibody binding site definition and exposure**) • 98-6: Appeared to be specific for a conformational or discontinuous epitope. [Xu1991] (**antibody binding site definition and exposure**) • 98-6: No neutralizing or enhancing activity. [Robinson1991] (**enhancing activity**) • 98-6: Two fold increase in binding to gp120 in the presence of bound sCD4. [Sattentau1991] (**antibody binding site definition and exposure**) • 98-6: Serves as target for antibody-dependent cellular cytotoxicity, ADCC. [Tyler1990] (**ADCC**) • 98-6: No neutralizing or enhancing activity for HIV-1 IIIB. [Robinson1990b] (**enhancing activity**) • 98-6: Toxic to HIV-infected T cells (H9) and monocytes (U937) when coupled to deglycosylated A chain of ricin. [Till1989] (**immunotoxin**) • 98-6: Kills HIV-infected cells when coupled to deglycosylated ricin A chain. [Gorny1989] (**immunotoxin**) • 98-6: Reacts preferentially with gp160 oligomer, compared to gp41 monomer. [Pinter1989] (**antibody binding site definition and exposure**)					
704	167-7 (SZ-167.7)	gp160 (644–663) **Ab type** cluster II **References** Eddleston1993, Xu1991	gp41 (644–663)	SLIEESQNQQEKNEQELLEL		HIV-1 infection	human (IgG2λ)
		• 167-7: Called SZ-167.7 – binds to a conformational domain within aa 644-663 of gp41, and reacts with astrocytes, as do 98-6 and ND-15G1. [Eddleston1993] • 167-7: Specific for a conformational epitope. [Xu1991]					
705	ND-15G1 (ND-15GI)	gp160 (644–663) **Ab type** cluster II **References** Gorny2004, Eddleston1993 **Keywords** antibody binding site definition and exposure, review.	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL		HIV-1 infection	human (IgG1κ)
		• ND-15G1: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• ND-15G1: Mapped to the conformational epitope within aa 644-663, and reacts with astrocytes, as do 98-6 and 167-7. [Eddleston1993] (**antibody binding site definition and exposure**)					
706	167-D (167)	gp160 (644–663)	gp41 (644–663 HXB2)	SLIEESQNQQEKNEQELLEL	no	HIV-1 infection	human (IgG1λ)
		Ab type cluster II, six-helix bundle **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU, NY **References** Gorny2004, Golding2002b, Nyambi2000, Gorny2000a, Gorny2000b, Manca1995a, Forthal1995, Spear1993 **Keywords** ADCC, antibody binding site definition and exposure, complement, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 167-D: Called 167. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • 167-D: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation. [Golding2002b] (**antibody binding site definition and exposure**) • 167-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs. [Nyambi2000] (**inter-clade comparisons**) • 167-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**) • 167-D: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. [Gorny2000b] (**antibody binding site definition and exposure**) • 167-D: Virions complexed to gp41 Ab facilitate presentation of p66 RT epitopes to Th cells. [Manca1995a] • 167-D: No neutralizing activity, no ADCC activity, and no viral enhancing activity. [Forthal1995] (**ADCC**, **enhancing activity**, **variant cross-recognition or cross-neutralization**) • 167-D: Did not mediate deposition of complement component C3 on HIV infected cells – complement mediated virolysis of MN and IIIB in the presence of sCD4. [Spear1993] (**complement**)					
707	2F5 (IAM 2F5, IAM-41-2F5, IAM2F5, c2F5)	gp160 (656–671)	gp41 (662–667 BH10)	NEQELLELDKWASLWN	L P	HIV-1 infection	human (IgG3κ)
		Ab type adjacent to cluster II, C-term **Research Contact** Hermann Katinger, Institute of Applied Microbiology, Vienna, or Polymun Scientific Inc., Vienna, Austria, or Viral Testing Systems Corp., Houson TX					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References deRosny2004, Zwick2004, Gorny2004, Wolbank2003, Ohagen2003, Montefiori2003, McGaughey2003, Kitabwalla2003, Wang2003, Richman2003, Mascola2003a, Hart2003, Ferrantelli2003, Dey2003, Binley2003, Stiegler2002, Li2002, Huang2002, Gorry2002, Finnegan2002, Follis2002, Cavacini2002, Bures2002, Liu2002, Ferrantelli2002, Zhang2002, Kunert2002, Mascola2002, Grundner2002, Xiang2002b, Clerici2002a, Joyce2002, Chakrabarti2002, Xu2002, Ho2002, Tian2002, Schulke2002, Golding2002b, Srivastava2002, Armbruster2002, Root2001, Xu2001, Hofmann-Lehmann2001, Stiegler2001, Verrier2001, Spenlehauer2001, Parker2001, Zeder-Lutz2001, Moore2001, Barnett2001, Mascola2001, Zwick2001c, Zwick2001b, York2001, Tumanova2001, Kolchinsky2001, Dong2001, Si2001, Yang2000, Xiao2000c, Coeffier2000, Sanhadji2000, Pai2002, Park2000, Nyambi2000, Lu2000b, Lu2000c, Liao2000, Kunert2000, Gorny2000b, Robert-Guroff2000, Baba2000, Mascola2000, Mascola1999, Parren1999, Muhlbacher1999, Beddows1999, Poignard1999, Montefiori1999, Frankel1998, Kunert1998, Geffin1998, Parren1998b, Jiang1998, Li1998, Takefman1998, Ernst1998, Fouts1998, Trkola1998, Yang1998, Parren1998a, Connor1998, Mondor1998, Andrus1998, Gorny1997, Earl1997, Burton1997, Ugolini1997, Turbica1997, Stamatatos1997, Mascola1997, Moore1997, Kessler II1997, Li1997, Mo1997, D'Souza1997, Schutten1997, Purtscher1996, Stoiber1996, McKeating1996b, Pincus1996, Conley1996, Sattentau1996, Poignard1996b, McKeating1996a, Calarota1996, Kessler1995, Neurath1995, Moore1995b, Sattentau1995c, Trkola1995, D'Souza1995, Beretta1994, Muster1994, Chen1994b, Thali1994, Conley1994b, D'Souza1994, Buchacher1994, Laal1994, Purtscher1994, Klasse1993a, Allaway1993, Muster1993, Buchacher1992

Keywords acute infection, antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, assay development, autologous responses, binding affinity, brain/CSF, co-receptor, complement, escape, HIV exposed persistently seronegative (HEPS), immunoprophylaxis, immunotherapy, immunotoxin, inter-clade comparisons, isotype switch, kinetics, mother-to-infant transmission, mucosal immunity, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization.

- 2F5: This paper reviews MAbs that bind to HIV-1 Env. 2F5 binds to a region of gp41 proximal to cluster II (aa 662-676), neighboring the binding site of the broadly neutralizing MAb 4E10 and of neutralizing Fab Z13. 2F5 is broadly neutralizing. [Gorny2004] (**review**)
- 2F5: The MAb 2F5 binds to the C-heptad and is neutralizing, but the MAb D50 binds to the C-heptad and is not neutralizing. 2F5 binds preferentially to native gp41 prior to receptor activation. D50 prefers the triggered form after receptor activation. Trapped fusion-intermediates suggest 2F5 remains present shortly after gp120 triggering by CD4, but may be lost by the time the six-helix bundle is formed. D50 binds equally to the fusion-intermediate and six-helix bundle. 2F5 neutralization seems to block a later step of the fusion process, but it does not inhibit binding of NC-1, a MAb specific for the six-helix bundle, so it does not prevent formation of the six-helix bundle. The results are most consistent with 2F5 inhibiting a post-fusion-intermediate step. [deRosny2004] (**antibody binding site definition and exposure**, **antibody interactions**)
- 2F5: The broadly neutralizing antibodies 2F5 and 2G12 were class-switched from IgG to IgA and IgM isotypes. Neutralizing potency was increased with valence for 2G12 so the IgM form was most potent, but for 2F5 the IgG form was most potent. Eight primary isolates were tested including two subtype A isolates. The polymeric IgM and IgA Abs, but not the corresponding IgGs, could interfere with HIV-1 entry across a mucosal epithelial layer, although they were limited in a standard neutralization assay. All isotypes could interact with activated human sera, presumably through complement, to inhibit HIV replication. [Wolbank2003] (**complement**, **isotype switch**, **variant cross-recognition or cross-neutralization**, **mucosal immunity**, **inter-clade comparisons**)
- 2F5: The antiviral response to intravenously administered MAbs 2F5 and 2G12 was evaluated in 7 HAART-naÃ¯ve asymptomatic HIV-1 infected patients during a treatment period of 28 days. MAb therapy reduced plasma HIV RNA in 3/7 patients during the treatment period, and transiently reduced viral load in two more. CD4 counts were up in 3/7 through day 28, and transiently increased in three more. Vigorous complement activation was observed after 48/56 Ab infusions. Before treatment, 2F5 neutralized isolates from five patients and no escape was observed during treatment. [Stiegler2002] (**complement**, **variant cross-recognition or cross-neutralization**, **escape**, **immunotherapy**)
- 2F5: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. 2F5 recognized most variants from 3/4 individuals by gp41 WB; the 4th individual had the ELDKWA variant Aldkwa in all three isolates. The other single Env that was not recognized carried eldRwa. [Ohagen2003] (**brain/CSF**, **escape**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2F5: AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessaton of therapy, which then declined to a low level. The polylconal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. [Montefiori2003] (**acute infection**, **escape**)
- 2F5: Cyclic peptides ELLELDKWASLW that adopt constrained beta-turn conformation of the 2F5 epitope beta-turn in the complexed crystal structure were synthesized and optimize 2F5 binding affinity. This peptide elicts high titer peptide-specific immune responses in guinea pigs that do not neutralize; the authors propose this may be the result of a short CDR3 loop in guinea pigs. [McGaughey2003] (**antibody binding site definition and exposure**, **vaccine antigen design**, **binding affinity**, **structure**)
- 2F5: A polyepitope vaccine was designed based on three repeats of the 2F5 core epitope ELDKWA combined with the V3 region peptide GPGRAFY. Abs raised in mice could recognize the peptides, sgp41, and CHO-WT cells that expressed HIV-1 Env on their surface. [Li2002] (**vaccine antigen design**)
- 2F5: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. [Kitabwalla2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- 2F5: A mouse MAb was raised against a variant of ELDKWA core epitope of the NAb 2F5, eldEwa, derived from the 2F5 neutralization resistant variant MVP5180. 2F5 does not bind to the variants eldEwa, elNkwa (B.TH.TH936705) or elEkwa, while 14D9 binds only to eldEwa and not ELDKWA. The eldEwa variant is common in the HIV-1 O group. [Huang2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 2F5: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. [Wang2003] (**vaccine antigen design**, **review**)
- 2F5: Most plasma samples of patients from early infection had NAb responses to early autologous viruses, and NAbs against heterologous strains tended to be delayed. Serial plasma samples were tested against serial isolates, and neutralization escape was shown to be rapid and continuous throughout infection. Autologous neutralization-susceptible and resistant viruses from four patients were tested for susceptability to neutralizing Ab responses using MAbs 2G12, IgG1b12 and 2F5. No correlation was established, all viruses tested were susceptible to at least one of the neutralizing MAbs. Two patients that did not have an autologous NAb response also did not evolve changes in susceptibility to these MAbs, while one patient with a pattern of autologous neutralization and escape acquired a 2G12 sensitive virus at month 6, and lost IgG1b12 sensitivity at month 21. [Richman2003] (**autologous responses**, **acute infection**, **escape**)
- 2F5: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. [Dey2003]
- 2F5: UK1-br and MACS2-br are R5 isolates derived from brain tissue samples from AIDS patients with dementia and HIV-1 encephalitis; both are neurotropic, but only UK1-br induced neuronal apoptosis and high levels of syncytium formation in macrophages. UK1-br Env had a greater affinity for CCR5 than MACS-br, and required low levels of CCR5 and CD4 for cell-to-cell fusion and single round infection. PBMC infected with UK1-br and MACS2-br virus isolates were resistant to neutralization by MAb 2G12. UK1-br was more sensitive than MACS2-br to IgG1b12, 2F5 and CD4-IgG2 neutralization. This pattern of Ab reactivity was similar to the to CD4-independent varient ADA197N/K, and thought to result from conformational changes which better expose the CCR5 binding regions, although the loss of the particular N-linked glycosylation site in the V1V2 stem region of ADA was experimentally shown to not be responsible for the the CD4-independent phenotype of UK1-br. [Gorry2002] (**brain/CSF**, **co-receptor**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2F5: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. 2F5 behaved very differently than these non-neutralizing antibodies: it bound to Env in the absence of target cells, and it was distributed evenly all over the cell surface, not localized in fusion domains. It did not interact with cells that exhibited cytoplasmic mixing. 2F5 was unusual in that it exhibited temperature dependence, and did not interact below 19 degrees C, in contrast to 2G12, M77 98-6 and IgG1b12 which bound strongly at temperatures ranging between 4-37 degrees. The authors suggest the temperature dependence of 2F5 may be due to encreased flexibility of the Envelope spike at warmer temperatures facilitating epitope exposure. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**)
- 2F5: A complex of the epitope peptide ELDKWAS bound to 2F5 was crystalized, and the peptide was found to interact with amino acids near the base of the very long (22 residue) CDR 3H region of the Ab. Ala substitution of the CDR H3 region confirmed the importance of these sites near the base of the H3 loop for interaction with the epitope in the context of intact gp41 as well as the peptide. A Phe at the apex of the loop was not located directly in the binding site, however binding of 2F5 to the epitope was very sensitive to non-conservative substitutions in this position (F100G, F100H, and F100R); these diminished both binding affinity and 2F5 neutralization, suggesting a role for the very long CDR 3H region. The authors suggest that particularly long CDR H3 regions may be a common feature of HIV-1 NAbs, based on the 22 residues in H3 of 2F5, the 18 H3 residues in b12, and the 22 H3 residues in X5. They express concern that because small animals like mice are be unable to elicit Ab responses with such long H3s, they may be poor model systems for HIV vaccine studies. [Zwick2004] (**antibody binding site definition and exposure**, **antibody interactions**, **antibody sequence, variable domain**, **structure**)
- 2F5: This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. [Mascola2003a] (**immunoprophylaxis**, **review**)
- 2F5: This study investigates the effects of glycosylation inhibitors on the binding between HIV-1 gp120 and mannose-binding lectin (MBL). Mannosidase I inhibitor deoxymannojirimycin (dMM) inhibits formation of complex and hybrid N-linked saccharides and yields virus with more mannose residues. dMM added during viral production significantly enhanced the binding 2F5 and 2G12, but not IgG1b12 in a viral capture assay. [Hart2003] (**antibody binding site definition and exposure**)
- 2F5: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. [Ferrantelli2003] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)
- 2F5: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate, with the exception of F240 which bound both equally well, which captured more virus than any other human MAb tested, and didn't neutralize either isolate. F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 and the gp41 MAb 2F5 for both R5X4 and R5 isolates. F240 also enhanced neutralization of the R5X4 isolate by 2F5, but had no effect on R5 virus. Anti-V3 MAb B4a1 did not impact 2F5 neutralization. [Cavacini2002] (**antibody binding site definition and exposure**, **antibody interactions**, **co-receptor**)
- 2F5: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other MAb against gp41 tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**)
- 2F5: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 NAbs 2F5 and 4E10 are able to potently neutralize the SOS pseudovirion post-attachment, although 2F5 performed relatively poorly in the pre-attachment assay, a further support for previous studies that indicated it does not bind well to native Env, and may bind best after the virus is attached to cells. [Binley2003] (**vaccine antigen design**)

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- 2F5: IgG1b12 neutralized many South African (5/8) and Malawian (4/8) clade C primary HIV-1 isolates, being more effective than 2F5 which neutralized only two Malawian and no South African isolates. 2G12 did not neutralize any of the 16 isolates. [Bures2002] (**inter-clade comparisons**)
- 2F5: NIH AIDS Research and Reference Reagent Program: 1475.
- 2F5: UK Medical Research Council AIDS reagent: ARP3063.
- 2F5: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. [Liu2002] (**immunoprophylaxis**, **vaccine antigen design**, **review**)
- 2F5: Review of NAbs that notes that 2F5 alone or in combination with other MAbs can protect some macaques against SHIV infection, that it is safe and well tolerated in humans, and that illustrates gp41's conformational change and exposure of the 2F5 epitope in the transient pre-hairpin form. [Ferrantelli2002] (**immunoprophylaxis**, **review**)
- 2F5: A 2F5 anti-idiotype murine MAb Ab2/3H6 was developed that blocks 2F5 binding to a synthetic epitope peptide and to gp160 in an ELISA competition assay – Ab2/3H6 diminished the neutralizing potency of 2F5 – Ab2/3H6 Fab fragments were capable of inducing neutralizing Abs and 2F5-epitope specific responses in immunized B6D2F1 mice. [Kunert2002] (**vaccine antigen design**)
- 2F5: Rhesus macaques were better protected from vaginal challenge with SHIV89.6D (MAb 2G12, 2/4; MAbs 2F5/2G12, 2/5; and HIVIG/2F5/2G12, 4/5 infected) than from intravenous challenge (MAb 2G12, 0/3; MAbs 2F5/2G12, 1/3; and HIVIG/2F5/2G12, 3/6 infected)– the animals that were infected by vaginal challenge after Ab infusion had low or undetectable viral RNA levels and modest CD4 T-cell decline. [Mascola2002] (**immunoprophylaxis**)
- 2F5: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads (except for the YU2 form that doesn't bind 2F5)—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface. [Grundner2002] (**vaccine antigen design**)
- 2F5: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b]
- 2F5: A combination of MAbs 2F5 and 2G12 given in multiple infusions was found to be safe and well tolerated even in high doses in a phase I study of seven HIV-1 infected healthy volunteers—the median elimination half-life was 7.94 days for 2F5, and 16.48 for 2G12—no anti-2F5 or anti-2G12 IgM or IgG responses were detected—although there was some transient increases, overall plasma viral RNA levels decreased in 6/7 volunteers, by a median of 0.62 log_10 [Armbruster2002] (**immunotherapy**)
- 2F5: Six sera from HIV-exposed uninfected individuals(EU) had IgA neutralizing activity dominated by recognition of a distinctive epitope within gp41, QARILAV – sera of QAFILAV-immunized BALB/c mice was neutralizing with the dose-dependent behavior similar to 2F5. [Clerici2002a] (**HIV exposed persistently seronegative (HEPS)**)
- 2F5: DP178 is a peptide derived from the C-term heptad repeat of gp41 that is a potent inhibitor of viral-mediated fusion—it contains the 2F5 epitope but fails to stimulate 2F5-like NAbs upon immunization—the peptide was extended to force an increase in helicity, and the modified peptide had a increase in affinity for 2F5, but upon guinea pig immunization although high peptide-specific Ab titers were achieved the sera were incapable of viral neutralization—the authors propose that 2F5 may bind with low affinity to a maturation intermediate, which may account for its breadth and why it is hard to recreate the epitope, but also suggests that the high concentrations required for neutralization are not relevant *in vivo* [Joyce2002] (**antibody binding site definition and exposure**)
- 2F5: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. [Chakrabarti2002] (**vaccine antigen design**)

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- 2F5: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. [Xu2002] (**antibody interactions**, **immunoprophylaxis**, **inter-clade comparisons**)
- 2F5: ELDKWAS was embedded into a beta-turn-like conformational site on a framework of an antibody specific for human leukocyte antigen HLA-DR – this construct was recognized by 2F5, and is suggested as an adjuvant-independent vaccine candidate. [Ho2002] (**vaccine antigen design**)
- 2F5: Expanding the minimal epitope ELDKWA to an end-capped, linear nonapeptide, Ac-LELDKWASL-amide attained maximal affinity within a set of native gp41-sequence peptides – scanning single residue substitutions confirmed that essential recognition requirements were the central DKW core sequence and the importance of the terminal Leu residues for high-affinity binding – high specificity binding pockets at central Lys and Trp side-chains and an absolute requirement for the carboxylate group of the Asp side chain were found – the nine residue fragment flanked by pairs of Ser and constrained by a disulfide bridge had high affinity for 2F5. [Tian2002] (**antibody binding site definition and exposure**)
- 2F5: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – SOS gp140-2F5-IgG1b12 formed multiple ring structures composed of two SOS gp140 proteins bridged by two Ab molecules, while 2F5 and 2G12 formed extended chains rather than closed rings. [Schulke2002] (**vaccine antigen design**)
- 2F5: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. [Golding2002b]
- 2F5: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 2F5 recognized o-gp140. [Srivastava2002] (**vaccine antigen design**)
- 2F5: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. [Xu2001] (**antibody interactions**)
- 2F5: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline. [Hofmann-Lehmann2001] (**immunoprophylaxis**)
- 2F5: 4E10 binds proximal to 2F5 and neutralizes primary isolates of clades A, B, C, D, and E – viruses that were resistant to 2F5 were neutralized by 4E10 and vice versa. [Stiegler2001] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 2F5: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 2F5: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12. [Spenlehauer2001] (**assay development**)
- 2F5: Matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) in combination with proteolytic protection was used to identify the functional epitope for MAb 2F5, NEQELLELDKWASLWN, in the disulfide bond associated gp120/gp41 protein SOS-gp140 (JRFL) – this minimal epitope is much larger than the ELDKWA core epitope previously defined by peptide ELISA, and this could help explain why ELDKWA-peptides are poor immunogens in terms of eliciting a 2F5-like antibody response. [Parker2001] (**antibody binding site definition and exposure**)

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- 2F5: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three mAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers. [Zeder-Lutz2001] (**antibody interactions**)
- 2F5: Moore and colleagues review the data concerning the lack of a clear relationship between genetic subtype and serotype – 2F5 is considered in some detail, as it represents a rare vulnerability from the neutralizing antibody perspective, although while it is apparently linear, attempts to present the peptide to the immune system have failed to elicit neutralizing Abs. [Moore2001] (**review**, **inter-clade comparisons**)
- 2F5: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines. [Mascola2001] (**review**)
- 2F5: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2. [Zwick2001c] (**antibody interactions**)
- 2F5: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – the minimal 2F5 epitope is determined to be EQELLELDKWASLW, based on screening a gp160 fragment expression library, longer than previous studies – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses. [Zwick2001b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 2F5: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001] (**variant cross-recognition or cross-neutralization**)
- 2F5: A phage peptide library was screened with MAb 2F5, and from the peptides that bound the amino acids DKW were found to be most critical for binding – the mimetic peptide RDWSFDRWSLSEFWL elicited a cross-reactive Ab response to gp41 when used to immunize rabbits. [Tumanova2001]
- 2F5: A peptide called 5-Helix was designed that binds to the C-peptide region of gp41 – 5-Helix is a potent inhibitor of HIV-1 entry that binds immediately COOH-terminal to the C-peptide region targeted by 5-Helix – the conformation of the bound 2F5 epitope is a hairpin turn. [Root2001]
- 2F5: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to antibody 2F5. [Kolchinsky2001] (**variant cross-recognition or cross-neutralization**)
- 2F5: ELNKWA is an escape variant not recognized by the broadly neutralizing MAb 2F5, which recognizes the core epitope ELDKWA – Abs were raised against the peptide escape variant CGELNKWAGELNKWA linked to KLH carrier – these polyclonal antibodies, like the monoclonal antibody TH-Ab1 also raised to ELNKWA, could recognize ELDKWA and escape mutant peptide epitopes ELEKWA and ELDEWA. [Dong2001] (**variant cross-recognition or cross-neutralization**)
- 2F5: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. [Si2001]
- 2F5: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) – 2F5 did not bind efficiently to these constructs, presumably because of the YU2 strain has a substitution in the 2F5 epitope (ALDKWA instead of ELDKWA) [Yang2000] (**vaccine antigen design**, **variant cross-recognition or cross-neutralization**)

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- 2F5: 2F5 or sCD4-IgG chimeric immunoadhesin were transferred into 3T3 cells, incorporated into a collagen structure called the neo-organ, and transplanted into SCIDhu mice that were then challenged with MN or LAI – the continuous production of the therapeutic molecules in this context resulted in dramatic reduction of viral load. [Sanhadji2000] (**immunotherapy**)
- 2F5: ELDKWAS co-crystallized bound to the Fab' 2F5 fragment showed the epitope peptide in a type I beta-turn conformation. [Pai2002] (**structure**)
- 2F5: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs. [Nyambi2000] (**inter-clade comparisons**)
- 2F5: ELDKWA peptide vaccine study. [Lu2000b] (**vaccine antigen design**)
- 2F5: ELDKWA peptide vaccine study. [Lu2000c] (**vaccine antigen design**)
- 2F5: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002]
- 2F5: Low levels of anti-ELDKWA antibodies are observed in HIV-1+ individuals, so a C-domain P2 peptide linked to a carrier was used to immunize mice and rabbits, and stimulated a high-level anti-ELDKWA response. [Liao2000] (**vaccine antigen design**)
- 2F5: 2F5 is a candidate for immunotherapy, but generally IgG1 has a longer half life in humans than IgG3, so the isotype was switched – rec CHO-derived MAb 2F5 IgG1kappa and hybridoma-derived MAb 2F5 IgG3kappa displayed identical specificity, *in vitro* function, and epitope (ELDKWA) – it remains to be determined if isotype switching will prolongs beta-clearance. [Kunert2000] (**immunotherapy**)
- 2F5: MAbs 98-6 and 2F5 both bind to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, and to C43 alone but not to N51 alone – 98-6 and 2F5 have comparable affinities for C43, but 98-6 has a higher affinity for the complex and 2F5 may bind to an epitope of C43 that is directly involved with complex formation –and IgG1 rec form of the Ab was used in this study. [Gorny2000b] (**antibody binding site definition and exposure**)
- 2F5: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge. [Robert-Guroff2000] (**review**)
- 2F5: Paper uses IgG1 form of 2F5 – a triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 4.2 +/- 0.8 days. [Baba2000] (**immunoprophylaxis**)
- 2F5: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and co-workers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa. [Mascola2000] (**immunoprophylaxis**, **mucosal immunity**)
- 2F5: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline. [Mascola1999] (**immunoprophylaxis**)
- 2F5: Review of the neutralizing Ab response to HIV-1. [Parren1999] (**review**)
- 2F5: In a study of 116 HIV-1+ individuals, Ab reactivity to a peptide encompassing the ELDKWA peptide decreased in CDC stage C patients compared with stage A patients, and longitudinal studies showed a decline in 6/8 patients, while overall Ab reactivity to rec soluble gp160 stayed constant. [Muhlbacher1999]

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- 2F5: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs. [Poignard1999] (**immunotherapy**)
- 2F5: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo*. [Montefiori1999] (**review**)
- 2F5: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs. [Beddows1999]
- 2F5: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. [Frankel1998] (**mucosal immunity**)
- 2F5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – in contrast to Geffin98, where multiple pediatric sera were found to compete with 2F5, cross-competition was noted to be very rare in sera from HIV+ adults – Kunert *et al.* propose that because there is a binding site of human complement factor H which overlaps the 2F5 binding site, it may generally be masked from the immune system – 2F5 also has a remarkably long CDR3 loop of 22 amino acids, and this region could not be readily assigned to any described D(H) fragment, leading to the suggestion of recombination of two fragments from novel regions. [Kunert1998] (**antibody sequence, variable domain**)
- 2F5: The natural immune response to the epitope of 2F5, ELDKWA, was studied in perinatally infected children and levels of reactivity to this epitope were correlated with absolute CD4 numbers over time and health status – 3/10 children who had no antibody reactivity to ELDKWA had substitutions in the epitope (ALDKWA, ELDQWA, and KLDKWA) – 2F5 competed with the ELDKWA-reactive sera depending on the serum titer. [Geffin1998]
- 2F5: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope. [Parren1998b] (**variant cross-recognition or cross-neutralization**)
- 2F5: Used as a control in the study of anti-gp41 MAb NC-1 – 2F5 does not react with HIV-2 gp41 or gp160. [Jiang1998] (**variant cross-recognition or cross-neutralization**)
- 2F5: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998] (**antibody interactions**)
- 2F5: Induces complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML. [Takefman1998] (**complement**)
- 2F5: The ELDKWA epitope was inserted into the antigenic site B of influenza hemagglutinin and expressed on baculovirus infected insect cells, flanked by 3 additional random amino acids, xELDKWAxx – FACS was used to isolate the clone that displayed the epitope with the most markedly increased binding capacity for 2F5, to identify particularly specific immunogenic constructs – PELDKWAPP was a high affinity form selected by FACS. [Ernst1998] (**vaccine antigen design**)
- 2F5: Points out that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity. [Fouts1998]
- 2F5: A wide range of neutralizing titers was observed that was independent of co-receptor usage – 2F5 was the most potent of the MAbs tested. [Trkola1998] (**variant cross-recognition or cross-neutralization**)
- 2F5: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998] (**assay development**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2F5: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. [Connor1998] (**variant cross-recognition or cross-neutralization**)
- 2F5: This MAb and the results of [Ugolini1997] are discussed – the authors propose that an Ab bound to gp41 would typically project less from the surface of the virion and so be unable to interfere with attachment [Parren1998a]. [Parren1998a, Ugolini1997] (**review**)
- 2F5: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect delivered 4 hours post infection. [Andrus1998] (**immunoprophylaxis**)
- 2F5: This review summarizes results about 2F5: it binds extracellularly, near the transmembrane domain, it is the only gp41 MAb that is neutralizing, it reacts with many non-B clade viruses and has a paradoxically weak binding to virus, given the neutralizing titers. [Burton1997] (**review**)
- 2F5: The only MAb out of a large panel to show no correlation between viral binding inhibition and neutralization. [Ugolini1997]
- 2F5: Used to standardize polyclonal response to CD4 BS. [Turbica1997]
- 2F5: Using concentrations of Abs achievable *in vivo*, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates. [Mascola1997] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 2F5: Binding of anti-gp120 MAbs IgG1b12 or 654-30D does not mediate significant exposure of the gp41 epitopes for MAbs 2F5 and 50-69. [Stamatatos1997] (**antibody interactions**)
- 2F5: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes. [Moore1997] (**review**)
- 2F5: IgG1b12 was more potent with greater breadth than MAb 2F5 in an infection reduction assay including 35 primary isolates. [Kessler II1997] (**variant cross-recognition or cross-neutralization**)
- 2F5: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2F5 has synergistic response with MAbs 694/98-D (anti-V3), 2G12, b12, and F105. [Li1997] (**antibody interactions**)
- 2F5: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy. [Mo1997] (**antibody interactions**)
- 2F5: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – the isolates with no 2F5 neutralizing susceptibility had the sequences ALGQWA or ELDTWA instead of EDLKWA – 7/9 primary isolates were neutralized, and ALDKWQ and ALDKWA were susceptible to neutralization. [D'Souza1997] (**variant cross-recognition or cross-neutralization**)
- 2F5: Of three neutralizing MAbs (257-D, IgG1b12, and 2F5), 2F5 was the only one to inhibit the entry of all viruses studied, both SI and NSI, with a potency proportional to its affinity for monomeric gp126. [Schutten1997] (**variant cross-recognition or cross-neutralization**)
- 2F5: Called IAM 2F5 – antibody mediated enhancement or inhibition seemed to be determined by isolate rather than antibody specificity – in this study, only 2F5 inhibited the entry of all the viruses studied, irrespective of their phenotype, and directly proportional to its affinity to monomeric HIV-1 gp160. [Schutten1997] (**variant cross-recognition or cross-neutralization**)
- 2F5: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] (**immunotoxin**)
- 2F5: 2F5 was infused into two chimpanzees which were then given an intravenous challenge with a primary HIV-1 isolate – both became infected, but with delayed detection and prolonged decrease in viral load relative to controls, indicating that preexisting, neutralizing antibodies (passively administered or actively elicited) affect the course of acute-phase virus replication and can be influential after the Ab can no longer be detected in the peripheral circulation. [Conley1996] (**immunoprophylaxis**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2F5: Review: only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. [Sattentau1996] (**review**)
- 2F5: Review: one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates. [Poignard1996b] (**review**)
- 2F5: Neutralizes HXB2, primary isolates, and chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b] (**variant cross-recognition or cross-neutralization**)
- 2F5: Primary isolates from clade A, B, and E are neutralized by 2F5 – neutralization requires the LDKW motif – neutralization resistant isolates or 2F5 selected variants all had substitutions in the D or K. [Purtscher1996] (**inter-clade comparisons**)
- 2F5: ELDKWAS is in a gp41 binding region for the negative regulator of complement factor H (CFH) – Abs to HIV generally do not cause efficient complement-mediated lysis, but binding of 2F5 can interfere with CHF binding, facilitating HIV destruction by complement. [Stoiber1996] (**complement**)
- 2F5: Only 4/20 Argentinian and 3/43 Swedish HIV+ sera reacted with LLELDKWASL – sera reacting with peptides that contained ELDKWA tended to have high neutralization titers – the region carboxyl terminal to EDLKWA was found to be more important for polyclonal sera AB binding, 670-675 WNWFDI – 2F5 bound most strongly to the peptide QELLELDKWA. [Calarota1996] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 2F5: Broad cross-clade neutralization of primary isolates – additive neutralization in combination with anti-CD4BS MAb IgG1b12 (Called BM12) [Kessler1995] (**inter-clade comparisons**)
- 2F5: MAb binding decreases the accessibility or alters the conformation of the gp41 fusion domain and of gp120 domains, including the binding site for the CD4 cell receptor. [Neurath1995] (**antibody binding site definition and exposure**)
- 2F5: Review: binds to the only generally accepted strong neutralizing epitope outside of gp120, one of only 3 MAbs with strong broad activity against primary viruses, the others are 2G12 and IgG1b12 – unique member of epitope cluster [Moore1995b] and John Moore, per comm 1996. [Moore1995b] (**review**)
- 2F5: Called IAM 41-2F5 – exposed in the presence of gp120 on the cell surface, while most of gp41 is masked – binds proximal to transmembrane region. [Sattentau1995c] (**antibody binding site definition and exposure**)
- 2F5: Cross-clade primary virus neutralizing activity – LDKW defined as the core epitope. [Trkola1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 2F5: Found to neutralize MN, JRCSF, and two B subtype primary isolates, but not a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. [D'Souza1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 2F5: 2F5 epitope ELDKWA inserted into an immunogenic loop in influenza virus hemagglutinin can elicit IIIB, MN and RF neutralizing sera in immunized mice. [Muster1994] (**vaccine antigen design**)
- 2F5: gp41 mutation (582 A/T) that reduces neutralization of anti-CD4 binding site MAbs does not alter 2F5's ability to neutralize. [Thali1994]
- 2F5: Called IAM-41-2F5 – neutralized lab and primary isolates – t 1/2 dissociation 122 min for the peptide, and 156 min for gp41 – core D(K/R)W – Ab resistant isolate had the sequence KLDNWA. [Conley1994b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 2F5: Included in a multi-lab study for antibody characterization binding and neutralization assay comparison. [D'Souza1994] (**assay development**)
- 2F5: MAb generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)
- 2F5: Failed to show synergy with anti-CD4 binding site IIIB neutralizing antibodies. [Laal1994] (**antibody interactions**)
- 2F5: Broadly reactive neutralizing activity, ELDKWA is relatively conserved – neutralized 2 primary isolates. [Purtscher1994] (**variant cross-recognition or cross-neutralization**)
- 2F5: Called IAM-41-2F5 – reports MAb to be IgG1 – the gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 2F5 is not affected. [Klasse1993a] (**variant cross-recognition or cross-neutralization**)
- 2F5: Synergy with combinations of CD4-based molecules in inhibition of HIV-1 Env mediated cell fusion. [Allaway1993] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2F5: DKWA defined as the core sequence – highly conserved epitope neutralizing MAb. [Buchacher1992, Muster1993] (**antibody binding site definition and exposure**)					
708	polyclonal	gp160 (659–670)	gp41 (659–670)	ELLELDKWASLW	no	Vaccine	guinea pig
		Vaccine *Vector/Type:* peptide *Strain:* B clade *HIV component:* gp41 *Adjuvant:* QS21 **References** McGaughey2003 **Keywords** antibody binding site definition and exposure, binding affinity, vaccine antigen design. • 2F5: Cyclic peptides ELLELDKWASLW that adopt constrained beta-turn conformation of the 2F5 epitope beta-turn in the complexed crystal structure were synthesized and optimize 2F5 binding affinity. This peptide elicts high titer peptide-specific immune responses in guinea pigs that do not neutralize; the authors propose this may be the result of a short CDR3 loop in guinea pigs and additional recessed contact points between 2F5 and gp41. [McGaughey2003] (**antibody binding site definition and exposure**, **vaccine antigen design**, **binding affinity**)					
709	14D9	gp160 (662–667)	gp41 (669–674 MVP5180)	ELDEWA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* natural variants *HIV component:* gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Ab type** adjacent to cluster II, C-term **References** Huang2002 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, variant cross-recognition or cross-neutralization. • 14D9: This mouse MAb was raised against a variant of ELDKWA core epitope of the NAb 2F5, eldEwa, derived from the 2F5 neutralization resistance variant MVP5180. The eldEwa peptide was conjugated to the carrier protein keyhole limpet hemocyanin (KLH) and adminstered to BALB/c mice and 14D9 was prepared using standard hybridoma methods. 2F5 does not bind to the variants eldEwa, elNkwa (B.TH.TH936705) or elEkwa, while 14D9 binds only to eldEwa and not ELDKWA. The eldEwa variant is common in the HIV-1 O group. [Huang2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					
710	polyclonal	gp160 (662–667)	gp41 (662–667)	ELDKWA	no	Vaccine	guinea pig
		Vaccine *HIV component:* gp41 **References** Joyce2002 • 2F5: DP178 is a peptide derived from the C-term heptad repeat of gp41 that is a potent inhibitor of viral-mediated fusion – it contains ELDKWA but fails to stimulate 2F5-like NAbs upon immunization – the peptide was extended to force an increase in helicity, and the modified peptide had a increase in affinity for 2F5, but upon guinea pig immunization although high peptide-specific Ab titers were achieved the sera were incapable of viral neutralization – the authors propose that 2F5 may be a low affinity maturation intermediate, which may account for its breadth and why it is hard to recreate the NAb response, but also suggests that the high concentrations required for neutralization are not relevant *in vivo*. [Joyce2002]					
711	5B2	gp160 (662–667)	Env (669–674 IIIB)	ELDKWA		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade IIIB *HIV component:* gp41 **Ab type** C-domain **References** Tian2001 • 5B2: Peptides GPGRAFY and ELDKWA were conjugated to keyhole limpet hemocyanin and used to raise mouse MAbs – MAb hybridomas were generated with defined specificity – 5B2 and 9G11 bind to the peptide and to rgp41. [Tian2001] • 5B2: There is an RT specific Ab [Szilvay1992] and a gp41 specific Ab [Tian2001] both called 5B2. [Tian2001]					
712	9G11	gp160 (662–667)	Env (669–674 IIIB)	ELDKWA		Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade IIIB *HIV component:* gp41					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type C-domain **References** Tian2001 • 9G11: Peptides GPGRAFY and ELDKWA were conjugated to KLH and used to raise mouse monoclonal Ab—MAb hybridomas were generated with defined specificity—5B2 and 9G11 bind to the peptide and to rgp41. [Tian2001]					
713	TH-Ab1	gp160 (662–667)	gp41 (669–674)	ELNKWA	L P	Vaccine	rabbit (IgG1)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *Strain:* B clade TH936705 *HIV component:* gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA) **Ab type** C-domain **References** Dong2001, Xiao2000a • TH-Ab1: ELNKWA is an escape variant not recognized by the broadly neutralizing MAb 2F5, which recognizes the core epitope ELDKWA—Abs were raised against the peptide escape variant CGELNKWAGELNKWA linked to KLH carrier—these polyclonal antibodies, like the MAb TH-Ab1 also raised to ELNKWA, could recognize ELDKWA and escape mutant peptide epitopes ELEKWA and ELDEWA. [Dong2001]					
714	polyclonal	gp160 (662–667)	gp41	ELDKWA	L P	Vaccine	rabbit
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **Ab type** C-domain **References** Liao2000 • Low levels of anti-ELDKWA antibodies are observed in HIV-1+ individuals, so a C-domain P2 peptide linked to a carrier was used to immunize mice and rabbits, and stimulated a high-level anti-ELDKWA response in mice and rabbits – vaccine was C-TSLIHSLIEESQNQQEKNEQELLELDKWA linked to carrier peptide K/G [(KGGG)_7-K] [Liao2000]					
715	polyclonal	gp160 (662–667)	gp41 (669–674)	ELDKWA		Vaccine	rabbit, mouse
		Vaccine *Vector/Type:* peptide *HIV component:* Env *Adjuvant:* BSA **Ab type** C-domain **References** Xiao2000b • Strong epitope-specific neutralizing antibody responses were induced using a Env peptide bound to BSA, C(ELDKWAG)_4-BSA, but not full gp160. [Xiao2000b]					
716	polyclonal	gp160 (662–667)	gp41 (662–667 BH10)	ELDKWA	L	Vaccine	mouse (IgA, IgG)
		Vaccine *Vector/Type:* influenza *Strain:* B clade BH10 *HIV component:* gp41 **Ab type** C-domain **References** Muster1995, Muster1994 • Sustained ELDKWA specific IgA response in mucosa of immunized mice. [Muster1995]					
717	polyclonal	gp160 (662–667)	gp120 (669–674)	ELDKWA		Vaccine	rabbit
		Vaccine *Vector/Type:* protein, polyepitope *HIV component:* gp160 *Adjuvant:* BSA **Ab type** C-domain **References** Lu2000b, Lu2000c • High titer response to ELDKWA and RILAVERYLKD was observed upon vaccination with multiple-epitope vaccine CG-GPGRAFY-G-ELDKWA-G-RILAVERYLKD conjugated to BSA, with a weak response to GPGRAFY – immunization with CG-(ELDKWA-GPGRAFY)_2-K was also tried, yielding a strong Ab response to both ELDKWA and GPGRAFY – gp160 vaccination yielded strong Ab response but not to any of the peptides studied here. [Lu2000c, Lu2000b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
718	4E10	gp160 (671–676)	gp160 (671–676 MN)	NWFDIT	P	HIV-1 infection	human (IgG3κ)

Ab type C-term **Research Contact** Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria, or Polymum Scientific Inc., Vienna, Austria

References Gorny2004, Kitabwalla2003, Wang2003, Fiebig2003, Ferrantelli2003, Binley2003, Ferrantelli2002, Xu2002, Xu2001, Zwick2001c, Zwick2001b, Stiegler2001, D'Souza1994, Buchacher1994, Buchacher1992

Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, immunoprophylaxis, inter-clade comparisons, mother-to-infant transmission, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- 4E10: This paper reviews MAbs that bind to HIV-1 Env. 4E10 binds to a region of gp41 proximal to cluster II (aa 662-676), neighboring the binding site of the broadly neutralizing MAb 2F5 and overlapping the epitope of neutralizing Fab Z13. 4E10 is the most broadly neutralizaing MAb, neutralizing primary isolates from clades A, B, C, D and CRF01 (E), although not the most potent. [Gorny2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 4E10: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. [Kitabwalla2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- 4E10: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. [Wang2003] (**vaccine antigen design**, **review**)
- 4E10: Porcine endogenous retroviruses (PERVS) are a concern in the context of procine xenotransplantation into humans; possible strategies for protection include PERV knockout animals or vaccines. Goats immunized with the PERV transmembrane protein revealed two NAb epitope, E1 and E2. E2's epitope (FEGWFN) binds to a sequence that is perfectly preserved in all PERVS and highly conserved in all gammaretroviruses: MuLV carries FEGLFN, FeLV FEGWFN, and it shares three amino acids with the core epitope for the anti-HIV human neutralizing MAB 4E10, (LWNWFN). [Fiebig2003]
- 4E10: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. [Ferrantelli2003] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)
- 4E10: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 NAbs 2F5 and 4E10 are able to potently neutralize the SOS pseudovirion post-attachment. [Binley2003] (**vaccine antigen design**)
- 4E10: Review of NAbs illustrating gp41's conformational change and exposure of the 4E10/Z13 epitope in the transient pre-hairpin form. [Ferrantelli2002] (**antibody binding site definition and exposure**)
- 4E10: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ —the combination b12+2G12+2F5 conferred partial protection against SHIV89.6—such combinations may be useful for prophylaxis at birth and against milk born transmission—the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. [Xu2002] (**antibody interactions**, **immunoprophylaxis**, **inter-clade comparisons**)
- 4E10: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. [Xu2001] (**antibody interactions**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 4E10: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2. [Zwick2001c] (**antibody interactions**)
- 4E10: MAbs 4E10 and Z13 both bind proximally to 2F5 to a conserved linear epitope that has some conformational aspects – both bind to MN virions, bind weakly to infected cells in a manner that is not disrupted by sCD4 and neutralize some primary isolates from clades B, C, and E – maps minimal 4E10 epitope to NWFDIT, contrary to an earlier report – different strains were refractive to neutralization by broadly neutralizing Abs IgG1b12, 2F5, Z13 and 4E10. [Zwick2001b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 4E10: 4E10 binds proximal to 2F5 and neutralizes primary isolates of clades A, B, C, D, and E – viruses that were resistant to 2F5 were neutralized by 4E10 and vice versa. [Stiegler2001] (**antibody binding site definition and exposure**)
- 4E10: Included in a multi-lab study for antibody characterization, binding and neutralization assay comparison. [D'Souza1994] (**variant cross-recognition or cross-neutralization**)
- 4E10: MAbs generated by hybridoma, electrofusion of PBL from HIV-1+ volunteers with CB-F7 heteromyeloma cells – also binds to MHC class II proteins – anti-class II Abs are only found in HIV-1 positive people – this paper maps 4E10's binding site to AEGTDRV, gp160(823-829), but the later Zwick *et al.* study in 2001 revised the epitope location. [Buchacher1994] (**antibody binding site definition and exposure**, **antibody generation**)

719	Z13	gp160 (671–676)	gp41 (671–676 MN)	NWFDIT	P	HIV-1 infection	human (IgG1κ)

Ab type C-term
References Gorny2004, Wang2003, Ferrantelli2002, Zwick2001b
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- Z13: This paper reviews MAbs and Fabs that bind to HIV-1 Env. Z13 binds to a region of gp41 proximal to cluster II (aa 662-676), neighboring the binding site of the broadly neutralizing MAb 2F5 and overlapping the epitope of neutralizing MAb 4E10. Z13 is broadly neutralizing, neutralizing primary isolates from clades A, B, C, D and CRF01 (E). [Gorny2004] (**antibody binding site definition and exposure**, **review**)
- Z13: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. [Wang2003] (**vaccine antigen design**, **review**)
- Z13: Review of NAbs that notes Z13 is a phage display generated FAb fragment from a B clade infected individual and that illustrates gp41's conformational change and exposure of the 4E10/Z13 epitope in the transient pre-hairpin form. [Ferrantelli2002] (**antibody binding site definition and exposure**, **antibody generation**)
- Z13: MAb 4E10 and FAb Z13 both bind proximally to 2F5 to a relatively conserved linear epitope that has some conformational aspects – both bind to MN virions, bind weakly to infected cells in a manner that is not disrupted by sCD4 and can neutralize some primary isolates from clades B, C, and E – Z13 was selected using a phage display library with the MN gp41 peptide LLELDKWASLWNWFDITNWSW from an HIV infected donor who had an exceptionally broad NAb response – different strains were refractive to neutralization by broadly neutralizing Abs IgG1b12, 2F5, Z13 and 4E10 – epitope location noted here is by analogy to MAb 4E10. [Zwick2001b] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**)

720	B30	gp160 (720–734)	gp41 (720–734 BH10)	HLPIPRGPDRPEGIE		Vaccine	mouse (IgG1)

Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160
Research Contact George Lewis
References Abacioglu1994

- B30: Epitope boundaries mapped by peptide scanning. [Abacioglu1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
721	polyclonal	gp160 (724–745)	gp41 (731–752)	PRGPDRPEGIEEEGGERDRDRS		Vaccine	mouse (IgA, IgG2a)
		Vaccine *Vector/Type:* Cowpea mosaic virus *Strain:* B clade IIIB *HIV component:* gp41 **References** Durrani1998 • Comparison of intranasal and oral immunization of HIV-1 peptide expressed in a plant viral vector – intranasal gave the better response. [Durrani1998]					
722	41S-2	gp160 (725–745)	gp160 (732–750)	RGPDRPEGIEEEGGERDRDRS	yes	Vaccine	mouse (IgG2bκ)
		Vaccine *Vector/Type:* peptide keyhole limpet hemocyanin (KLH) conjugate *HIV component:* gp41 **References** Hifumi2003, Hifumi2002, Hifumi2000b, Hifumi2000a **Keywords** anti-idiotype, antibody sequence, variable domain. • 41S-2: A murine Ab called i41SL1-2 was raised against the complementary determining region of the 41S-2 light chain, CRDL-1 (RSSKSLLYSNGNTYLY). As with 41S-2-L, the light chain of i41SL1-2 also had catalytic activity and degraded the immunizing peptide, initally cleaving between the Arg1 and Ser2. i41SL1-2 did not cross-react with gp41 peptide, gp120 V3 loop peptide and bound weakly to 41S-2-L.i41SL1-2 shows homology to the anti-VIP Ab (VIP, vasoactive intestinal peptide) that also has peptidase character. Both light chains contain a catalytic triad composed of Asp, Ser, and His (for i41SL1-2: Asp73, Ser 76 or Ser70 and His 79). Intact i41SL1-2 was unable to degrade CDRL-1, possibly due to an immobile inactive conformation of the catalytic triad. [Hifumi2003] (**anti-idiotype**, **antibody sequence, variable domain**) • 41S-2: 41S-2-L refers to the light chain of 41S-2, which can enzymatically decompose the gp41 protein of HIV-1, but doesn't degrade unrealted proteins. The peptide RGPDRPEGIEEEGGERDRDRS, against which the MAb was raised, can also be cleaved, initially between Glu12-Gly13, followed by successive cleavage reactions. [Hifumi2002] • 41S-2: The complementary determining region of 41S-2-L, the light chain of 41S-2, is strongly involved in gp41 recognition. This light chain can serve as a molecular catalyst for gp41 degredation. [Hifumi2000b] • 41S-2: BALBc mice were immunized with gp41 peptide and a MAb specific for the peptide was generated – isolated MAb light chains displayed proteolytic activity toward the peptide epitope which may be due to a catalytic triad on light chain (Asp73, Ser76, and His79) – no catalytic activity was observed for the whole antibody. [Hifumi2000a]					
723	447-52D (447/52-DII, 447-52-D, 447d, 447-52-D, 447-D, 447, 447D)	gp160 (726–729)	gp120 (MN)	GPXR	L P	HIV-1 infection	human (IgG3λ)
		Ab type V3 **Research Contact** Dr. Susan Zolla-Pazner, NYU Med Center NY, NY; Veteran Affairs Med Center NY, NY; or Cellular Products Inc, Buffalo, NY, USA **References** Gorny2004, Pantophlet2003b, Zwick2003, Kessler2003, Binley2003, Poignard2003, Ferrantelli2002, He2002, Gorny2002, Sharon2002, Srivastava2002, Verrier2001, York2001, Park2000, Nyambi2000, Ly2000, Hioe2000, Grovit-Ferbas2000, Gorny2000a, Beddows1999, Hioe1999, Nyambi1998, Gorny1998, Connor1998, Zolla-Pazner1999b, Zolla-Pazner1999a, Parren1998a, Smith1998, Mondor1998, Inouye1998, Ugolini1997, Gorny1997, Hill1997, Parren1997c, Boots1997, Hioe1997b, Hioe1997a, Fouts1997, Binley1997a, D'Souza1997, Sattentau1996, Trkola1996a, Jagodzinski1996, Forthal1995, Moore1995b, Moore1995a, Zolla-Pazner1995b, Zolla-Pazner1995a, Sattentau1995c, Saarloos1995, Fontenot1995, Sattentau1995a, Moore1994a, Gorny1994, VanCott1994, Laal1994, Conley1994a, Spear1993, Cavacini1993a, Keller1993, Gorny1993, Karwowska1992b, Buchbinder1992, Gorny1992 **Keywords** acute infection, ADCC, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, assay development, assay standardization, binding affinity, co-receptor, complement, enhancing activity, inter-clade comparisons, kinetics, mimotopes, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization. • 447-52D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary isolates. Although 447-52D was selected using a peptide, it has conformational characteristics. Inter-clade cross-neutralization by anti-V3 conformation-dependent MAbs is reduced. [Gorny2004] (**antibody binding site definition and exposure**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 447-52D: This paper attempts to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Adding a glycosylation sequon (P313N) to the V3 loop knocked out binding to anti-V3 MAbs loop 2, 19b and 447-52-D. [Pantophlet2003b] (**vaccine antigen design**)
- 447-52D: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. [Zwick2003] (**antibody interactions**)
- 447-52D: The Fv fragment (composed of just the light and heavy variable regions, and the smallest intact binding unit of an Ab) of 447-52 D was expressed and purified. Preliminary NMR with the peptide epitope indicates that an NMR structure determination is feasible. [Kessler2003] (**antibody sequence, variable domain**, **structure**)
- 447-52D: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. 447-52D was able to neutralize the SOS protein better than the wildtype, but did not neutralize SOS well when added post-attachment, as the V3 loop is involved in co-receptor engagement. [Binley2003] (**vaccine antigen design**)
- 447-52D: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – Ab 447-52D was able to potently neutralize 89.6 and to neutralize JR-CSF at a high concentration but poorly neutralized ADA – b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, but anti-V3 Abs 447-52D and 19b, which did not neutralize JR-CSF and ADA, captured amounts of p24 equal to or higher than the amounts captured by the neutralizing Ab b12. [Poignard2003] (**antibody binding site definition and exposure**, **assay development**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Review of NAbs. [Ferrantelli2002]
- 447-52D: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002]
- 447-52D: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 447-52D bound to primary isolates from all clades except CRF01 (E), was conformationally sensitive and showed the some of the most potent neutralizing activity. [Gorny2002] (**variant cross-recognition or cross-neutralization**)
- 447-52D: The feasibility of determining the NMR structure of the V3(MN) peptide bound to the 447-52D Fab fragment was tested and a general strategy for obtaining NMR structures of V3 peptide-Fab fragments developed – preliminary NMR spectra for 447-52D complexed to a 23 amino acid V3 peptide was obtained. [Sharon2002] (**structure**)
- 447-52D: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent—antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs—447-D recognized the gp120 monomer much more readily than o-gp140, suggesting the V3 loop is less exposed on o-gp140 and on intact virions. [Srivastava2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 447-52D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – the dissociation constant, Kd of 447-52D for the cell associated primary and TCLA Envs was equal, 3nM. [York2001] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **binding affinity**)
- 447-52D: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000] (**antibody binding site definition and exposure**)
- 447-52D: A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 447-52D showed the highest cross-reactivity, bound to 24/26 viruses tested, but achieved 90% neutralization only against MN, 50% against CA5, and no neutralization was observed for 3 other isolates tested. [Nyambi2000] (**inter-clade comparisons**)
- 447-52D: Called 447D – SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000] (**antibody binding site definition and exposure**)
- 447-52D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – V3 MAbs 447-52-D and 268-10-D did not effect proliferation. [Hioe2000]
- 447-52D: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. [Grovit-Ferbas2000] (**vaccine antigen design**)
- 447-52D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**)
- 447-52D: rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced 447-52D neutralization sensitivity relative to PBMC-adapted lines (32X increase between HIV-1(M2424/PBMC(p0)) and HIV-1(M2424/H9(p9)) and a >128X increase between HIV-1(W61D/PBMC) and HIV-1(W61D/SupT1) isolates) [Beddows1999] (**variant cross-recognition or cross-neutralization**)
- 447-52D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs. [Hioe1999]
- 447-52D: MAb peptide-reactivity pattern clustered with the immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group – 447 reacted with peptides containing GPGR, but also with many lacking this sequence (GPGQ, for example), and it failed to react with 2/14 peptides containing GPGR, illustrating the importance of context. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 447-52D: Review of clade specificity and anti-V3 HIV-1-Abs. [Zolla-Pazner1999a] (**review**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 447-52D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – 447-52D was the most potent and cross-reactive of 18 human MAbs tested and was the only MAb which bound to virions from isolates CA20 (subtype F), CA13 (subtype H), and VI526 (subtype G) [Nyambi1998] (**inter-clade comparisons**)
- 447-52D: Kinetic parameters were measured, and the association rates were similar, but dissociation rate constants were quite variable for V3 MAbs, 1324E was comparable to 447-52D. [Gorny1998] (**kinetics**)
- 447-52D: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. [Connor1998]
- 447-52D: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**antibody binding site definition and exposure**)
- 447-52D: Called 447-52-D – The tip of the MN V3 loop was inserted into cold causing human rhinovirus 14 (HRV14) – chimeras were immunoselected, and chimeric viruses were neutralized by anti-V3 loop antibodies, and 447-52D was among the Abs used – chimeric viruses elicited potent NAbs in guinea pigs against ALA-1 and MN. [Smith1998] (**vaccine antigen design**)
- 447-52D: Inhibits binding of Hx10 to both CD4 positive and negative HeLa cells. [Mondor1998] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Called 447-D – 447-D resistance took longer to acquire in virus with the M184V substituted RT, and had the form (AAC N to TAC Y) at position 5 of the V3 loop, rather than the GPGR to GPGR resistance found with wildtype RT. [Inouye1998]
- 447-52D: Used as a control for comparison to five V3 RF selected antibodies – 447-52D was reactive with A, B, and C clade peptides, but not E. [Gorny1997] (**inter-clade comparisons**)
- 447-52D: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – 447-52D has an epitope involving the tip of the V3 loop, that was previously studied with this method [Keller1993] – in Keller *et al.*, with no competition, LxGPxR was the most common six-mer, 38% of the peptides – after competition with a gp120 IIIB ligand (QRGPGR)i, RGPxR was the most common and one peptide had the sequence QRGPGR, showing type specific mimotopes can be enriched by strain specific ligand competition protocols [Boots1997]. [Boots1997, Keller1993] (**antibody binding site definition and exposure**, **mimotopes**)
- 447-52D: Called 447 – gp120 can inhibit MIP-1alpha from binding to CCR5, but this inhibitory effect is blocked by pre-incubation of gp120 with three anti-V3 MAbs: 447, 257, 1027 – MAb 670 which binds in the C5 region had no effect. [Hill1997] (**co-receptor**)
- 447-52D: Neutralizes TCLA strains but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Viral binding inhibition by 447-D was correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997] (**antibody binding site definition and exposure**)
- 447-52D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**)
- 447-52D: Tested using a resting cell neutralization assay. [Hioe1997a] (**assay standardization**)
- 447-52D: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 447-52D bound monomer, oligomer, and neutralized JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- 447-52D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – many of these isolates had the GPGR motif at the apex of the V3 loop. [D'Souza1997] (**variant cross-recognition or cross-neutralization**, **assay standardization**)
- 447-52D: Review: called 447-52-D – only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. [Sattentau1996] (**variant cross-recognition or cross-neutralization**, **review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 447-52D: Neutralizes JR-FL – strongly inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**co-receptor**, **variant cross-recognition or cross-neutralization**) • 447-52D: Called 447-52-D – The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – CRDS inhibits 447-52D binding. [Jagodzinski1996] (**antibody binding site definition and exposure**) • 447-52D: Neutralizing (- complement), no ADCC activity, and no viral enhancing activity. [Forthal1995] (**ADCC**, **complement**, **enhancing activity**) • 447-52D: Review: the V3 loop motif GPGR is not common outside subtype B isolates, MAb 19b is more cross-reactive than 447-52D. [Moore1995b] (**variant cross-recognition or cross-neutralization**) • 447-52D: Binding affected by identity of amino acids flanking GPGR core – poor breadth of primary virus neutralization. [Moore1995a] (**variant cross-recognition or cross-neutralization**) • 447-52D: Neutralization of primary and prototype laboratory HIV-1 isolates using a resting cell assay enhances sensitivity. [Zolla-Pazner1995b] (**assay development**, **variant cross-recognition or cross-neutralization**) • 447-52D: Serotyping study using flow-cytometry – bound only to GPGR V3 loop tips. [Zolla-Pazner1995a] (**antibody binding site definition and exposure**) • 447-52D: Ab-mediated activation of complement on HIV+ cells is higher than Ab independent activation—what has been termed "Ab independent" in fact results in part from IgM in normal human serum that is HIV-cross-reactive. [Saarloos1995] (**complement**) • 447-52D: Called 447 – The tip of the V3 loop was presented in a mucin backbone – higher valency correlates with stronger affinity constant. [Fontenot1995] (**vaccine antigen design**) • 447-52D: Called 447d – Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. [Sattentau1995c] (**vaccine antigen design**) • 447-52D: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies. [Moore1994a] (**acute infection**) • 447-52D: Mild oxidation of carbohydrate moieties does not alter binding. [Gorny1994] (**antibody binding site definition and exposure**) • 447-52D: GPGQ in MAL resulted in enhanced dissociation – GPGQ in CM234 or K14T did not bind – binding affected by identity of amino acids flanking GPGR core. [VanCott1994] (**antibody binding site definition and exposure**) • 447-52D: Neutralization synergy in combination with CD4 binding domain MAbs. [Laal1994] (**antibody interactions**) • 447-52D: Requires GPxR at the tip of the V3 loop, common in B clade – neutralized primary isolates. [Conley1994a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • 447-52D: Complement mediated virolysis of IIIB, but not in the presence of sCD4. [Spear1993] (**complement**) • 447-52D: Additive neutralization of MN and SF2 when combined with CD4 binding site MAb F105 – supra-additive neutralization of RF. [Cavacini1993a] (**antibody interactions**) • 447-52D: Peptide phage library showed that any of the residues ADGLMNQRS in the X position tolerated in peptides that react well with the antibody. [Keller1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • 447-52D: Neutralizes MN and IIIB: GPGR, and binds SF2: GPGR. [Gorny1993] (**variant cross-recognition or cross-neutralization**) • 447-52D: Reacts with MN, NY5, CDC4, SF2, RF, WM52, and HXB2. [Karwowska1992b] (**variant cross-recognition or cross-neutralization**) • 447-52D: 60-fold increase in neutralization potency when combined 1:1 with human MAb 588-D. [Buchbinder1992] (**antibody interactions**) • 447-52D: Requires GPXR at the tip of the V3 loop – neutralizes a broad array of B clade lab isolates. [Gorny1992] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)			
724	C8	gp160 (727–732)	gp41 (727–732 BH10)	PDRPEG	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **References** McLain2001, Abacioglu1994, Pincus1993b, Pincus1993a					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• C8: The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. [McLain2001] • C8: Epitope boundaries mapped by peptide scanning. [Abacioglu1994] • C8: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – C8 was used as a control – the dominant response among vaccinees was to this mid-gp41 region, but not among the infected lab workers – Abs binding this region do not neutralize, bind to infected cells, nor serve as immunotoxins. [Pincus1993b] • C8: Immunotoxin of C8 coupled to ricin-A does not mediate cells killing, and is not affected by sCD4. [Pincus1993a]					
725	B31	gp160 (727–734)	gp41 (727–734 BH10)	PDRPEGIE		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **References** Abacioglu1994 • B31: Epitope boundaries mapped by peptide scanning. [Abacioglu1994]					
726	B33	gp160 (727–734)	gp41 (727–734 BH10)	PDRPEGIE	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp160 **References** Bristow1994, Abacioglu1994 • B33: Epitope boundaries mapped by peptide scanning IgG1. [Abacioglu1994] • B33: There are two MAbs in the literature named B33, see also gp120, positions 123-142 – MAb generated in a study of the humoral immune response to Baculovirus-expressed mis-folded rgp160 IIIB:NL43, MicroGenSys. [Bristow1994]					
727	1576	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Vella1993 • 1576: Not neutralizing. [Vella1993]					
728	1578	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Vella1993, Evans1989 • 1578: Core epitope: IEEE – in this study, neutralized IIIB, but not RF or MN. [Vella1993] • 1578: No neutralizing activity – epitope may be formed by regions from both poliovirus and HIV. [Evans1989]					
729	1579	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Vella1993 • 1579: Core epitope: IEEE – neutralized IIIB, but not RF or MN. [Vella1993]					
730	1583	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Sattentau1995c, Vella1993, Evans1989 • 1583: Cytoplasmic domain, epitope not exposed at the surface of HIV-1 infected cells. [Sattentau1995c] • 1583: Core epitope: ERDRD – Could neutralize HIV IIIB but not HIV RF. [Vella1993] • 1583: Neutralizing activity, less broad than 1577. [Evans1989]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
731	1899	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Vella1993 • 1899: Could neutralize HIV IIIB and HIV RF. [Vella1993]					
732	1907	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Vella1993 • 1907: Could not neutralize HIV IIIB, RF or MN. [Vella1993]					
733	1908	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Sattentau1995c, Vella1993, Evans1989 • 1908: Cytoplasmic domain, epitope not exposed at the surface of HIV-1 infected cells. [Sattentau1995c] • 1908: Neutralized IIIB, but not RF or MN. [Vella1993]					
734	1909	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **References** Vella1993 • 1909: Neutralized HIV IIIB but not HIV RF. [Vella1993]					
735	41-1	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse (IgMκ)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* gp41 **References** Dalgleish1988, Mani1994 • 41-1: Neutralizes HIV-1 but not HIV-2 strains. [Dalgleish1988] • 41-1: This antibody gp41(735-752 IIIB) [Dalgleish1988] seems to have been named the same as a different MAb to gp41(584-609) [Mani1994]. [Dalgleish1988, Mani1994]					
736	41-2	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse (IgMκ)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* gp41 **References** Dalgleish1988 • 41-2: Neutralizes HIV-1 but not HIV-2 strains. [Dalgleish1988]					
737	41-3	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse (IgMκ)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* gp41 **References** Dalgleish1988 • 41-3: Neutralizes HIV-1 but not HIV-2 strains. [Dalgleish1988]					
738	ED6	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no		mouse (IgM)
		References Evans1989					
739	LA9 (121-134)	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no		mouse (IgM)
		References Evans1989					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
740	1575	gp160 (728–745)	gp41 (735–752 IIIB)	DRPEGIEEEGGERDRDRS	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **Ab type** C-term **Research Contact** C. Vella, NIBSC, Potters Bar UK **References** Cleveland2000a, Buratti1997, Vella1993, Evans1989 • 1575: Ab binding to IEEE suppresses neutralizing Ab binding to adjacent epitope ERDRD. [Cleveland2000a] • 1575: Study shows that MAb 1575 can recognize the IEEE sequence in both gp41, and in the HPG30 region of the p17 protein – motif is conserved in both regions in different HIV-1 clades. [Buratti1997] • 1575: Core epitope: IEEE – neutralized IIIB, but not RF or MN. [Vella1993] • 1575: Neutralizing activity, less broad than 1577. [Evans1989]			
741	88-158/02	gp160 (732–747)	gp41 (732–752 IIIB)	GIEEEGGERDRDRSIR		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp41 **References** Niedrig1992a • 88-158/02: Mild inhibition of *in vitro* activity at high MAb concentrations – profound enhancing activity at low concentrations – significant reactivity to virion – domain non-immunogenic in humans. [Niedrig1992a]					
742	88-158/022	gp160 (732–747)	gp41 (732–752 IIIB)	GIEEEGGERDRDRSIR		Vaccine	mouse (IgG2b)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp41 **References** Niedrig1992a • 88-158/022: Mild inhibition of *in vitro* activity at high MAb concentrations – profound enhancing activity at low concentrations – significant reactivity to virion – domain non-immunogenic in humans. [Niedrig1992a]					
743	88-158/079	gp160 (732–747)	gp41 (732–752 IIIB)	GIEEEGGERDRDRSIR		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp41 **References** Niedrig1992a • 88-158/079: Mild inhibition of HIV *in vitro* at high MAb concentrations – profound enhancing activity at low concentrations – weak binding to virion – domain non-immunogenic in humans. [Niedrig1992a]					
744	polyclonal	gp160 (733–736)	gp41 (735–752 IIIB)	IEEE	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* Cowpea mosaic virus *HIV component:* gp41 **Ab type** C-term **References** McLain2001, Cleveland2000b • The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. [McLain2001] • When PRGPDRPEGIEEEGGERDRDRS was used as antigen an immunodominant, non-neutralizing response to IEEE was observed, but immunization GERDRDR shifts the response to ERDRD. [Cleveland2000b]					
745	polyclonal	gp160 (733–736)	gp41 (735–752 NL43)	IEEE	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* Cowpea mosaic virus *HIV component:* gp41 **Ab type** C-term **References** McLain2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. [McLain2001]					
746	B8	gp160 (733–741)	gp41 (733–741 BH10)	IEEEGGERD	no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI *HIV component:* gp160 **References** Abacioglu1994, Pincus1993b • B8: Epitope boundaries mapped by peptide scanning. [Abacioglu1994] • B8: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – B8 was used as a control – the dominant response among vaccinees was to this mid-gp41 region, but not among the infected lab workers – Abs binding this region do not neutralize, bind to infected cells, nor serve as immunotoxins. [Pincus1993b]					
747	1577	gp160 (739–743)	gp41 (735–752 IIIB)	ERDRD	no	Vaccine	mouse
		Vaccine *Vector/Type:* poliovirus *Strain:* B clade IIIB *HIV component:* gp41 **Ab type** C-term **Research Contact** C. Vella or Morag Ferguson (NIBSC, Potters Bar UK) **References** Cleveland2000a, Vella1993, D'Souza1991, Evans1989 • 1577: NIH AIDS Research and Reference Reagent Program: 1172. • 1577: UK Medical Research Council AIDS reagent: ARP317. • 1577: Ab binding to IEEE suppresses neutralizing Ab binding to adjacent epitope ERDRD. [Cleveland2000a] • 1577: Core epitope: ERDRD – could neutralize HIV IIIB and HIV RF. [Vella1993] • 1577: Non-neutralizing in this multi-lab study. [D'Souza1991] • 1577: Raised against IIIB peptide chimera – neutralized African and American HIV-1 lab strains. [Evans1989]					
748	polyclonal	gp160 (739–743)	gp41 (735–752 IIIB)	ERDRD	L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* Cowpea mosaic virus *HIV component:* gp41 **Ab type** C-term **References** McLain2001, Cleveland2000b • The substitution 725 RG (P[R–>G]GPDRPEGIEEEGGERDRDRS) alters the antigenic exposure of this region on the virion resulting in the loss of the downstream neutralizing epitope ERDRD, increased exposure of the epitope GPDRPEG in the virion, while the epitope IEEE remains unchanged. [McLain2001] • ERDRD-specific IgG recognizes an externalized loop of the gp41 C-terminal tail with high affinity – neutralized HIV-1 B clade strains IIIB, NL-4.3, RF, MN and D clade virus CBL-4, but HXB-2D (clade B) was not recognized – when PRGPDRPEGIEEEGGERDRDRS was used as antigen an immunodominant, non-neutralizing response to IEEE was observed, but immunization GERDRDR shifts the response to ERDRD – NAb does not inhibit attachment of free virus, but does inhibit by an event that precedes fusion-entry. [Cleveland2000b]					
749	DZ	gp160 (822–855)	gp41 (827–860 BRU)	VAEGTDRVIEVVQGACRAIRHIPRR-IRQGLERIL	L	Vaccine	human (IgG1λ)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* Env **References** Boyer1991 • DZ: Weakly neutralizing IIIB – binds to peptides 827-843 and 846-860 of BRU – reacted specifically with IIIB and RF. [Boyer1991]					

IV-C-16 Env Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
750		Env	gp120 (IIIB)			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF **References** Rodríguez1999 • The murine Ab response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the Ab response was greater, in particular to the C-term region of gp120 – a cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by Elispot assay. [Rodríguez1999]				
751		Env	Env (384–467)			Vaccine	macaque, rabbit
		Vaccine *Vector/Type:* hepatitis B surface antigen lipoprotein particles (HsBAg) *HIV component:* V3 **References** Michel1993 • Immunization with recombinant HIV1 V3/HBsAg hybrid particles into rabbits or macaques elicited and maintained for several months anti-V3 or HIV-1 Env proliferative, CTL and Ab responses. [Michel1993]				
752		Env			Y	HIV-1 infection, Vaccine	human
		References Burton2000 • This review article touches on why natural immune responses do not tend to favor potent neutralizing Ab production, and discusses possible vaccine strategies to counter this problem. [Burton2000]				
753		Env			P	HIV-1 infection	human
		References Pellegrin1996 • Detection of an autologous NAb response in 12 patients with primary infections was delayed – for patients with a viral isolate obtained at month 1, autologous NAbs to viral isolates were generally not observed before month 6, and there was no apparent relationship between the emergence of neutralizing activity and the decrease of plasma viral load. [Pellegrin1996]				
754		Env	Env			HIV-1 infection	
		References Berger2002 **Keywords** immunotherapy. • This medical hypothesis proposes that HIV shares domains with human proteins are masked from the immune response as they are seen as self. They propose blocking the shared determinants on human proteins in the thymus with antibodies, to allow anti-self responses which are normally inhibited to occur in HIV+ people. (**immunotherapy**)				
755	1008-D	Env	gp120			HIV-1 infection	human
		Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Zwick2003, Zolla-Pazner1995a **Keywords** antibody interactions. • scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
756	102-135	Env	gp41 (HAM112, O group)			Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160 **References** Scheffel1999 • 102-135: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity – 102-135 bound to two non-contiguous peptides in combination, assumed to form some type of helical structure, and not to either individually. [Scheffel1999]					
757	1025	Env	gp120				
		References Berman1997 • 1025: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial. [Berman1997]					
758	105-134	Env	gp41 (652–681 HAM112, O group)			Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160 **References** Scheffel1999 • 105-134: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. [Scheffel1999]					
759	10E9	Env	gp41			HIV-1 infection	mouse (IgG1)
		References Papsidero1988 • 10E9: 100/100 HIV+ human sera could inhibit 10E9 binding. [Papsidero1988]					
760	1125H (1125h)	Env	gp120		L (MN)	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **Research Contact** Shermaine Tilley, Public Health Research Institute, USA **References** Gorny2004, Yang1998, Alsmadi1998, Wyatt1998a, Pincus1996, Warrier1996, D'Souza1995, Pinter1993b, Wyatt1992, Thali1992a, Tilley1991a, Tilley1991b **Keywords** ADCC, antibody binding site definition and exposure, antibody interactions, assay development, immunotoxin, inter-clade comparisons, review, structure, variant cross-recognition or cross-neutralization. • 1125H: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 1125H: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998] (**assay development**) • 1125H: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. [Alsmadi1998] (**ADCC**) • 1125H: Called 1125h – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] (**structure**) • 1125H: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] (**immunotoxin**) • 1125H: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. [Warrier1996] (**antibody interactions**) • 1125H: Neutralization was MN specific – failed to neutralize JRCSF, and 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs. [D'Souza1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**) • 1125H: Precipitation of Delta 297-329 env glycoprotein, with has a deleted V3 loop, is much more efficient that precipitation of wild type. [Wyatt1992] (**antibody binding site definition and exposure**) • 1125H: Binding to soluble gp120 enhanced by the presence of an anti-V3 HuMAb, 41148D. [Pinter1993b] (**antibody interactions**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1125H: Amino acid substitutions in HXB2 that strongly inhibit binding: 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480. [Thali1992a] (**antibody binding site definition and exposure**) • 1125H: Binding to gp120 inhibited by CD4 – epitope is destroyed by reduction, but not by removal of N-linked sugars – neutralization of MN, RF, SF-2 and IIIB – neutralization synergy with anti-V3 MAb 4117C. [Tilley1991a] (**antibody binding site definition and exposure**, **antibody interactions**, **variant cross-recognition or cross-neutralization**)					
761	126-50	Env	gp41 (HXB2)		no	HIV-1 infection	human (IgG2κ)
		References Xu1991, Robinson1991, Tyler1990, Robinson1990b • 126-50: Specific for a conformational epitope. [Xu1991] • 126-50: No enhancing or neutralizing activity. [Robinson1991] • 126-50: Serves as target for antibody-dependent cellular cytotoxicity ADCC. [Tyler1990] • 126-50: No enhancing activity for HIV-1 IIIB. [Robinson1990b]					
762	12H2	Env	gp41 (530–677 HXB2)		no	Vaccine	mouse (IgMκ)
		Vaccine *Vector/Type:* Semliki-Forest Virus *HIV component:* Env **References** Giraud1999 • 12H2: Env in a Semliki-Forest Virus (SFV) vector was used to vaccinate mice intramuscularly as naked RNA, and an Ab response was induced to Env from which 12H2 was derived – and advantage of this method is that the protein is properly expressed. [Giraud1999]					
763	13.10 (No. 13)	Env	gp120		no	HIV-1 infection	human (IgG1λ)
		Research Contact Evan Hersh and Yoh-Ichi Matsumoto **References** Wisnewski1996, Moran1993, Lake1989 • 13.10: NIH AIDS Research and Reference Reagent Program: 377. • 13.10: 13.10 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] • 13.10: Heavy (V HI) and light (V lambdaII) chain sequenced – no enhancing or neutralizing activity – called No. 13. [Moran1993] • 13.10: First HIV-1 specific human-mouse hybridoma that produces a MAb that binds to gp120 and gp160. [Lake1989]					
764	1B1	Env	Env		L	HIV-1 infection	human
		Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria **References** Kunert1998, Purtscher1994, Buchacher1994 • 1B1: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods. [Kunert1998] • 1B1: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994]					
765	1F7	Env	Env		L	HIV-1 infection	human
		Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria **References** Grant2000, Kunert1998, Purtscher1994, Buchacher1994 • 1F7: There is an anti-idiotype MAb named 1F7 that was raised against pooled IgG from HIV-1+ subjects that recognizes a set of antibodies against HIV Gag, Pol, and Env, and this MAb is reported to inhibit anti-HIV CTL activity—this is not the same as the 1F7 described by Buchacher *et al.* [Grant2000] • 1F7: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods. [Kunert1998] • 1F7: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
766	2.2B	Env	gp41		no		

Ab type cluster II **Research Contact** James Robinson, Tulane University, Tulane, LA
References Binley2003, Schulke2002, Binley1999
Keywords vaccine antigen design.

- 2.2B: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 Abs 7B2 and 2.2B did not neutralize in any format, WT, SOS, nor when added postbinding. [Binley2003] (**vaccine antigen design**)
- 2.2B: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. [Schulke2002] (**vaccine antigen design**)
- 2.2B: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**vaccine antigen design**)

767	30D	Env	gp120		no		

References Yang2002

- 30D: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002]

768	31710B	Env	gp41				human (IgG1)

References Alsmadi1998

- 31710B: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. [Alsmadi1998]

769	38B5/C9	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 38B5/C9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—38B5/C9 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
770	39H10/A11	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 39H10/A11: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—39H10/A11 bound to three R5 and three X4 B clade viruses, as well as two E clade viruses. [He2002]

771	3D5	Env	Env		L	HIV-1 infection	human

Research Contact Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, Vienna, Austria
References Kunert1998, Purtscher1994, Buchacher1994

- 3D5: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods. [Kunert1998]
- 3D5: Generated by electrofusion of PBL from HIV-1 positive volunteers with CB-F7 cells. [Buchacher1994]

772	3H6	Env	gp41				mouse

References Pinter1995

- 3H6: Generated in response to virus grown in protein-free medium. [Pinter1995]
- 3H6: There is another MAb with this ID that recognizes Rev.

773	40D3/C11	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 40D3/C11: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—40D3/C11 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]

774	49B11/A1	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 49B11/A1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—49B11/A1 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]					
775	4KG5	Env	gp120 (JR-FL)		no	HIV-1 infection	human (IgG)
		Ab type C4, V3, V1-V2 **References** Zwick2003 **Keywords** antibody binding site definition and exposure, antibody generation, antibody interactions, structure, variant cross-recognition or cross-neutralization. • 4KG5: 4KG5, a single-chain Fv (scFv), reacts with a conformational epitope which is formed by the V1, V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. 4KG5 was derived from derived from the serum of HIV-1 infected patient FDA2, who showed broad neutralizng activity, but is not itself neutralizing. Denaturation of gp120 abolished binding of 4KG5 and Fab b12. Addtionally, binding of 4KG5 was abrogated when any of the V1, V2 or V3 loops were deleted. Of a panel of Abs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished or abroated binding: V2 loop MAbs (G3-4, G3-136), V3 loop MAbs (19b, 447-52D, hNM01, AH48, loop2, F425 B4e8, 694-88D), V3-C4 (G3-299, G3-42, G3-519, G3-537), CD4BS (b6, b3, F91, F105, 15e, L33, 1008-D, 654-30D, 559-64D, 1027-30D, Ia3, Ia7, FG39, Fbb14). MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1, V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. 4KG5 recognized HIV-1 envelope proteins derived from JR-FL, JR-CSF, BaL, ADA and R2, but not MN, DH123, HxB2, YU2, SF2 and 89.6. Binding of 4KG5 to different strains of HIV-1 env is probably due sequence differences in V3 and C4, rather than V1 or V2. [Zwick2003] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **variant cross-recognition or cross-neutralization**, **structure**)					
776	52G5/B9	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 52G5/B9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—52G5/B9 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]					
777	55E4/H1	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 55E4/H1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—55E4/H1 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]					
778	56C4/C8	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 56C4/C8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—56C4/C8 bound to some R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]					
779	57B6/F1	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 57B6/F1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—57B6/F1 bound some R5 and X4 B clade viruses, and no E clade viruses. [He2002]					
780	57H5/D7	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					
		• 57H5/D7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—57H5/D7 bound to most R5 and X4 B clade viruses, as well as one of two E clade viruses. [He2002]					
781	63G4/E2	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 63G4/E2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—63G4/E2 bound to three R5 and three X4 B clade viruses, as well as two E clade viruses. [He2002]				
782	65B12/C5	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 65B12/C5: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—11 of the MAbs were conformation dependent, but did not block sCD4 binding—these MAbs were part of the same competition group, and enhanced binding of the CD4BS MAb 38G3/A9 and anti-CD4BS MAbs also enhanced their binding—these MAbs tended to be very cross-reactive but could not neutralize autologous SF162—65B12/C5 bound some R5 and X4 B clade viruses, and no E clade viruses. [He2002]				
783	6E10	Env	gp120		L	Vaccine	
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **Research Contact** Phil Berman **References** Berman1991					
784	7-1054	Env	gp36 (HIV-2)		no		mouse
		References Scheffel1999 • Binds HIV-2 gp36, used as a control in a study of group O MAbs. [Scheffel1999]					
785	7B2	Env	gp41		no		
		Ab type cluster I **References** Binley2003, Binley1999 **Keywords** antibody binding site definition and exposure, vaccine antigen design. • 7B2: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. gp41 Abs 7B2 and 2.2B did not neutralize in any format, WT, SOS, nor when added postbinding. [Binley2003] (**vaccine antigen design**) • 7B2: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**antibody binding site definition and exposure**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
786	85G11/D8	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 85G11/D8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses. [He2002]

787	87E4/A8	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 87E4/A8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses. [He2002]

788	97B1/E8	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* deglycosylated gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Research Contact Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References He2002

- 97B1/E8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—three of the MAbs were conformation dependent, but did not block sCD4 binding and were part of the same competition group—these MAbs were all raised against a deglycosylated form of gp120—they could not neutralize autologous SF162 and bound some R5 and X4 B clade viruses, and no E clade viruses. [He2002]

789	A1g8	Env	gp120			HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** James Robinson, Tulane University Med School, New Orleans, LA, USA
References Cavacini2003, Cavacini2002
Keywords antibody interactions, co-receptor, variant cross-recognition or cross-neutralization.

- A1g8: The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to R5X4 virus 92HT593, but only of 48d to the R5 virus 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. [Cavacini2003] (**antibody interactions**, **co-receptor**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• A1g8: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-V3 MAb B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, but only A1g8 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. Anti-gp41 MAb F240 had a synergistic effect on neutralization with CD4i MAbs 48d and 17b, but not with A1g8 for the R5X4 virus. [Cavacini2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)					
790	A9	Env	gp120 (IIIB)			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF **References** delReal1999 • A9: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – A9 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183-2. [delReal1999]					
791	AG10H9	Env	gp41 (717–751)				
		Research Contact BabCO **References** Ohagen2003 **Keywords** brain/CSF, variant cross-recognition or cross-neutralization. • AG10H9: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. AG10H9 recognized most variants gp41 and gp160 from 3/4 individuals by WB, but not the 4th. [Ohagen2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)					
792	AH48	Env	gp120 (V3)			HIV-1 infection	human
		References Zwick2003 **Keywords** antibody generation, antibody interactions. • AH-48: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. AH48 is a novel anti-V3 Fab first used in this study. [Zwick2003] (**antibody generation**, **antibody interactions**)					
793	Ag1211	Env	gp120 (V3 loop) (JRFL)				
		Ab type V3 **References** Kwong2002 **Keywords** antibody binding site definition and exposure.					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- Ag1211: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)

794 B4 Env gp120 (IIIB) Vaccine mouse (IgM)

Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120
References delReal1999

- B4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B4 was an anti-gp120 from a BALBc reconstructed nude mouse and had VH gene J606. [delReal1999]

795 B4a1 Env gp120 (V3) HIV-1 infection human

Ab type V3 **Research Contact** James Robinson, Tulane University Med School, New Orleans, LA, USA
References Cavacini2003, Cavacini2002
Keywords antibody interactions, co-receptor, variant cross-recognition or cross-neutralization.

- B4a1: The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. The anti-V3 MAb B4a1 cross-competes with B4e8. [Cavacini2003] (**antibody interactions**)
- B4a1: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 binding was not affected by the binding of the V3 loop MAb B4a1, but preincubation with F240 could enhance B4a1 binding of the R5 isolate. B4a1 reacts with many B clade isolates, and preincubation with sCD4 enhances binding to both the R5 and R5X4 isolates. B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, as well as CD4BS MAbs IgG1b12 and F105 to R5X4 virions, but only A1g8 and IgG1b12 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. B4a1 had an additive affect on neutralization with 2G12 with the R5X4 virus but not the R5 virus, and did not impact 2F5 neutralization. [Cavacini2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)

796 B4e8 (F425 B4e8) Env gp120 (V3 loop) P HIV-1 infection human (IgG2κ)

Ab type V3 **Research Contact** Lisa Cavacini, Beth Isreal Deconess Medical Center, Boston MA, USA
References Zwick2003, Liu2003, Cavacini2003
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, co-receptor, variant cross-recognition or cross-neutralization.

- B4e8: Called F425 B4e8. scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the V3 MAbs used. [Zwick2003] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• B4e8: The effect of isotype (IgG1 and IgG3) and subtype (IgA) switching of parental F425B4e8 (IgG2)on HIV-1 binding and neutralization was investigated. IgG1-and IgA-F425B4e8 mutants showed virus-specific binding levels and TCLA SF2 isolate compared to the parental IgG2. Comparable levels of neutralization of primary isolates 92HT593 (R5X4) and 92US660 (R5) was achieved by all isotypes and subtypes of F425B4e8. [Liu2003] (**variant cross-recognition or cross-neutralization**, **antibody sequence, variable domain**) • B4e8: This MAb binds to the base of the V3 loop, and binds and neutralizes multiple primary isolates. The anti-V3 MAb B4a1 cross-competes with B4e8. B4e8 and 2G12 enhanced each others binding, and gave synergistic neutralization. B4e8 could neutralize R5X4 virus 92HT593 better than 2G12, while 2G12 was better at neutralizing R5 virus 92US660. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to 92HT593, but only of 48d to the 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. CD4BS MAb IgG1b12 had no effect on B4e8 binding. Anti-gp41 MAb F240 inhibited B4e8 neutralization. [Cavacini2003] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)			
797	B5	Env	gp120 (IIIB)			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF **References** delReal1999 • B5: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B5 was a gp120 specific MAb from a BALBc mouse and had VH gene J558. [delReal1999]				
798	B6	Env	gp120 (IIIB)			Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 **References** delReal1999 • B6: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – B6 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558. [delReal1999]				
799	BAT267	Env	gp120		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Fung1987					
800	BAT401	Env	gp120		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Fung1987					
801	BAT509	Env	gp120		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* inactivated HIV *Strain:* B clade IIIB *HIV component:* HIV-1 **References** Fung1987					
802	C31	Env	gp120		no	HIV-1 infection	human (IgG1κ)
		References Boyer1991 • C31: Broadly-reactive group specific MAb – high yield cultivation of human MAb. [Boyer1991]					
803	D1	Env	gp41 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Otteken1996					
		• D1: MAbs D1, D16, had T37 bind to oligomeric gp160 equally well – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half life of 30 min. [Otteken1996]					
804	D12	Env	gp41 (IIIB)		L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140					
		Research Contact Patricia Earl and Christopher Broder, NIH					
		References Yang2000, LaBranche1999, Otteken1996, Earl1997, Richardson1996, Broder1994, Earl1994					
		Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, vaccine antigen design.					
		• D12: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000] (**vaccine antigen design**)					
		• D12: D12 was used in WB of HIV-1 transmembrane proteins in a study which showed that determinants of HIV-1 CD4 independence map outside regions required for coreceptor specificity – IIIBx, a CD4-independent variant of IIIB, has a truncated gp41. [LaBranche1999]					
		• D12: MAbs D4, D10, D11, D12, and D41 all bind only to complete oligomer – pulse label experiments of MAb binding to noncleavable gp160 revealed that these MAbs bound with a delay, epitopes forming with a half life of 30 min. [Otteken1996] (**antibody binding site definition and exposure**)					
		• D12: MAbs D10 and D12 are very easily blocked by human sera from HIV+ individuals. [Earl1997]					
		• D12: This antibody was blocked more strongly by human sera than other anti-gp41 MAbs (D20, D43, D61, and T4) in a oligomeric ELISA assay. [Richardson1996] (**antibody interactions**)					
		• D12: One of 18 MAbs (e. g. D4 and D40) that bind to a conformation-dependent epitope in gp41 that bind preferentially, but not exclusively, to oligomers – neutralizes IIIB and SF2. [Broder1994] (**antibody binding site definition and exposure**)					
		• D12: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)					
805	D16	Env	gp41 (IIIB)		L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env					
		Research Contact Patricia Earl and Christopher Broder, NIH					
		References Earl1997, Weissenhorn1996, Earl1994					
		• D16: One of eleven MAbs (D16, D17, D31, D36, D37, D40, D44, D55, D59, T37, and T45) that are conformation dependent and that can block the binding of the MAb D50 that binds to the linear peptide gp41(642-665) – reactive with 9/10 HIV-1 strains all except HIV-1 ADA, which has the change E659D and E662A that may result in the loss of binding (ELLE to DLLA) [Earl1997]					
		• D16: Precipitates both oligomeric gp140 and soluble monomeric gp41(21-166)that lacks the fusion peptide and membrane anchor, along with MAbs D16, D38, D40, D41, and D54. [Weissenhorn1996]					
		• D16: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
806	D4	Env	gp120 (IIIB)			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120					
		References delReal1999					
		• D4: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – D4 was a gp120 from a BALBc reconstructed nude mouse and had VH gene J558. [delReal1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
807	D43	Env	gp41 (HXB2)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* dimeric Env **Research Contact** Patricia Earl and Christopher Broder, NIH **References** Earl1997, Richardson1996, Earl1994 • D43: Partially conformation dependent – doesn't bind to short peptides, but does bind to the region spanning 641-683 – binding can be blocked by MAbs T3, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL. [Earl1997] • D43: This is a linear gp41 epitope, mapping in the region 635-678 – human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4. [Richardson1996] • D43: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]				
808	F223	Env	gp120		no	HIV-1 infection	human (IgG3λ)
		References Cavacini1999 • F223: binds to HIV-1 gp120 and to uninfected lymphocytes binding to a 159-kd auto-antigen expressed on most B cells and a small fraction of T and NK cells – the antibody enhances HIV-1 infection in a complement-dependent manner – F223 light chains have a strong homology with VLgamma2, the heavy chain to the germline gene VH3-H.11 – N-linked carbohydrates are key for recognition of both gp120 and the autoantigen – MAb 3D6 also uses VH3 and has autoreactivity. [Cavacini1999]					
809	F285	Env	Env			HIV-1 infection	human (IgG1)
		References Wisnewski1996, Wisnewski1995 • F285: F285 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996]					
810	F7	Env	gp120 (IIIB)			Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF **References** delReal1999 • F7: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – F7 was a gp120 specific MAb from a BALBc mouse and had VH gene 7183(81X), previously found expressed only in fetal liver. [delReal1999]					
811	FG39	Env	gp120			HIV-1 infection	human
		Ab type CD4BS **References** Zwick2003 **Keywords** antibody interactions. • FG39: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. [Zwick2003] (**antibody interactions**)					
812	Fab A12	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		References Binley1996 • Fab A12: Uncharacterized epitope – variable regions sequenced. [Binley1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
813	Fab A2	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1λ)
		References Binley1996					
		• Fab A2: Uncharacterized epitope – variable regions sequenced. [Binley1996]					
814	Fab L9	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		References Binley1996					
		• Fab L9: Uncharacterized epitope – variable regions sequenced. [Binley1996]					
815	Fbb14	Env	gp120			HIV-1 infection	human
		Ab type CD4BS					
		References Zwick2003					
		Keywords antibody interactions.					
		• Fbb14: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. Fbb14 was unusual among CDBS ABs in that it didn't enhance 4KG5's binding, like b12, but it did not inhibit it either as the other 13 CD4BS Abs did, it remained neutral. [Zwick2003] (**antibody interactions**)					
816	Fbb21	Env	gp120			HIV-1 infection	human
		Ab type CD4i					
		References Zwick2003					
		Keywords antibody interactions.					
		• Fbb21: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4i Fab first used in this study. Fbb21, like other CD4i MAbs, did not inhibit or enhance 4KG5 binding. [Zwick2003] (**antibody interactions**)					
817	Fbb21	Env	gp120			HIV-1 infection	human
		Ab type CD4i					
		References Zwick2003					
		Keywords antibody interactions.					
		• Fbb21: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4i Fab first used in this study. Fbb21, like other CD4i MAbs, did not inhibit or enhance 4KG5 binding. [Zwick2003] (**antibody interactions**)					
818	G12	Env	gp120 (IIIB)			Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120					
		References delReal1999					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• G12: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G12 was a gp120 from a BALBc reconstructed nude mouse and had VH gene 7183-6. [delReal1999]					
819	G2	Env	gp120 (IIIB)			Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 **References** delReal1999 • G2: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – G2 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52. [delReal1999]					
820	H2	Env	gp41				human (IgMκ)
		Research Contact BioInvent, Lund, Sweden, commercial **References** Muller1991 • H2: Anti-idiotypic MAbs (10B3 and 2All) against MAb H2 were generated by immunization of BALBc mice with H2 – they also react with seropositive sera. [Muller1991]					
821	H8	Env	gp120 (IIIB)			Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* chimeric GM-CSF *Strain:* B clade IIIB *HIV component:* gp120 **References** delReal1999 • H8: Murine antibody response to the chimeric construction granulocyte-macrophage colony stimulating factor GM-CSF/gp120 was tested, MAbs from normal mice were gp120 specific, MAbs from nude mice bound gp120 but were polyreactive, and from reconstituted mice were half way between – the anti-gp120 response used a high frequency of VH81X, VHQ52, and VH7183 genes, a family used during fetal life and associated with autoimmunity – H8 was a gp120 from a BALBc reconstructed nude mouse and had VH gene Q52. [delReal1999]					
822	HBW4	Env	gp120 (IIIB)			HIV-1 infection	human (IgG1λ)
		References Wisnewski1996, Wisnewski1995, Moran1993 • HBW4: HBW4 is V H2 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] • HBW4: Heavy (V HII) and light (V lambdaII) chain sequenced. [Moran1993]					
823	HIVIG	Env	gp120		P	HIV-1 infection	human
		References Nichols2002 • NYBC-HIVIG derived from patients with high NAb titers and NABI-HIVIG derived from patients with high anti-p24 Ab titers were compared in neutralizing assay against a panel of six primary isolates – both could neutralize all isolates tested but the NYBC-HIVIG dose required for 50% neutralization was of 3.2 fold lower, showing source plasmas influence the effective concentration of NAb present in HIVIG. [Nichols2002]					
824	IVI-4G6	Env	gp41			Vaccine	mouse (IgG2b)
		Research Contact K. Miyakoshi (Feji-Rebio Co, Tokyo, Japan) **References** Yin2001 • IVI-4G6: A bi-specific Ab (BFA) was made by combining Fab fragments of gp41-specific MAb IVI-4G6 and CD3-specific Mab UCHT1 – the BFA suppressed HIV-1 propagation culture and eliminated latently infected cells. [Yin2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
825	Ia3	Env	gp120			HIV-1 infection	human
		Ab type CD4BS **References** Zwick2003 **Keywords** antibody interactions. • Ia3: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. [Zwick2003] (**antibody interactions**)				
826	Ia7	Env	gp120			HIV-1 infection	human
		Ab type CD4BS **References** Zwick2003 **Keywords** antibody interactions. • Ia7: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This is a novel CD4BS Fab first used in this study. [Zwick2003] (**antibody interactions**)				
827	IgA6/30lambda	Env	gp120		1	HIV-1 exposed seronegative	human
		References Berry2003 **Keywords** antibody generation, antibody sequence, variable domain, genital and mucosal immunity, HIV exposed persistently seronegative (HEPS). **Country** Kenya. • A panel of anti-gp120 single-chain variable fragment (scFv) Ab were isolated from cervical B lymphocytes of unexposed uninfected Kenyan prostitutes. These Abs recognize gp120 in ELISA and using flow cytometry. IgG1b12 does not inhibit binding of the new clones to HIV, so the epitopes are distinct. Sequencing of the V genes of the scFv clones show they are unique. [Berry2003] (**antibody generation**, **genital and mucosal immunity**, **HIV exposed persistently seronegative (HEPS)**, **antibody sequence, variable domain**)				
828	IgA6/5k	Env	gp120		1	HIV-1 exposed seronegative	human
		References Berry2003 **Keywords** antibody generation, antibody sequence, variable domain, genital and mucosal immunity, HIV exposed persistently seronegative (HEPS). **Country** Kenya. • A panel of anti-gp120 single-chain variable fragment (scFv) Ab were isolated from cervical B lymphocytes of unexposed uninfected Kenyan prostitutes. These Abs recognize gp120 in ELISA and using flow cytometry. IgG1b12 does not inhibit binding of the new clones to HIV, so the epitopes are distinct. Sequencing of the V genes of the scFv clones show they are unique. [Berry2003] (**antibody generation**, **genital and mucosal immunity**, **HIV exposed persistently seronegative (HEPS)**, **antibody sequence, variable domain**)				
829	IgA6/L4	Env	gp120		1	HIV-1 exposed seronegative	human
		References Berry2003					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Keywords antibody generation, antibody sequence, variable domain, genital and mucosal immunity, HIV exposed persistently seronegative (HEPS). **Country** Kenya. • A panel of anti-gp120 single-chain variable fragment (scFv) Ab were isolated from cervical B lymphocytes of unexposed uninfected Kenyan prostitutes. These Abs recognize gp120 in ELISA and using flow cytometry. IgG1b12 does not inhibit binding of the new clones to HIV, so the epitopes are distinct. IgA6/4L is neutralizing. Sequencing of the V genes of the scFv clones show they are unique. [Berry2003] (**antibody generation**, **genital and mucosal immunity**, **HIV exposed persistently seronegative (HEPS)**, **antibody sequence, variable domain**)					
830	K14	Env	gp41		no		human (IgG1)
		References Schutten1997, Schutten1996, Schutten1995b, Schutten1995a, Teeuwsen1990 • K14: In a study of NSI and SI virus neutralization, K14 did not influence viral entry. [Schutten1997] • K14: Reduced affinity for both SI and NSI viruses relative to MAb MN215, failed to neutralize SI strain. [Schutten1995b] • K14: Did not bind to peptides spanning gp41, but it does not react with Env deletion mutant 643-692 – does not react with HIV-2 – competition experiments showed this was an immunodominant conserved epitope in HIV-1 positive sera from Europe and Africa. [Teeuwsen1990]					
831	M25	Env	gp41			Vaccine	mouse (IgGκ)
		Vaccine *Vector/Type:* purified HIV-1 **References** Watkins1996, diMarzo Veronese1985 • M25: heavy and light chains cloned and sequenced – binding requires heavy and light chain in combination, in contrast to M77. [Watkins1996]					
832	MAG 6B	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 6B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or G or A, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V. [Kang1994]					
833	MO28	Env	gp41		no	in vitro stimulation or selectio	human (IgM)
		References Ohlin1989 • MO28: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera. [Ohlin1989]					
834	MO30	Env	gp41		no	in vitro stimulation or selectio	human (IgM)
		References Ohlin1989 • MO30: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera. [Ohlin1989]					
835	MO43	Env	gp41		no	in vitro stimulation or selectio	human (IgM)
		References Ohlin1989 • MO43: This antibody was raised by *in vitro* stimulation with a recombinant Env penv9 – the discontinuous epitope of MO43 involves hydrophobic regions 632-646, 677-681 and 687-691, proximal to and spanning the transmembrane region – this specificity is unusual in HIV-1 positive sera. [Ohlin1989]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
836	N2-4	Env	gp41		no	HIV-1 infection	human (IgG1κ)
		Research Contact Evan Hersh and Yoh-Ichi Matsumoto **References** Robinson1990b • N2-4: NIH AIDS Research and Reference Reagent Program: 528. • N2-4: No enhancing activity for HIV-1 IIIB. [Robinson1990b]					
837	N70-2.3a	Env	gp120		no	HIV-1 infection	human (IgG1)
		Research Contact James Robinson, Tulane University, LA **References** Takeda1992, Robinson1990a • N70-2.3a: Fc receptor mediated enhancement of HIV-1 infection – binds a conformational site in the carboxyl half of gp120, distinct from 1.5e. [Takeda1992] • N70-2.3a: Broad reactivity. [Robinson1990a]					
838	P35	Env	Env				human
		Ab type C1 **References** Zwick2003, Kwong2002 **Keywords** antibody binding site definition and exposure, antibody interactions. • P35: called p35. scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C1-binding Fab with a discontinuous epitope that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**) • P35:Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminal, linear. [Kwong2002] (**antibody binding site definition and exposure**)					
839	P43110	Env	gp120				
		Research Contact Advanced Biosciences (Kensington, MD) **References** VanCott1995, diMarzo Veronese1992 • P43110: Does not recognized denatured form of the gp120 protein. [VanCott1995]					
840	P5-3	Env	gp120			HIV-1 infection	human (IgG1λ)
		Research Contact Evan Hersh and Yoh-Ichi Matsumoto **References** Pincus1991, Robinson1990b • P5-3: NIH AIDS Research and Reference Reagent Program: 378. • P5-3: Poor immunotoxin activity when coupled to RAC – isotype specified as: IgG3lambda. [Pincus1991] • P5-3: No enhancing activity for HIV-1 IIIB. [Robinson1990b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
841	T15G1	Env	gp41		no		

References Binley1999

- T15G1: The MABs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999]

842	T20	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Otteken1996, Earl1994

- T20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T20 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding. [Sugiura1999]
- T20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. [Otteken1996]
- T20: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

843	T26	Env	gp41			Vaccine	mouse

Vaccine *Vector/Type:* protein
Ab type C-term **Research Contact** Patricia Earl, National Institute of Allergy and Infectious Diseases
References Kilgore2003, Earl1997, Earl1994
Keywords antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization.

- T26: Mab is restricted in its binding to gp41 of the LAI isolate and not to gp41 of the MN, Ada and RF isolates. Antibody specificity may be determined by LAI residues D637E, N641D and H648Y. T26 binds to the N-terminal half of the C helix (aa630-680) of the LAI envelope, specifically targeting a confomational epitope within the six-helix bundle of gp41. Addition of the C-helical peptide inhibitor from LAI (T26 reactive) rescued the binding activity of MAb T26 to cell-surface expressed RF envelope (T26 non-reactive) triggered with sCD4 or cell-surface expressed receptors in a surface immunoprecipitation assay. This supports that C-peptide entry inhibitors bind to the gp41 N-helical coiled-coil, disrupting native six-helix bundles. [Kilgore2003] (**antibody binding site definition and exposure**)
- T26: A panel of 138 MAb raised against different forms of soluble Env. [Earl1994] (**antibody generation**)
- T26: T26 was raised against the gp140 tetramer, binds to gp41 and is a highly strain specific. [Earl1997] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

844	T27	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Research Contact P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Earl1994

- T27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T27 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding. [Sugiura1999]
- T27: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
845	T3	Env	gp41 (HXB2)			Vaccine	mouse (IgG)

Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env
References Yang2000, Zwick2001b, Earl1997, Earl1994

- T3: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000]
- T3: T3 partially competes with MAb Z13, but not MAb 4E10, both of which bind to gp41 proximally to the 2F5 epitope and have a broad neutralizing potential. [Zwick2001b]
- T3: Partially conformation dependent – doesn't bind to short peptides, but does bind to the region spanning 641-683 – binding can be blocked by MAbs D43, D38 and D45 – MAbs in this competition group reacted with 9/10 HIV-1 strains, not binding to JRFL. [Earl1997]
- T3: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
846	T30	Env	gp41		no	Vaccine	mouse

Vaccine *Vector/Type:* tetrameric Env *HIV component:* Env
Research Contact C. Broder
References Ohagen2003, Earl1997, Earl1994
Keywords antibody binding site definition and exposure, antibody generation, brain/CSF, escape.

- T30: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. T30 recognized most variants (10/13) gp41 by WB, and all of the gp160s. [Ohagen2003] (**brain/CSF**, **escape**)
- T30: Binds in the region 580 to 640, but does not bind to peptides spanning this region – binding depends on N-linked glycosylation of Asn 616 – no other antibody tested inhibited binding, but binding could be inhibited by sera from HIV+ individuals. [Earl1997] (**antibody binding site definition and exposure**)
- T30: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
847	T4	Env	gp41 (IIIB)		L	Vaccine	mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
References Srivastava2002, Yang2000, Stamatatos2000, Binley1999, Earl1997, Otteken1996, Weissenhorn1996, Richardson1996, Broder1994, Earl1994
Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, vaccine antigen design.

- T4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – T4 recognized o-gp140. [Srivastava2002] (**antibody binding site definition and exposure**)
- T4: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – gp41 MAbs T4, D12, T3, and D50 bound less efficiently to gp140-GNC4 than did pooled sera, but T4 and D12 recognized the gp140-GNC4 timer equivalently to gp140(-), and T3 and D50 recognized the trimer at greater levels than gp140(-) [Yang2000] (**vaccine antigen design**)
- T4: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form. [Stamatatos2000] (**vaccine antigen design**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• T4: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**vaccine antigen design**) • T4: This antibody, along with 7 others (M10, D41, D54, T6, T9, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1+ individuals. [Earl1997] (**antibody interactions**) • T4: MAbs T4 and T6 bind only to oligomer, and pulse chase experiments indicate that the epitope is very slow to form, requiring one to two hours. [Otteken1996] (**antibody binding site definition and exposure**) • T4: Does not bind to soluble monomeric gp41(21-166) that lacks the fusion peptide and membrane anchor, only to the oligomer gp140, as does T6. [Weissenhorn1996] (**antibody binding site definition and exposure**) • T4: one of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2. [Broder1994] (**antibody binding site definition and exposure**) • T4: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)				
848	m18	Env	Env			HIV-1 infection	human
		References Zhang2003 **Keywords** antibody generation, inter-clade comparisons, variant cross-recognition or cross-neutralization. • m18: m18 was selected from a human Fab phage display library by a new method called sequential antigen panning (SAP), using a series of antigens to screen the library to pick broadly cross-reactive isolates. The epitope of m18 is independent of CD4 binding. The phage display library was constructed using the combined bone marrow of three long term non-progressors with potent NAb activity in their sera. m18 bound to gp140s from primary isolates from clades A-F with nM affinities. The ability to block cell mediated fusion by m18 was compared to Fabs X5 and b12 for a clade A, CRF01 EA, G, and 6 clade B isolates, and the inhibitory activity of m18 was slightly lower but comparable to neutralizing Fabs b12 and X5. It also showed broad cross-neutralization; 11/15 pseudotyped Envs from primary isolates from clades A-F were inhibited in an IC50 assay at concentration less than or equal to 100 ug/ml; X5 was also tested and somewhat more potent, generally requiring lower concentrations and inhibiting 13/15 primary isolates. [Zhang2003] (**antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)				
849	multiple Fabs	Env	gp120			HIV-1 infection	human
		References Burton1991 • A panel of anti-gp120 Fabs was generated by antigen selection from a random combinatorial library prepared from bone marrow from an asymptomatic individual. [Burton1991]					
850	multiple MAbs	Env	gp120			Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp120 **References** Denisova1996 • When gp120 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: G1B12, G2F7, G9G8, G12F12, G1B8, G11F11, G9E8, G1B11, G1B6, G6F2, G2E7. [Denisova1996]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
851	multiple MAbs	Env	gp120			Vaccine	mouse
		Vaccine *Vector/Type:* gp120-CD4 complex *HIV component:* gp120 **References** Denisova1996 • When gp120-CD4 was used as an immunogen, in contrast to gp120 bound to an anti-V3 MAb, few MAbs were generated and all bound better to the native than to the denatured protein – MAbs generated were: CG43, CG41, CG49, CG53, CG42, CG4, CG46, CG40, CG52, CG51, CG48, CG50, CG125, CG124, CG121. [Denisova1996]					
852	multiple MAbs	Env	gp120			Vaccine	mouse
		Vaccine *Vector/Type:* protein-Ab complex *HIV component:* gp120-Mab complex **References** Denisova1996 • When anti-V3 MAb M77 was bound to gp120 and used as an immunogen, it stimulated many MAbs to linear epitopes, as well as an array of MAbs to discontinuous epitope – 10 of 36 MAbs were mapped to linear epitopes and are mentioned elsewhere in this database, the others are: GV5H1, GV4D5, GV4G10, GV1A8, GV10H5, GV8E11, GV2H4, GV6E6, GV1F7, GV1G9, GV4G5, GV6B12, GV1E8, GV2B7, GV1B11, GV6H5, GV6G2, GV6B5, GV1E10, GV5E3, GV5B9, GV5F4, GV6G4, GV1A12, GV5C11, GV6B6, GV3C10. [Denisova1996]					
853	polyclonal	Env	Env		L P	HIV-1 infection	human (IgG3)
		References Scharf2001 • IgG3: HIVIG was separated into immunoglobulin classes and IgG3 neutralization of HIV strains X4, R5 and X4R5 strains was superior to IgG1 and IgG2, and IgG3 was also a more potent inhibitor of viral fusion – the IgG3 advantage was lost when only Fabs were considered, indicating the IgG3 neutralization efficacy is enhanced due to a longer hinge region of the heavy chain in comparison to IgG1 and IgG2. [Scharf2001]					
854	polyclonal	Env	gp140 (IIIB)		L	Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120, gp140 *Adjuvant:* MPL-SE adjuvant, QS21 **References** Earl2001 • Immunization of rabbits with oligomeric gp140 induced production of higher levels of cross-reactive neutralizing Abs than immunization with gp120 – immunization of Rhesus macaques with gp140 yielded strong NAb against IIIB, modest against other lab-adapted strains, and no NAb activity against primary isolates – most neutralizing activity could not be blocked by a V3 peptide – 3/4 vaccinated macaques showed no viral replication upon intravenous challenge with SHIV-HXB2. [Earl2001]					
855	polyclonal	Env	gp160 (IIIB)			HIV-1 infection, Vaccine	human
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* gp160 *Adjuvant:* aluminum hydroxide **References** Cox1999 • 60 asymptomatic HIV-1 infected patients were vaccinated with rec gp160 in alum, produced in a baculovirus expression vector in insect cells (VaxSyn), 64 received placebo, and all were followed in a 5 year longitudinal study – a mean of 78% of vaccinated and 82% of those receiving placebo had demonstrable ADCC at the different time intervals in the study, and the vaccine did not enhance ADCC production – patients with rapid and slow disease progression showed similar ADCC levels. [Cox1999]					
856	polyclonal	Env	gp160 (89.6)		yes	Vaccine	macaque
		Vaccine *Vector/Type:* modified vaccinia Ankara (MVA) *Strain:* B clade 89.6 *HIV component:* Env, Gag-Pol *Adjuvant:* IL2/Ig **References** Barouch2001b					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Four rhesus macaques were vaccinated with a modified vaccinia Ankara (MVA) vaccine that elicited strong CTL responses as well as antibody responses. The animals were infected when challenged with pathogenic SHIV-89.6P, but had potent CTL responses, secondary NAb responses upon challenge, partial preservation of CD4+ T-cell counts, lower viral loads, and no evidence of disease or mortality by day 168 after challenge—monkeys that got a sham vaccine had high viral load, progressed to disease, and 2/4 were dead by day 168. [Barouch2001b]					
857	polyclonal	Env	gp160		no	HIV-1 infection	human
		References Ahmad2001					
		• High CD4+ T-cell count and low viral load was correlated with high ADCC anti-HIV-1 Env Ab titers in a study of 46 HIV-1 infected individuals from all disease stages. [Ahmad2001]					
858	polyclonal	Env	gp160		P	HIV-1 infection	human (IgG)
		References Beirnaert2001					
		• Neutralizing antibodies are thought to inhibit HIV entry by blocking either binding or fusion – six broadly cross-neutralizing sera that can neutralize group M and O viruses inhibit the binding to PBMCs – the nine primary isolates tested in this study represented very diverse subtypes and recombinant forms, and different co-receptor usage. [Beirnaert2001]					
859	polyclonal	Env	gp160		P	HIV-1 infection	human (IgG)
		References Beirnaert2000					
		• Sera from 66 HIV individuals from diverse geographic locations could neutralize primary isolates to different extents: broad cross-neutralizing isolates could neutralize 14 primary isolates from HIV-1 group M clades A-H and three O isolates, limited cross-neutralizing sera neutralized some isolates, and non-neutralizing sera—6/7 broadly neutralizing sera were from African women, despite only 14/66 study subjects being women—ability to neutralize three key isolates, MN lab (envB/gagB, X4 coreceptor), VI525 (envG/gagH, envA/gagA, R5X4) and CA9 (Group O, R5) was predictive of being able to neutralize an additional set of 14 primary isolates. [Beirnaert2000]					
860	polyclonal	Env	gp120 (SF2)		L	Vaccine	mouse, baboon
		Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* MF59, PLG					
		References O'Hagan2000					
		• Microparticles were used as an adjuvant for entrapped HIV-1 gp120 and induced strong serum IgG responses in mice – polylactide co-glycolide polymer (PLG) microparticles in combination with MF-59 had the highest response. [O'Hagan2000]					
861	polyclonal	Env	gp120 (SF2, US4)			Vaccine	macaque, guinea pig, mouse
		Vaccine *Vector/Type:* DNA, protein *Strain:* B clade SF2, B clade US4 *HIV component:* gp120 *Adjuvant:* aluminum phosphate, MF59, PLG					
		References O'Hagan2001					
		• DNA vaccines of codon-optimized Env and Gag genes driven by CMV promotors and absorbed on to PLG microparticles were more effective than naked DNA at eliciting strong Ab responses (more rapid, higher titer, more stable), comparable to gp120 in MF-59. [O'Hagan2001]					
862	polyclonal	Env	gp120		L	HIV-1 infection	chimpanzee (IgG)
		References Moore1999, Shibata1999					
		• polyclonal: Commentary discussing this finding noting the particularly high neutralization titer and limited breadth of the chimpanzee sera used in this study. [Moore1999]					
		• polyclonal: Purified IgG from chimpanzee sera infected with several HIV-1 strains was used for passive administration to macaques which were subsequently challenged with the virulent SHIV bearing the HIV-1 env DH12 – *in vitro* neutralization correlated with protection *in vivo*. [Shibata1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
863	polyclonal	Env	gp160 (MN)		L P	HIV-1 infection	human (IgA)
		References Moja2000					
		• 15 samples isolated from parotid saliva were selected for study as they had anti-Env IgA – IgA neutralizing activity was detected that was not directed at either EDELKWA or the V3 loop. [Moja2000]					
864	polyclonal	Env	gp120		L	Vaccine	
		Vaccine *Vector/Type:* protein *Strain:* B clade MN, B clade SF2 *HIV component:* gp120					
		References McElrath2000					
		• After 3 immunizations, 210/241 (87%) HIV-1 uninfected vaccinees in a phase II trial developed NAbs – of 140 patients receiving 4 vaccinations, 53% had persistent neutralizing antibodies to homologous virus, and 34% to heterologous virus, measured at day 728 after initial immunization – immunogens were well tolerated– but IVDUs had a decreased Ab response relative to lower risk groups. [McElrath2000]					
865	polyclonal	Env	gp120			Vaccine	mouse
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* gp120 *Adjuvant:* GM-CSF/gp120 chimera					
		References Rodríguez1999					
		• The murine Ab response to a chimeric of granulocyte-macrophage colony stimulating factor GM-CSF/gp120 in vaccinia was not higher titer that the response to a gp120-vaccinia construct, but the breadth of the Ab response was greater – a cellular response of greater intensity was trigged to the GM-CSF/gp120 vaccinia construct, as measured by proliferation and Elispot. [Rodríguez1999]					
866	polyclonal	Env	gp120 (YU2)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* stabilized Env trimer *Strain:* B clade HXBc2, B clade YU2 *HIV component:* Env					
		Research Contact Joseph Sodroski, Harvard Medical School					
		References Yang2001					
		• Soluble Env trimers were created that were designed to mimic functional Env oligomers – stabilized timers could induce neutralizing antibodies more effectively than gp120, and Abs to the YU2 trimer were cross-reactive within clade B and could neutralize several primary and TCLA reactive strains – the stabilized primers did not neutralize primary isolates outside the B clade, from clades C, D, and E – HXBc2 stabilized trimer antigen elicited strong neutralizing Abs against the homologous isolate HXBc2 TCLA strain, but not against primary isolates. [Yang2001]					
867	polyclonal	Env	gp120 (MN)			Vaccine	human
		Vaccine *Vector/Type:* protein *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* aluminum hydroxide, QS21					
		References Evans2001					
		• Vaccination with QS21 adjuvant and rsgp120 elicited stronger and more sustained neutralizing antibody responses and lymphocyte proliferation with lower doses of rsgp120 than alum formulations, suggesting QS21 may be a means to reduce the does of soluble protein. [Evans2001]					
868	polyclonal	Env	gp120		yes	HIV-1 infection	human
		References Binley2000					
		• HAART inhibited the development of anti-gp120 Ab when initiated during primary infection and sometimes in patients treated within 2 years of HIV-1 infection – HAART during primary infection usually did not inhibit the development of weak NAb responses against autologous virus – 3/4 patients intermittently adherent developed high titers of autologous NAbs, largely coincident with brief viremic periods. [Binley2000]					
869	polyclonal	Env	gp120 (SIV)		yes	HIV-1 infection	macaque
		References Reitter1998					
		• This study concerned an SIV mutated strain that lacked 4th, 5th and 6th sites for N-linked glycosylation – monkeys infected with the mutant viruses had increased neutralizing activity in their sera relative to monkeys infected with the parental strain. [Reitter1998]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
870	polyclonal	Env	Env		yes	HIV-1 infection	human
		References Kim2001					
		• After HAART reduction of viral load to <400 for three visits over a 12 month interval, 2/11 patients were found to have increased anti-Env Ab binding titers, and neutralizing Abs titers increased against primary isolates US1, and CM237 – no NAB titer increase was seen to more readily neutralized isolate BZ167 – this suggests that in certain individuals the control of HIV-1 by HAART may augment immune control of HIV. [Kim2001]					
871	polyclonal	Env	Env		yes	HIV-1 exposed seronegative	human (IgA)
		References Kaul2001b					
		• Kaul *et al.* provide a concise summary of the findings concerning the presence of Mucosal IgA in highly exposed, uninfected subjects, arguing for a role in protection. [Kaul2001b]					
872	polyclonal	Env	gp120		yes	Vaccine	human
		Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* gp120 *Adjuvant:* MF59					
		References Nitayaphan2000					
		• A phase I/II trial was conducted in 52 seronegative Thais immunizing with rgp120 SF2 – the vaccine was safe and 39/40 developed NAb responses to the autologous SF2, while 22/40 were able to cross-neutralize the heterologous strain MN. [Nitayaphan2000]					
873	polyclonal	Env	gp120 (SF2)		yes	Vaccine	macaque
		Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* gp120, p24 Gag *Adjuvant:* Immune stimulating complexes (ISCOM)					
		References Heeney1998a					
		• The immune responses induced in Rhesus monkeys using two different immunization strategies was studied – one vaccine group was completely protected from challenge infection, the other vaccinees and controls became infected – protected animals had high titers of heterologous NAbs, and HIV-1-specific T helper responses – increases in RANTES, MIP 1 alpha and MIP 1 beta produced by circulating CD8+ T cells were also associated with protection. [Heeney1998a]					
874	polyclonal	Env	gp120			Vaccine	macaque
		Vaccine *Vector/Type:* peptide, protein *Strain:* B clade SF2, B clade SF33 *HIV component:* gp120 *Adjuvant:* Immune stimulating complexes (ISCOM), MF59					
		References Verschoor1999					
		• Attempts were made to broaden immune responses induced in Rhesus monkeys by immunization of animals previously immunized that had resisted homologous challenge, with a second immunization with ISCOM-peptides or a boost with gp120 from SF33 – animals didn't survive a second challenge heterologous challenge virus SHIV(SF33) raising concerns about early antigenic sin. [Verschoor1999]					
875	polyclonal	Env	gp120		yes	Vaccine	baboon
		Vaccine *Vector/Type:* protein *Strain:* B clade SF2, CRF01 CM235 *HIV component:* gp120 *Adjuvant:* MF59					
		References VanCott1999					
		• Immunization with rgp120 CM235 (CRF01) induced Abs capable of neutralizing TCLA subtype E (CRF01) and subtype B isolates, while rgp120SF2 induced Abs could only neutralize subtype B TCLA isolates – neither immunogen induced Abs capable of neutralizing primary HIV-1 isolates – both rgp120CM235 and rgp120SF2 induced Abs to regions within C1, V1/V2, V3, and C5, but unique responses were induced by rgp120CM235 to epitopes within C2, and by rgp120SF2 to multiple epitopes within C3, V4, and C4 – CM235 baboon sera bound 3- to 12-fold more strongly than the SF2 baboon sera to all subtype E gp120s while binding to subtype B gp120s (except SF2) were within two to threefold for the SF2 and CM235 baboon sera. [VanCott1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
876	polyclonal	Env	gp140 (SF162DeltaV2)		yes	Vaccine	macaque, rabbit (IgG)

Vaccine *Vector/Type:* DNA with CMV promotor *Strain:* B clade SF162 *HIV component:* gp140 *Adjuvant:* MF59
References Barnett2001

- SF162ΔV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization—when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162ΔV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162ΔV2, but not intact SF162, was used as the immunogen—Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162ΔV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5)—the pattern of cross-recognition shifted after the second boost. [Barnett2001]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
877	polyclonal	Env	gp120			HIV-1 infection	human (IgG)

References Binley1997b

- Retention of anti-Env antibodies and loss of anti-Gag antibodies during progression was studied, and suggested to be the result of the loss of T-cell help and the unique ability of Env to stimulate B cells even in a backdrop of declining CD4 cells, because of the ability of Env to bind to the CD4 molecule. [Binley1997b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
878	polyclonal	Env	gp120 (W61D)		L	Vaccine	human

Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120
References Beddows1999

- rgp120 derived from a R5X4 subtype B virus, HIV-1 W61D, was used to vaccinate healthy volunteers and the resulting sera were compared with HIV-1 positive subjects – vaccinee sera had more potent responses to linear V1/V2 and V3 epitopes than did the sera from HIV-1+ individuals, but could only neutralize homologous or heterologous virus only after adaptation to T-cell lines – neutralization activity was lost after re-adaptation to growth in PBMCs – in contrast, sera from infected individuals could neutralize both PBMC and T-cell line adapted viruses. [Beddows1999]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
879	polyclonal	Env	gp120		L	Vaccine	macaque

Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* Gag, gp120, V3
References Wagner1998b

- A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock. [Wagner1998b]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
880	polyclonal	Env	gp120 (IIIB)			Vaccine	mouse

Vaccine *Vector/Type:* DNA *HIV component:* gp120, gp160
References Shiver1997

- DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T cell proliferative response with Th1-like secretion of gamma interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs. [Shiver1997]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
881	polyclonal	Env	gp120		L	Vaccine	mouse

Vaccine *Vector/Type:* DNA *HIV component:* Env, Gag, Pol, Vif *Adjuvant:* B7, IL-12
References Kim1997b

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• A gag/pol, vif or CMN160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice – the Ab response was detected by ELISA, but the CMN160 DNA vaccinated mice showed a neutralizing Ab response. [Kim1997b]					
882	polyclonal	Env	gp120		P	HIV-1 infection	human
		References Bradney1999					
		• Sera were taken from long term non-progressors and evidence for viral escape was noted – serum could neutralize earlier autologous isolates, but not contemporary isolates. [Bradney1999]					
883	polyclonal	Env	gp120		L P	Vaccine	human
		Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade SF2 *HIV component:* Env, Gag					
		References Belshe1998					
		• NAbs were obtained by a HIV-1 gag/env in canary pox vaccination of eight volunteers after boosting with rgp120 against lab strains – 1/8 primary isolates was neutralized, BZ167. [Belshe1998]					
884	polyclonal	Env	gp120		L	Vaccine	human
		Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, Protease *Adjuvant:* MF59					
		References Belshe2001, Belshe1998					
		• A phase 2 trial was conducted in 435 volunteers with vCP201, a canary pox vector carrying gp120 (MN in vCP201, and SF2 in the boost), p55 (LAI) and protease (LAI), either alone or with a gp120 boost – NAbs against MN were obtained in 56% of those who received vCP201 alone, and in 94% of those who got the prime with the gp120 boost. [Belshe1998]					
885	polyclonal	Env	gp120				human
		References Neshat2000					
		• HIV-1 gp120 appears to be a B cell superantigen that binds to members of the V_{H3} Ig gene family—the gp120 binding site was localized to the Fab portion of the Ab, and discontinuous residues in the V_H region were critical. [Neshat2000]					
886	polyclonal	Env	gp41 (539–684 BH10)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* gp41					
		References Bai2000					
		• Murine rsgp41 antisera recognized a common epitope on human IFNα (aa 29-35 and aa 123-140) and on human IFNβ (aa 31-37 and aa 125-142), suggesting that elevated levels of Ab to IFNs found in HIV+ individuals may be due to a cross-reactive gp41 response. [Bai2000]					
887	polyclonal	Env	gp120 (BH10)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* B clade 89.6, B clade ADA, B clade IIIB *HIV component:* gp120 *Adjuvant:* C3d fusion					
		References Ross2001					
		• gp120 was fused with murine complement protein C3d in a DNA vaccine to enhance the titers of Ab to Env – fusion to C3d resulted in a more rapid onset of Ab response and avidity maturation, after three immunizations in BALB/c mice with DNA on a gold bead delivered with a gene gun, but not in strong neutralizing Ab response. [Ross2001]					
888	polyclonal	Env	gp120 (SF162DeltaV2)			Vaccine	macaque
		Vaccine *Vector/Type:* DNA prime with protein boost *Strain:* B clade SF162 *HIV component:* gp140 *Adjuvant:* MF59					
		References Cherpelis2001a, Cherpelis2001b					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• HIV-1 SF162ΔV2 gp140 envelope was used in a DNA-prime plus protein-boost vaccination methodology in Rhesus macaques, the animals were depleted of their CD8+ T lymphocytes, and challenged with pathogenic SHIV(SF162P4)—the vaccinated macaques had lower peak viremia, rapidly cleared virus from the periphery, and developed delayed seroconversion to SIV core antigens relative to non-vaccinated controls. [Cherpelis2001a] • Two animals were immunized both intradermally and intramuscularly at weeks 0, 4, and 8 with a codon optimized DNA vector expressing the SF162V2 gp140 envelope with an intact gp120-gp41 cleavage site, and both developed lymphoproliferative responses and potent neutralizing Abs – CD8+ T lymphocytes were depleted in the animals and they were challenged with SHIV162P4 – at peak viremia, plasma viral levels in the vaccinated animals were 1 to 4 logs lower than those in the unvaccinated animals. [Cherpelis2001b]					
889	polyclonal	Env	gp120		P	HIV-1 infection	human
		References Sarmati2001 • Some HIV-1 infected patients have increasing CD4 counts despite failing ARV, and CD4 levels are correlated with HIV-1 specific NAbs – no correlation was found between NAbs and viral load in this patients. [Sarmati2001]					
890	polyclonal	Env	gp41 (539–684 BH10)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein *HIV component:* gp41 **References** Bai2000 • There is a common epitope in HIV-1 gp41, and IFNalpha and IFNbeta. [Bai2000]					
891	polyclonal	Env	gp120 (IIIB)		no		human (IgM)
		References Llorente1999 • Combinatorial antibody analysis by phage display and flow cytometry demonstrated that gp120 in HIV-1 negative people is recognized by IgM, but not IgG Abs – IgM Fab reactivity is observed throughout the entire sequence of HIV-1 IIIB gp120 and is characterized by low affinity binding and near germline configuration reflecting a lack of maturation of the IgM repertoire – no neutralizing activity was observed in a non-infected individual before isotope switching. [Llorente1999]					
892	polyclonal	Env	gp120 (SF2)		L	Vaccine	human (IgM)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF2 *HIV component:* gp120 **References** Locher1999 • High risk volunteers were vaccinated with SF2 gp120 – 3 breakthrough cases were studied – SF2 neutralizing Abs were observed, but Ab titers to autologous virus were never high and took 6 months after HIV-1 infection to develop – viral loads were similar to HIV-1 infected individuals who had not been vaccinated. [Locher1999]					
893	polyclonal	Env	gp120 (subtype A, B, C, D, CRF01)		yes	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* formaldehyde-fixed whole-cell *HIV component:* gp120 **References** Nunberg2002, LaCasse1999 • A retraction was printed (Science 296:1025, 2002) noting that an unknown cytotoxic effect of these complex sera accounted for a major fraction of the neutralization reported in [LaCasse1999] [Nunberg2002]. [LaCasse1999, Nunberg2002] • In this study, immunogens were generated that were thought to capture transient envelope-CD4-coreceptor structures that arise during HIV binding and fusion by formaldehyde-fixation of co-cultures of cells expressing HIV-1 Env and those expressing CD4 and CCR5 receptors – these cells elicited NAbs in CD4- and CCR5-transgenic mice that neutralized 23/24 primary isolates from clades A-E. [LaCasse1999]					
894	polyclonal	Env	(B consensus)		P	HIV-1 infection	human
		References Morris2001					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Ab responses before HAART therapy and after one year of therapy were measured in 8 individuals that were classified HAART successes, and 10 patients who were classified as HAART failures – V3 peptide antibody binding titers to the B-consensus and MN and SF2 variants, and neutralization of HIV-1 MN and four subtype B clinical isolates were tested – subjects with strong anti-V3 and NAb humoral immune responses before starting HAART were more likely to achieve sustained viral suppression to <500 copies RNA/ml on HAART – HIV-specific Ab responses declined after 1 year of successful viral suppression on HAART. [Morris2001]					
895	polyclonal	Env			P	HIV-1 infection	human (IgG)
		References Pilgrim1997					
		• Sera from long-term nonprogressors(LTNP) had broader NAbs against heterologous primary isolates and were more likely to neutralize the contemporaneous autologous isolate than were sera from short-term nonprogressors and normal progressors – in 4 individuals followed from acute infection, NAbs were detected against the early autologous isolate by 5-40 weeks, and not detected in an additional 2 cases after 27-45 weeks. [Pilgrim1997]					
896	polyclonal	Env			P	HIV-1 infection	human
		References Moog1997					
		• Autologous and heterologous NAbs were studied in 18 individuals who were sampled early after sero-conversion and followed longitudinally – autologous NAbs were not detected in sera collected at the same time as the viruses were isolated – NAbs detected against the seroconversion autologous strains were not detected one year after seroconversion, and were highly specific to the virus present at the early phase of HIV infection – heterologous neutralization of primary isolates were not detected until after 2 years. [Moog1997]					
897	polyclonal	Env			yes	HIV-1 infection	human
		References Montefiori2001					
		• In 7/9 patients in whom HAART was initiated during early seroconversion, NAbs to autologous strains were not found immediately following treatment interuption after 1-3 years, and Env and Gag Abs were low or undetected by ELISA indicating, that early HAART suppresses the normal antibody response to HIV-1, presumably by limiting the concentration of viral antigens needed to drive B-cell maturation – in 3 patients with a viral rebound autologous NAbs rapidly appeared and correlated with spontaneous down-regulation of viremia – prolonged control of viremia after stopping treatment persisted in the absence of detectable NAbs, suggesting that cellular immune responses alone can control viremia under certain circumstances – these results support the notion that virus-specific B-cell priming, combined with CD8+ CTL induction, may be beneficial for HIV-1 vaccines that aim to suppress viremia in the absence of complete protection to prevent disease and reduce the rate of virus transmission. [Montefiori2001]					
898	polyclonal	Env				HIV-1 infection	human (IgG)
		References Scala1999					
		• Random peptide libraries were screened using sera from HIV-infected subjects to identify mimotopes, peptides that mimic conformational or linear epitopes specifically recognized by Abs from HIV-1 infected individuals – the sera of simian SHIV-infected monkeys also recognized the specific peptides, and mice immunized with the selected peptides elicited HIV-specific Abs that neutralized HIV-1 isolates IIIB and NL4-3. [Scala1999]					
899	polyclonal	Env			L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* mimotopes					
		References Scala1999					
		• Random peptide libraries were screened using sera from HIV-infected subjects to identify mimotopes, peptides that mimic conformational or linear epitopes specifically recognized by Abs from HIV-1 infected individuals – the sera of simian SHIV-infected monkeys also recognized the specific peptides, and mice immunized with the selected peptides elicited HIV-specific Abs that neutralized HIV-1 isolates IIIB and NL4-3. [Scala1999]					
900	polyclonal	Env				Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* virus-like particle (VLP) *HIV component:* Env, Gag *Adjuvant:* Complete Freund's Adjuvant (CFA)					
		References Lebedev2000					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Virus-like particles (VLPs) in the form of spherical particles with yeast dsRNA enveloped in a polysaccharide matrix carrying the protein TBI, that contains fragments of HIV Env and Gag, were used to immunize BALB/c mice and induced specific Abs against HIV-1 as measured by ELISA with TBI. [Lebedev2000]					
901	polyclonal	Env			P	HIV-1 infection	human
		References Donners2002					
		• A difference in neutralization patterns between African and European plasma is observed, especially in African women, who tended to have cross-neutralizing Abs against primary isolates. [Donners2002]					
902	polyclonal	Env			L	HIV-1 infection	human (IgG)
		References Dianzani2002					
		• Immune complexes(ICs) in the plasma contained HIV RNA (80%-100%) in association with HIV-specific IgG NAbs indicating that the HIV in the plasma of carriers is frequently composed of antibody-neutralized HIV as ICs. [Dianzani2002]					
903	polyclonal	Env	Env		P	HIV-1 infection	human (IgG)
		References Kimura2002					
		• Significant neutralization activity against autologous isolates was observed in 13/19 HIV+ patients at initiation of HAART therapy which persisted during therapy, increasing in one patient, and declining in one patient – 3/6 patients with no detectable NAb at the start of therapy developed NAb responses – of the four patients with increased NAb responses, three had low level viral rebounds (blips) [Kimura2002]					
904	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Devito2000b					
		• Mucosal and plasma HIV-specific IgA that can neutralize primary isolates is present saliva (11/15 tested) and plasma (11/15) and cervicovaginal fluid (11/14) from highly exposed persistently seronegative (HEPS) individuals. [Devito2000b]					
905	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Devito2000a					
		• IgA from the genital tract, saliva and plasma from highly exposed persistently seronegative (HEPS) individuals can inhibit transcytosis of HIV-1 across a transwall system that provides a tight epithelial cell layer—50% of the IgA samples studied were able to inhibit transcytosis of at least one of two primary isolates tested, indicating this may be an important mechanism against sexual acquisition of HIV-1. [Devito2000a]					
906	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Broliden2001					
		• IgA isolated from the saliva, genital tract, and plasma of most highly exposed persistently seronegative (HEPS) sex workers in a Kenyan cohort could neutralize a B, A and D clade primary isolates and could inhibit transcytosis of HIV across a transwall model of the human mucosal epithelium. [Broliden2001]					
907	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Devito2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• IgA isolated from the saliva, genital tract, and plasma of most highly exposed persistently seronegative (HEPS) Kenyan sex workers mediated broad cross-clade neutralization of primary isolates (A, B, C, D, and CRF01) – 6/10 HEPS individuals that were persistently exposed to a stable HIV+ B clade infected partner showed less breadth of neutralization, and were able to neutralize clade A and B primary isolates, but not clades C, D, or CRF01. [Devito2002]					
908	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Mazzoli1999					
		• Serum HIV-specific IgA is present in highly exposed persistently seronegative individuals (HEPS) in the absence of serum IgG – serum IgA can be found in productively infected individuals and exposed seronegatives at similar titers – 5/15 sera from HEPS had neutralizing activity, 2 of these in purified IgA – HIV-1 specific serum IgA concentrations declined after one year of interruption of at-risk sex. [Mazzoli1999]					
909	polyclonal	Env			P	HIV-1 exposed seronegative	human (IgA)
		References Beyrer1999					
		• HIV-specific anti-gp160 IgA is present in cervical lavage from 6/13 HIV-exposed seronegative Thai female sex workers. [Beyrer1999]					
910	polyclonal	Env				Vaccine	mouse
		Vaccine *Vector/Type:* DNA *Strain:* B clade HXB2/Bal					
		References Chakrabarti2002					
		• A modified gp140 (gp140ΔCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. [Chakrabarti2002]					
911	polyclonal	Env				Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade 89.6, B clade IIIB *HIV component:* Env *Adjuvant:* alpha2-macroglobin, Complete Freund's Adjuvant (CFA), monophosphoryl lipid A with GM-CSF					
		References Liao2002					
		• HIV-envelope peptides coupled to α2-macroglobin were much more immunogenic when formulated in monophosphoryl lipid A with GM-CSF than in complete or incomplete Freund's adjuvant or in monophosphoryl lipid A with GM-CSF alone. [Liao2002]					
912	polyclonal	Env	gp120		P	Vaccine	macaque
		Vaccine *Vector/Type:* gp120-CD4 complex, gp140-CD4 complex *Strain:* B clade IIIB *HIV component:* gp120, gp140 *Adjuvant:* QS21					
		References Fouts2002					
		• gp120-CD4 and gp140-CD4 complexes were used for i.m. vaccination of rhesus macaques and neutralizing Ig was recovered using affinity chromatography using a chimeric HIV-BAL gp120 with a mimetic peptide that induces a CD4-triggered mimetic structure – the sera and affinity purified Ab were broadly neutralizing against primary X4, R5, and R5X4 isolates from multiple subtypes but did not react as well against lab-adapted isolates. [Fouts2002]					
913	polyclonal	Env			P	HIV-1 infection	human
		References Pastori2002					
		• HAART initiated during primary infection was studied in seven patients and had different effects on NAb production—in some cases, α-Env Abs were inhibited during primary infection, and in some cases strong NAbs against autologous virus were induced. [Pastori2002]					
914	polyclonal	Env	gp120		L	HIV-1 infection	chimpanzee (IgG)
		References Moore1999, Igarashi1999					
		• polyclonal: Commentary discussing this finding noting the particularly high neutralization titer and limited breadth of the chimpanzee sera used in this study. [Moore1999]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• The rate of virus clearance in the circulation in rhesus macaques receiving a continuous infusion of cell-free viral dual-tropic virus isolate HIV-1DH12 particles in the presence and absence of virus-specific antibodies was measured – the clearance of physical and infectious viral particles is very rapid in naive animals, with half-lives ranging from 13 to 26 minutes, but clearance cold be acheived with a half life of 3.9-7.2 minutes when chimpanzee neutralizing Abs were present to help to remove virions from the blood. [Igarashi1999]					
915	polyclonal	Env	gp120		L	Vaccine	human
		Vaccine *Vector/Type:* canarypox prime with gp120 boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* gp120, gp41 *Adjuvant:* MF59 **References** Gupta2002					
		• Vaccine trial protocol 022A in 150 HIV-1 uninfected adults (130 completed the study) showed high titer ALVAC vaccine in combination with gp120 was safe and immunogenic in HIV-1 negative volunteers – NAb responses were detected in 95% of vaccinees, with higher titers in recipients of sequential versus simultaneous dosing of the two vaccines and in vaccinia naive volunteers. [Gupta2002]					
		• Different HIV strains were used for different regions: gp120 MN and gp41 LAI, rgp120 SF2.					
916	polyclonal	Env	gp120		yes	Vaccine	mouse (IgA, IgG, IgG1, IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade 89.6 *HIV component:* gp120, gp140 *Adjuvant:* Cholera toxin (CT), IL-12 **References** Albu2003 **Keywords** genital and mucosal immunity, mucosal immunity, Th1, Th2.					
		• Mice were intranasally immunized with gp120 or gp140 with IL-12 and Cholera toxin as adjuvants. Adjuvants enhanced NAb stimulation in mucosa and genital tissues and in serum. [Albu2003] (**genital and mucosal immunity**, **mucosal immunity**, **Th1**, **Th2**)					
917	polyclonal	Env	gp120 (V3 loop)			HIV-1 infection	human
		Ab type V3 **References** Bongertz2003 **Keywords** inter-clade comparisons, rate of progression. **Country** Brazil.					
		• Ab responses at diluations above 1:1000 against the consensus V3 loops of subtypes A, B, C, D, F, and Brazilian B and F, were detected in only 6/60 individuals infected with HIV by sexual exposure, while a significantly higher (38/46) reactivity and frequency of peptide recognition was observed in the plasma of IDUs. High Ab titers (> 1:10,000) were directed against V3B, V3Bbr and V3F peptides. The IDU group also displayed broader NAb responses, in comparison to the sexually transmitted group. This may contribute to a slower disease progression in IDUs. [Bongertz2003] (**inter-clade comparisons**, **rate of progression**)					
918	polyclonal	Env	gp120		yes	Vaccine	mouse
		Vaccine *Vector/Type:* virus-like particle (VLP) *Strain:* A clade UG5.94UG018 *HIV component:* Gag, gp120 **References** Buonaguro2002 **Keywords** inter-clade comparisons. **Country** Uganda.					
		• BALB/c mice were immunized with VLPs carrying a subtype A gp120. Humoral immune responses directed against B-clade derived Gag (p24) peptides or gp120-Env V3 loop peptide were readily induced following a multi-dose immunization with VLP particles presenting a gp120 molecule from a HIV-1 isolate of clade A. VLP-immunized mice showed autologous and heterologous (against B-clade HIV-1 IIIB strain) neutralization activity. Proliferative responses and CTL were also observed. [Buonaguro2002] (**inter-clade comparisons**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
919	polyclonal	Env	gp120			Vaccine	human

Vaccine *Vector/Type:* canarypox, protein *Strain:* B clade LAI, B clade MN *HIV component:* Env, Gag, Protease
References Cao2003
Keywords inter-clade comparisons.
Country Uganda.

- 20 Ugandan seronegative individuals were intramuscularly immunized in this study with an ALVAC HIV GagPol and Env vaccine carrying B clade agtigens.3/20 of subjects produced neutralizing antibodies against the autologous HIV-1 clade B strain MN that was T-cell line adapted; 2 also had NAb reactivity against a primary B clade cell line. No NAb cross-reaction was observed with primary viral isolates UG92029 (subtype A) or UG92046 (subtype D). 4/20 had detectable CTL activity against B clade antigen, and one of these cross-reacted with A clade antigen, one with D clade. [Cao2003] (**inter-clade comparisons**)

920	polyclonal	Env	gp160			SHIV infection	macaque

References Crawford1999
Keywords variant cross-recognition or cross-neutralization.

- Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate or TCLA SHIV variants. SHIV infected macaques could neutralize autologous virus very effectively, but serum from HXB2c or 89.6 infected animals could not neutralize heterologous SHIVs. Serum from KU infected animals could neutralize only HXB2c, and serum from 89.6PD infected animals could neutralize 89.6, 89.6P, 89.6PD and KB9 (all derived from 89.6) well. Many sera from the SHIV infected macaques could also neutralize HIV-1 strains MN and SF2. [Crawford1999] (**variant cross-recognition or cross-neutralization**)

921	polyclonal	Env	gp160			HIV-1 infection	human

References Crawford1999
Keywords variant cross-recognition or cross-neutralization.

- Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate or TCLA SHIV variants. Serum from 9 HIV-1 infected people were tested for their ability to neutralize SHIVs. KU2 was least sensitive, 89.6, 89.6P, 89.6PD and KB9 (all derived from 89.6) were moderately susceptible, and SHIV HXB2c was less sensitive than IIIB, the strain from which it was derived. [Crawford1999] (**variant cross-recognition or cross-neutralization**)

922	polyclonal	Env	Env		yes	Vaccine	rabbit, mouse (IgG)

Vaccine *Vector/Type:* Venezuelan equine encephalitis virus (VEE) *Strain:* B clade R2 *HIV component:* gp160ΔCT
References Dong2003
Keywords inter-clade comparisons, variant cross-recognition or cross-neutralization.

- C3H/He mice immunized with replicons expressing RT env protein or the VEE env vector pGP expressing either gp140 or gp160 showed cross-reactive neutralizing Ab responses to five clade B env proteins, a chinese clade C strain and weakly against a chinese clade E (CRF-1) strain.
- Subcutaneous or intradermal immunization with VEE replicons expressing HIV-1 R2 gp140 and with HIV-1 R2 gp160 lacking the cytoplasmic tail. Sera from 3/3 rabbits inhibited SF162 infectivity and 2/3 rabbits were able to neutralize the R2 strain.
- Mice and rabbits were immunized with Venezuelan equine encephalitis virus (VEE) replicon system particles expressing HIV-1 Env from the clone R2 that was derived from a virus that was neutralization sensitive and isolated from an individual that made strong NAb resposnes. Stronger and faster NAb responses were induced with replicons expressing gp160 with the cytoplasmic tail deleted than with gp160 or gp140. NAb responses against heterologous strain SF162 were similar in BALB/c and C3H/He mice and enhanced compared to responses elicited in C57BL/6 mice. Serum from mice neutralized 5 primary clade B env proteins, a chinese clade C strain, but not a chinese clade E (CRF-1) strain. Sera from 3/3 immunized rabbits could neutralize SF162, and from 2/3 neutralized the autologous R2 strain. [Dong2003] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
923	polyclonal	Env			P	HIV-1 infection	human

References Donners2003
Keywords assay development, assay standardization, co-receptor, inter-clade comparisons, kinetics.
Country Belgium.

- Plasma samples from six HIV-1+ Belgians showed broad cross-neutralization ability against primary isolates from group M (subtypes A-H) and Group O. Viruses with R5, X4, and R5X4 co-receptor usage were all represented in the test panel. Kinetics of neutralization showed that NAb responses detected useing a PBMC assay with a short incubation period could be lost upon extended culture. No preincubation with Ab was needed to see some inhibition of virus replication, indicating that at least partial neutralization occurs post-virus binding to target cells. [Donners2003] (**assay development**, **co-receptor**, **kinetics**, **inter-clade comparisons**, **assay standardization**)

924	polyclonal	Env	Env			HIV-1 infection	human

Research Contact Rebeca Geffin, Miami School of Medicine
References Geffin2003
Keywords autologous responses, escape, rate of progression, responses in children.

- A longitudinal study of NAb responses in perinatally HIV-1 infected infants and children was undertaken, including 7 with rapid progression (RP) and 9 who did not progress rapidly (NRP). A subset of both RPs and NRPs had some plasma samples that could neutralize contemporaneous autologous viral isolates after 6 months of age, but most isolates could not be neutralized by contemporaneous plasma, only by later samples. The non-contemporaneous NAbs would persist for years, had highest titers against earlier isolates, and tended to be more potent in NRP children. This study indicates that there is ongoing NAb escape in HIV-1+ children. No correlation between HIV RNA levels and Ab production was established, although this might have been complicated by treatment. [Geffin2003] (**autologous responses**, **escape**, **responses in children**, **rate of progression**)

925	polyclonal	Env				HIV-1 infection	

Research Contact Mascola2003b
References Mascola2003b
Keywords escape, review.

- This paper reviews the paper by Wei *et al.* (Nature 2003) that substantiates the notion that HIV evolves to change the number and position of glycosylation sites in Envelope and this facilitates neutralization escape *in vivo*. This NAb escape mechanism is called a glycan shield. [Mascola2003b] (**escape**, **review**)

926	polyclonal	Env					macaque

References Mascola2003a
Keywords immunoprophylaxis, review.

- This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. The binding properties and SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. [Mascola2003a] (**immunoprophylaxis**, **review**)

927	polyclonal	Env	gp120			Vaccine	rabbit

Vaccine *Vector/Type:* DNA prime with virus-like particle (VLP) boost, fowlpoxvirus prime with virus-like particle (VLP) boost *Strain:* B clade 89.6P *HIV component:* Env
References Radaelli2003
Keywords Th1, Th2.

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Three different immunization protocols using two recombinant fowlpox (FP) constructs and two expression plasmids (SIV mac239 gg/pol or HIV-1 env 89.6P) for priming and VLP particles for boosting were tested for their ability to elicit neutralizing Ab and cell-mediated immune responses. NAb responses against SHIV 89.6P were elicited in all protocols tested. Plasmid DNA (pcDNA3gag/pl SIV) was more efficient than the FP vector (FPgag/polSIV) in inducing Ab responses to against the gag core protein (p27). DNA plasmid followed by a VLP boost elicited a Th0 profile. [Radaelli2003] (**Th1**, **Th2**)					
928	polyclonal	Env				HIV-1 infection	human
		References Polonis2003 **Keywords** co-receptor, escape, inter-clade comparisons. **Country** Thailand. • Neutralization of 49 subtype E HIV-1 isolates from various stages of disease and 21 subtype B viruses was compared using polyclonal Ab pools and single subtype E plasmas. Non-syncytium-inducing (NSI) CRF01 (subtype E) HIV-1 isolates showed increased sensitivity to neutralization (42%) than syncytium-inducing (SI) subtype E isolates (9%). In contrast, the viral phenotype of subtype B isolates did not correlate with neutralizaiton sensitivity. SI viruses were primarily X4 (one X4R5 was identified), NSI were R5. Low CD4+ T cell numbers in subtype E infected patients correlated with concurrent isolate resistance to neutralizing Ab responses. [Polonis2003] (**co-receptor**, **escape**, **inter-clade comparisons**)					
929	polyclonal	Env	gp120			Vaccine	macaque (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade W61D *HIV component:* gp120, Nef, Tat *Adjuvant:* AS02A (oil-in-water emulsion, 3D-monophosphoryl lipid A, QS21), AS06 (CpG, aluminum hydroxide) **References** Voss2003 **Keywords** adjuvant comparison, variant cross-recognition or cross-neutralization. • Monkeys were immunized with different combinations of gp120/NefTat/SIV-Tat three times over a three-month time period and intravenously challenged with SHIV 89.6P four weeks after the last immunzation. Vaccination induced anti-Tat, -Nef and -gp120 Ab responses which decreased until challenge. Neutralizing Ab responses against HIV-1 MN and HIV-1 W61D were observed. Vaccination with the combination of all three proteins reduced viral load and kept animals from a CD4+ T cell decline, preventing AIDS for more than 2.5 years. The adjuvant AS02A elicited NAbs and protected from disease, while AS06 did not. gp120 alone or TatNef/SIV-Tat without gp120 could not protect from disease. [Voss2003] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)					
930	polyclonal	Env	Env			Vaccine	mouse
		Vaccine *Vector/Type:* peptide *Adjuvant:* QS21 **References** Cunto-Amesty2001 **Keywords** mimotopes, vaccine antigen design. • Concanavalin A binds to mannose/glucose, and binds to HIV-1. Con A was used to select peptide mimics of carbohydrates that bound to Con A, and the mimetic peptides were then used for BALB/c mouse immunization. Abs raised against the mimetic peptides binds to HIV+ cells, and could weakly neutralize T cell lab adapted strains. [Cunto-Amesty2001] (**mimotopes**, **vaccine antigen design**)					
931	polyclonal	Env	gp41			Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *HIV component:* gp41 **Ab type** alpha-helical hairpin intermediate **References** Louis2003 **Keywords** vaccine antigen design. • Polyclonal Abs raised against soluble trivalently linked N35CCG-N13 and N34CCG, the internal trimeric core of the coiled-coil ectodomain, inhibit HIV-1 Env-mediated cell fusion at levels comparable to 2G12. [Louis2003] (**vaccine antigen design**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
932	polyclonal	Env	Env			Vaccine	mouse

Vaccine *Vector/Type:* E. Coli recombinant protein *HIV component:* gp120, gp41 *Adjuvant:* Complete Freund's Adjuvant (CFA), Incomplete Freund's Adjuvant (IFA)
References Li2002
Keywords vaccine antigen design.

- A polyepitope vaccine was designed based on a recombinant GST fusion protein containing three repeats of the 2F5 core epitope ELDKWA combined with the V3 region peptide GPGRAFY. Abs raised in mice could recognize the peptides, sgp41, and CHO-WT cells that expressed HIV-1 Env on their surface. [Li2002] (**vaccine antigen design**)

933	polyclonal	Env	Env			HIV-1 infection	human

References Montefiori2003
Keywords acute infection, autologous responses, escape.

- AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessaton of therapy, which then declined to a low level. The polylconal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. [Montefiori2003] (**autologous responses**, **acute infection**, **escape**)

934	polyclonal	Env	gp120 (dis DH012)			HIV-1 infection, Vaccine	chimpanzee

Vaccine *Vector/Type:* protein
References Zhu2003
Keywords vaccine-specific epitope characteristics.

- This study compares the immunogenicity of the HIV DH012 strain in chimpanzees during a natural infection with DH012 vaccinations. Naturally infected chimpanzees have sera containing potent anti-DH012 neutralization Abs, but the primary epitope is a discontinuous conformational epitope called CEV that involves the V1/V2 region, the bridging sheet, and the V3 loop. Abs that are raised upon gp120 vaccination, in contrast, are primarily against V3. DH012 has preserved the epitopes for the MAbs IgG1b12, 2G12, 17b, however natural DH012 infection in chimpanzees and DH012 gp120 vaccination in guinea pigs does not give rise to Abs against these epitopes. [Zhu2003] (**vaccine-specific epitope characteristics**)

935	101-342	Env	gp120 (476–505 HAM112, O group)			Vaccine	mouse (IgG2aκ)

Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160
Ab type C-term
References Scheffel1999

- 101-342: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. [Scheffel1999]

936	101-451	Env	gp120 (498–527 HAM112, O group)			Vaccine	mouse (IgG2bκ)

Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160
Ab type C-term
References Scheffel1999

- 101-451: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. [Scheffel1999]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
937	120-1	Env	gp120 (503–532)		no	Vaccine	mouse (IgMκ)

Vaccine *Vector/Type:* peptide
Ab type C-term
References Dalgleish1988, Chanh1986

938 212A — Env — gp120 — no — HIV-1 infection — human

Ab type C1 **Research Contact** James Robinson, Tulane University, LA
References Pantophlet2003b, Binley1998, Sullivan1998b, Parren1997c, Wyatt1997, Ditzel1997, Fouts1997, Binley1997a, Moore1996, Moore1994d, Robinson1992
Keywords vaccine antigen design.

- 212A: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 212A: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998]
- 212A: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10. [Sullivan1998b]
- 212A: Does not neutralize TCLA strains or primary isolates. [Parren1997c]
- 212A: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted. [Wyatt1997]
- 212A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 212A bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997]
- 212A: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs. [Moore1996]
- 212A: Mutations that inhibit binding: C1 (45 W/S) and V5 (463 N/D) – and enhance binding: V2 (179/180 LD/DL) and C5 (495 G/K) [Moore1994d]

939 522-149 — Env — gp120 — no — Vaccine — mouse

Vaccine *Vector/Type:* protein *HIV component:* Env
Ab type C1 **Research Contact** G. Robey, Abbott Inc.
References Pantophlet2003b, Zwick2003, Yang2000, Binley1998, Trkola1996a, Moore1996
Keywords antibody interactions, vaccine antigen design.

- 522-149: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 522-149: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C1-binding Fab that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- 522-149: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000]
- 522-149: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 522-149: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] • 522-149: Binding is enhanced by C5 antibodies M91 and 1C1 – mutual binding-inhibition with anti-C1 antibody 133/290 – binding is destroyed by a W/L (position 61, LAI) gp120 amino acid substitution – other C1 antibodies enhance binding to gp120. [Moore1996]					
940	L19	Env	gp120 (HXBc2)			HIV-1 infection	human (IgG1)
		Ab type C1 **References** Ditzel1997 • L19: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for the selection of Fabs – six N-term Fabs, L19 L34, L35, L52, L59, and L69, were obtained that have a similar epitope to Fab p7. [Ditzel1997]					
941	M90	Env	gp120		no	Vaccine	(IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Env **Ab type** C1 **Research Contact** Fulvia di Marzo Veronese **References** Pantophlet2003b, Yang2000, Binley1999, Binley1998, Wyatt1997, Ditzel1997, Moore1996, DeVico1995, diMarzo Veronese1992 • M90: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] • M90: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] • M90: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] • M90: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998] • M90: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-82, are deleted. [Wyatt1997] • M90: Reciprocal inhibition of binding of other anti-C1 MAbs – inhibits CD4 binding site MAbs – enhances binding of V2 MAbs G3-4 and SC258. [Moore1996] • M90: Reacted with both non-reduced (but not denatured) covalently cross-linked gp120-CD4 complex. [DeVico1995] • M90: Reactive only with native gp120, so binds to a discontinuous epitope – reacts with multiple strains. [diMarzo Veronese1992]					
942	MAG 104	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** C1 **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• MAG 104: Only observed amino acid substitution that reduces binding: 88 N/P and 106 E/A – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. [Kang1994]					
943	MAG 45 (#45)	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** C1 **Research Contact** C. Y. Kang, IDEC Inc **References** Yang2000, Wyatt1997, Moore1996, Kang1994 • MAG 45: Called #45 – a combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] • MAG 45: Called #45 – binds to efficiently sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-50, are deleted. [Wyatt1997] • MAG 45: Reciprocal binding inhibition with anti-C1-C5 and anti-C1-C4 discontinuous MAbs – binding enhanced by anti-V3 5G11 – inhibits binding of anti-CD4 binding site MAbs. [Moore1996] • MAG 45: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. [Kang1994]					
944	MAG 95	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** C1 **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 95: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. [Kang1994]					
945	MAG 97	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** C1 **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 97: Only observed amino acid substitution that reduces binding: 88 N/P – does not bind to C1 region 20 mer peptides, tentative classification conformationally sensitive anti-C1 MAb. [Kang1994]					
946	T9	Env	gp41			Vaccine	mouse (IgG)
		Vaccine *HIV component:* oligomeric gp140 **Ab type** C1 **Research Contact** Patricia Earl and Christopher Broder, NIH **References** Golding2002b, Earl1997, Broder1994 **Keywords** antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization. • T9: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b – nor did it alter two gp41 MAbs, T9 and D61, inability to inhibit fusion. [Golding2002b] (**antibody binding site definition and exposure**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• T9: This antibody, along with 7 others (M10, D41, D54, T6, T4, T10 and T35), can block the linear murine MAb D61, and the human MAb 246-D, which both bind to the immunodominant region near the two Cys in gp41 – most of these antibodies are oligomer dependent – all of the MAbs are reactive with ten different HIV-1 strains – members of this competition group are blocked by sera from HIV-1+ individuals. [Earl1997] (**antibody binding site definition and exposure**) • T9: One of five MAbs (T4, T6, T9, T10 and T35) in a competition group that bind to a conformation-dependent epitope in gp41 and is oligomer specific – neutralizes IIIB and SF2. [Broder1994] (**antibody generation**, **variant cross-recognition or cross-neutralization**) • There are two HIV-Abs with the name T9, one binds to gp41, one to gp120.				
947	p7	Env	gp120 (HXBc2)			HIV-1 infection	human (IgG1)
		Ab type C1 **References** Parren1997c, Ditzel1997 • p7: Does not neutralize TCLA strains or primary isolates. [Parren1997c] • p7: gp120 immobilized on solid phase by capture with sCD4 was used for selection of Fabs – three novel N-term Fabs were obtained that bind to similar epitopes, p7, p20, and p35 – a C1 W/S substitution at position 45 abolished binding, a Y/D at position 45 reduced binding, and C5 region substitutions 475 M/S and 493 P/K enhanced binding – compete with MAbs M85, M90 and 212A, but not M91 and G3-299. [Ditzel1997]					
948	L100	Env	gp120 (HXBc2)			HIV-1 infection	human (IgG1)
		Ab type C1-C2 **References** Kwong2002, Parren1997a, Parren1997c, Ditzel1997 **Keywords** antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization. • L100: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminal, discontinuous. [Kwong2002] (**antibody binding site definition and exposure**) • L100: gp120 immobilized on solid phase by capture with sCD4 and then masked with Fab p7 allowed selection of a new Fab, L100, with a novel specificity for C1 and C2 – gp120 C1 substitutions 69 W/L and 76 P/Y abolish L100 binding, and C2 substitutions 252 R/W, 256 S/Y, 262 N/T and 267 E/L abolish or strongly inhibit L100 binding – inhibits binding of MAbs M90 and G3-299, but not M85, 212A, and M91. [Ditzel1997, Parren1997a] (**antibody binding site definition and exposure**, **antibody generation**) • L100: Does not neutralize TCLA strains or primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)					
949	2/11c (211c, 2.11c, 211/c, 2-11c)	Env	gp120		L (weak)	HIV-1 infection	human
		Ab type C1-C4 **Research Contact** James Robinson, Tulane University, LA **References** Kwong2002, Xiang2002a, Binley1998, Wyatt1997, Li1997, Fouts1997, Binley1997a, Trkola1996a, Moore1996 **Keywords** antibody binding site definition and exposure.					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2/11c: Called 211/c. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminus, discontinuous. [Kwong2002] (**antibody binding site definition and exposure**)
- 2/11c: Used as a negative control in a study of CD4i MAbs. [Xiang2002a]
- 2/11c: Called 211/c – a panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998]
- 2/11c: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-74, are deleted. [Wyatt1997]
- 2/11c: Called 2.11c – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 mug/ml. [Li1997]
- 2/11c: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 2/11c bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997]
- 2/11c: Called 211c – does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a]
- 2/11c: Inhibits binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and CD4i MAbs (48d and 17b) – similar reactivity pattern to A32, but less cross-reactive and lower affinity – A32 and 211/c are unique among known human and rodent MAbs. [Moore1996]

950	A32	Env	gp120		no	HIV-1 infection	human (IgG1)

Ab type C1-C4, CD4i **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA

References Pantophlet2003b, Zwick2003, Kwong2002, Grundner2002, Yang2002, Yang2000, Binley1999, Binley1998, Sullivan1998b, Parren1997c, Boots1997, Wyatt1997, Burton1997, Fouts1997, Binley1997a, Trkola1996a, Wu1996, Moore1996, Moore1995b, Wyatt1995, Moore1994b

Keywords antibody binding site definition and exposure, antibody interactions, co-receptor, inter-clade comparisons, mimotopes, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- A32: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- A32: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. A32 is described as having a C1-C4 discontinuous CD4i epitope, and had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- A32: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-terminal, discontinuous. [Kwong2002] (**antibody binding site definition and exposure**)
- A32: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface – non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12 – the MAb 17b was sCD4 inducible on gp160deltaCT PL. [Grundner2002] (**vaccine antigen design**)
- A32: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002] (**antibody binding site definition and exposure**)
- A32: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] (**vaccine antigen design**)
- A32: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**antibody binding site definition and exposure**)
- A32: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer. [Binley1998] (**antibody binding site definition and exposure**)
- A32: Enhances binding of CD4i MAbs 17b and 48d, and a MAb generated in response to gp120-CD4 complex, CG10. [Sullivan1998b] (**antibody interactions**)
- A32: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – A32 has a unique epitope involving mostly C2 but C1 and C4 contribute – six quite variable phage inserts were recognized, with a consensus of LPWYN – a central Trp was the most conserved element, consistent with W427 being an important residue for binding gp120. [Boots1997] (**antibody binding site definition and exposure**, **mimotopes**)
- A32: Does not neutralize TCLA strains or primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- A32: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. [Wyatt1997] (**antibody binding site definition and exposure**)
- A32: Review. [Burton1997] (**review**)
- A32: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – A32 bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- A32: Does not neutralize JR-FL, or any strain strongly – partial inhibition of gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**co-receptor**)
- A32: Not neutralizing – binds domains that interact with gp41 – MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 and binding of A32 does not block this inhibition. [Wu1996] (**antibody binding site definition and exposure**)
- A32: Reciprocal inhibition of binding of anti-C1, -C5, -C4, -V3 and anti-CD4 binding site MAbs – induces binding of some anti-V2 and sCD4 inducible MAbs (48d and 17b) – very similar competition pattern between 2/11c, A32 and 211/c are unique among known human and rodent MAbs. [Moore1996] (**antibody binding site definition and exposure**, **antibody interactions**)
- A32: Review: epitope is distinct from CD4BS MAbs, 48d and 17b, and 2G12. [Moore1995b] (**antibody binding site definition and exposure**)
- A32: Epitope is better exposed upon CD4 binding to gp120 – binding of A32 enhances binding of 48d and 17b – studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2. [Wyatt1995] (**antibody binding site definition and exposure**, **antibody interactions**)
- A32: Reacted with virtually every gp120 monomer of every clade tested, most conserved gp120 monomer epitope known. [Moore1994b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
951	C11 (c11)	Env	gp120		no	HIV-1 infection	human

Ab type C1-C5 **Research Contact** James Robinson, Tulane University, LA

References Pantophlet2003b, Ohagen2003, Raja2003, Kwong2002, Basmaciogullari2002, Grundner2002, Yang2002, Binley1999, Sullivan1998b, Parren1997c, Wyatt1997, Fouts1997, Binley1997a, Wu1996, Trkola1996a, Moore1996, Moore1994d, Robinson1992

Keywords antibody binding site definition and exposure, antibody interactions, brain/CSF, co-receptor, vaccine antigen design, variant cross-recognition or cross-neutralization.

- C11: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- C11: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. C11 recognized most variants,some from each of the four individuals, by gp120 immunoprecipitation. [Ohagen2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)
- C11: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-299) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. Authors describe the epitope as N-term and C-term binding. [Kwong2002] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- C11: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. C11 was used as a negative control, as C11 binding did not alter binding of CD4-independent gp120 to CCR5, nor binding to CCR5-expressing Cf2Th cells. [Raja2003] (**co-receptor**)
- C11: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding – basic residues in the V3 loop and the beta19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding – MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants – C11 was used to detect gp120 binding to CXCR4 or CCR5 on PMPLs. [Basmaciogullari2002] (**antibody binding site definition and exposure**)
- C11: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface – non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12 – the MAb 17b was sCD4 inducible on gp160deltaCT PL. [Grundner2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- C11: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002] (**antibody binding site definition and exposure**)
- C11: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**vaccine antigen design**)
- C11: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10. [Sullivan1998b] (**antibody interactions**)
- C11: Does not neutralize TCLA strains or primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- C11: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial re-exposure if sCD4 was bound – does not bind to HXBc2 gp120 if the 19 C-term amino acids are deleted. [Wyatt1997] (**antibody binding site definition and exposure**)
- C11: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – C11 bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- C11: Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**antibody binding site definition and exposure**)
- C11: Did not block ability of gp120-sCD4 complexes to inhibit MIP-1alpha binding – binds to gp41-binding domain. [Wu1996] (**antibody binding site definition and exposure**)
- C11: Binding enhanced by anti-V3 MAb 5G11 – reciprocal inhibition with anti-C1 MAbs. [Moore1996] (**antibody interactions**)
- C11: Mutations that inhibit binding: C1 (45 W/S, 88 N/P) – V5 (463 N/D) – and C5 (491 I/F, 493 P/K and 495 G/K) and enhance binding: C1 (36 V/L) – V1-V2 (152/153 GE/SM) – and DeltaV1/V2/V3. [Moore1994d] (**antibody binding site definition and exposure**)

952	L81	Env	gp120		no	HIV-1 infection	human (IgG1)

Ab type C1-C5
References Parren1997c, Ditzel1997

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L81: Does not neutralize TCLA strains or primary isolates. [Parren1997c] • L81: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – L81 binding is abolished by C1 substitution 45 W/S, C5 substitution 491 I/F, and C3 substitution L/A. [Ditzel1997]					
953	2F19C	Env	gp120 (HIV2ROD)	APGK	no	Vaccine	mouse
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C3 **References** Matsushita1995 • 2F19C: Binds in WB, but binds poorly to Env on the cell surface, APGK is the core binding region. [Matsushita1995]					
954	B2C	Env	gp120 (HIV2ROD)	HYQ(core)	L	Vaccine	mouse
		Vaccine *Vector/Type:* peptide *Strain:* HIV-2 ROD **Ab type** C3 **References** Matsushita1995 • B2C: Viral neutralization was type-specific for HIV-2 ROD. [Matsushita1995]					
955	polyclonal	Env			P	HIV-1 infection	human (IgG)
		Ab type C3 **References** Wang2002b • Autologous NAbs were studied in 3 patients on HAART that rebounded – phylogenetic analysis of env (V1-V5) sequences indicated that rebound viruses had evolved from or preexisted in baseline populations – HIV-1 rebound viruses from all 3 patients were resistant to neutralization by autologous IgG, unlike the baseline viruses – mutations in the C3 region was responsible for conferring neutralization resistance against autologous antibody in 2 of 3 patients. [Wang2002b]					
956	1024	Env	gp120				
		Ab type C4 **References** Berman1997 • 1024: Binds to 1/7 isolates from breakthrough cases from a MN gp120 vaccine trial. [Berman1997]					
957	23A (2.3A)	Env	gp120		no		
		Ab type C5 **Research Contact** James Robinson, Tulane University, LA **References** Schulke2002, Binley1999, Fouts1997, Trkola1996a, Wu1996, Thali1993, Thali1992a • 23A: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. [Schulke2002] • 23A: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] • 23A: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric env binding – 23A bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 23A: C5 binding MAb – does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a]
- 23A: Called 2.3A – Did not block ability of gp120-sCD4 complexes to inhibit MIP-1alpha binding – binds to gp41-binding domain of gp120. [Wu1996]

958 D7324 Env gp120 Vaccine sheep

Vaccine *HIV component:* gp120
Ab type C5 **Research Contact** Aalto BioReagents Ltd, Dublin, Ireland or Cliniqa Inc., Fallbrook, CA, USA
References Zwick2003, Herrera2003, Poignard2003, Basmaciogullari2002, Xiang2002a, Gram2002, Sanders2002, Binley1998, Mondor1998, Ugolini1997, Ditzel1997, Trkola1996a, Wyatt1995, Moore1993c, Moore1993b, Sattentau1991, Moore1990a
Keywords antibody interactions.

- D7324: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a C5-binding polyclonal Ab that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- D7324: Used to capture gp120 onto solid phase for epitope mapping. [Basmaciogullari2002, Binley1998, Ditzel1997, Herrera2003, Moore1993b, Moore1993c, Poignard2003, Sanders2002, Xiang2002a]
- D7324: Called NEA9205 – gp120 capture ELISAs with MAbs D7324 (anti-C-term) or 9205 (anti-V3) were compared in a study of orientation of glycosylation sites – CD4 binding could only inhibit deglycosylation when gp120 was bound to the plate by D7324, not by 9205, while Abs from HIV-1 infected people inhibited deglycosylation most effectively when gp120 was caught by 9205. [Gram2002]
- D7324: Epitope in C5 – Does not neutralize JR-FL nor block gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a]
- D7324: Binds to the last 15 amino acids in gp120 – used for antigen capture ELISA. [Wyatt1995]
- D7324: Binding unaltered by gp120 binding to sCD4, in contrast to 110.5, 9284, 50-69 and 98-6. [Sattentau1991]

959 10/46c Env gp120 Vaccine rat

Vaccine *Vector/Type:* protein *HIV component:* gp120
Ab type CD4BS
References Peet1998, Jeffs1996, Cordell1991

- 10/46c: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 10/46c was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]
- 10/46c: Increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. [Jeffs1996]

960 1027-30-D (1027-30D) Env Env human (IgG1κ)

Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Zwick2003, Hioe2000
Keywords antibody interactions, review.

- 1027-30D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 1027-30-D: Called 1027-30D. scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1027-30-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. [Hioe2000]					
961	1125H (1125h)	Env	gp120		L (MN)	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **Research Contact** Shermaine Tilley, Public Health Research Institute, USA **References** Yang1998, Alsmadi1998, Wyatt1998a, Pincus1996, Warrier1996, D'Souza1995, Pinter1993b, Wyatt1992, Thali1992a, Tilley1991a, Tilley1991b • 1125H: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998] • 1125H: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. [Alsmadi1998] • 1125H: Called 1125h – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] • 1125H: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] • 1125H: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. [Warrier1996] • 1125H: Neutralization was MN specific – failed to neutralize JRCSF, and 2 B subtype and 1 D subtype primary isolates in a multi-laboratory study involving 11 labs. [D'Souza1995] • 1125H: Precipitation of Delta 297-329 env glycoprotein, with has a deleted V3 loop, is much more efficient that precipitation of wild type. [Wyatt1992] • 1125H: Binding to soluble gp120 enhanced by the presence of an anti-V3 HuMAb, 41148D. [Pinter1993b] • 1125H: Amino acid substitutions in HXB2 that strongly inhibit binding: 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480. [Thali1992a] • 1125H: Binding to gp120 inhibited by CD4 – epitope is destroyed by reduction, but not by removal of N-linked sugars – potent neutralization of MN, RF, SF-2 and IIIB – neutralization synergy with anti-V3 MAb 4117C. [Tilley1991a]				
962	120-1B1	Env	gp120		L		human
		Ab type CD4BS **Research Contact** Virus Testing Systems Corp., Houston, TX **References** Gorny2004, Watkins1993 **Keywords** antibody binding site definition and exposure, review. • 120-1B1: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 120-1B1: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 120-1B1 was not affected by this mutation. [Watkins1993] (**antibody binding site definition and exposure**)				
963	1202-D (1202-30-D)	Env	Env				human (IgG1κ)
		Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Hioe2000, Nyambi1998 **Keywords** inter-clade comparisons, review. • 1202-D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 1202-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. [Nyambi2000] (**inter-clade comparisons**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1202-D: Called 1202-30D – Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. [Hioe2000] • 1202-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 1202-D did not bind to any B clade viruses, and weakly bound A, C, and G clade isolates – 559/64-D, 558-D and 1202-D had similar reactivities. [Nyambi1998] (**inter-clade comparisons**)					
964	1331E	Env	gp120 (IIIB)			HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Gorny2000a **Keywords** antibody binding site definition and exposure, review. • 1331E: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 1331E: Inhibits sCD4 binding to rec gp120 LAI – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**)					
965	1570 (1570A, 1570C, 1570D)	Env	Env (PR12, BH10)			HIV-1 infection	human
		Ab type CD4BS **References** Gorny2004, Jeffs2001 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 1570: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 1570: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – three MAbs were isolated from one individual, 1570A, C and D but all were determined to have the same V(H)3 region – 1570 was able to bind to a panel of recombinant proteins from the A, B, C, D, and E subtypes. [Jeffs2001] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					
966	1595	Env	Env (PR12, BH10)			HIV-1 infection	human
		Ab type CD4BS **References** Gorny2004, Jeffs2001 **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 1595: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 1595: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1595 was able to bind gp120 from the A, B, and D clades from a panel of recombinant proteins from the A, B, C, D, and E subtypes. [Jeffs2001] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
967	1599	Env	Env (PR12, BH10)			HIV-1 infection	human

Ab type CD4BS
References Gorny2004, Jeffs2001
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 1599: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 1599: BH10 was mutated to form the PR12 protein with the first 74 C-terminal amino acids and the V1, V2 and V3 hypervariable loops deleted and a very well exposed CD4 binding domain (CD4bd) – this proteins was used to select three new human CD4BS MAbs 1570, 1595 and 1599 – 1599 was able to bind gp120 only from the B clade from a panel of recombinant proteins from the A, B, C, D, and E subtypes. [Jeffs2001] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
968	15e (1.5e, 1.5E, 15E)	Env	gp120		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Research Contact** James Robinson, Tulane University, LA, and David Ho, ADARC, NY, NY
References Gorny2004, Pantophlet2003b, Zwick2003, Raja2003, Pantophlet2003a, Kwong2002, Zhang2002, Xiang2002b, Kolchinsky2001, Park2000, Sullivan1998a, Fouts1998, Trkola1998, Binley1998, Sullivan1998b, Parren1998a, Wyatt1998a, Parren1997c, Berman1997, Wyatt1997, Li1997, Fouts1997, Binley1997a, Wisnewski1996, McDougal1996, Trkola1996a, Poignard1996a, Moore1996, McKeating1996b, Lee1995, Sattentau1995b, Moore1994a, Moore1994b, Cook1994, Thali1994, Bagley1994, Wyatt1993, Watkins1993, Thali1993, Moore1993a, Takeda1992, Thali1992a, Wyatt1992, Ho1992, Koup1991, Ho1991b, Cordell1991, Thali1991, Robinson1990a
Keywords ADCC, adjuvant comparison, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, brain/CSF, co-receptor, enhancing activity, inter-clade comparisons, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization.

- 15e: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 15e: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 15e: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)
- 15e: Called 1.5e. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 15e: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. [Raja2003] (**co-receptor**)
- 15e: UK Medical Research Council AIDS reagent: ARP3016.
- 15e: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished. [Pantophlet2003a] (**antibody binding site definition and exposure**)
- 15e: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**antibody binding site definition and exposure**)
- 15e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**)
- 15e: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 15e. [Kolchinsky2001] (**antibody binding site definition and exposure**)
- 15e: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000] (**antibody binding site definition and exposure**)
- 15e: Called 1.5e – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 1.5e enhances and does not neutralize YU2 env even at 50 ug/ml. [Sullivan1998a] (**antibody binding site definition and exposure**)
- 15e: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer. [Fouts1998] (**antibody binding site definition and exposure**)
- 15e: No detectable neutralizing activity among primary isolates with different co-receptor usage – some neutralization of TCLA strains. [Trkola1998] (**variant cross-recognition or cross-neutralization**)
- 15e: Competes with CG-10 binding, a MAb raised against a gp120 CD4 complex, this was probably due to the disruption of CD4-gp120 by 15e. [Sullivan1998b] (**antibody binding site definition and exposure**, **antibody interactions**)
- 15e: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type. [Binley1998] (**antibody binding site definition and exposure**)
- 15e: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**antibody binding site definition and exposure**)
- 15e: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] (**structure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 15e: Neutralizes TCLA strains, but not primary isolates. [Parren1997c]
- 15e: Called 1.5E – Binds to 7/7 isolates from breakthrough cases from a MN gp120 vaccine trial. [Berman1997] (**variant cross-recognition or cross-neutralization**)
- 15e: Does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-93, are deleted. [Wyatt1997] (**antibody binding site definition and exposure**)
- 15e: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 15e could only achieve 50% neutralization, but could act synergistically with anti-V3 MAb 694/98-D to achieve 90% [Li1997] (**antibody interactions**)
- 15e: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 15e bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- 15e: 15e is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- 15e: Neutralizes HIV-1 LAI less potently than V3 specific MAbs. [McDougal1996]
- 15e: Inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**antibody binding site definition and exposure**)
- 15e: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs. [Poignard1996a] (**antibody interactions**)
- 15e: gp120 binding enhanced by anti-V3 MAb 5G11 and anti-V2 MAb G3-136 – binding inhibited by other CD4 binding site MAbs, antibodies that bind to gp120 only when CD4 is bound, and CD4-IgG. [Moore1996] (**antibody interactions**)
- 15e: Called 1.5e – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b] (**variant cross-recognition or cross-neutralization**)
- 15e: The V4 and V5 domains are essential for 1.5e binding, in contrast to the V1, V2, and V3 loops. [Lee1995] (**antibody binding site definition and exposure**)
- 15e: Binds with higher affinity to monomer than to oligomer, moderate association rate. [Sattentau1995b] (**antibody binding site definition and exposure**)
- 15e: Cross-reactive with gp120 proteins from clades B and D, less so with A and C, and not reactive with clade E and F. [Moore1994b] (**inter-clade comparisons**)
- 15e: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block 15e binding. [Cook1994] (**antibody binding site definition and exposure**, **brain/CSF**)
- 15e: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 17b) [Thali1994] (**antibody binding site definition and exposure**)
- 15e: Heavy chain is V HIV, V2-1 – light chain is V_kappaI, Hum01/012. Compared to 21h and F105. [Bagley1994] (**antibody sequence, variable domain**)
- 15e: Called 15E – a neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – 15E neutralization was not affected by this mutation. [Watkins1993] (**antibody binding site definition and exposure**)
- 15e: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120. [Wyatt1993] (**antibody binding site definition and exposure**)
- 15e: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120. [Moore1993a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 15e: Called N70-1.5e – does not enhance infection of HIV-1 IIIB and MN. [Thali1992a] (**enhancing activity**)
- 15e: Amino acid substitutions in HXB2 that strongly inhibit binding, similar to [Ho1992], some additional, 88, 102, 117, 113, 257, 368, 370, 421, 427, 457, 470, 480 [Thali1992a]. [Ho1992, Thali1992a] (**antibody binding site definition and exposure**)
- 15e: Precipitation of Delta 297-329 env glycoprotein, with a deleted V3 loop, is much more efficient that precipitation of wild type. [Wyatt1992] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 15e: gp120 mutants that affect 15e epitope binding: 113, 257, 368, 370, 421, 427, 475 – four of these coincide with amino acids important for the CD4 binding domain. [Ho1992] (**antibody binding site definition and exposure**)
- 15e: Binds to gp120 of HIV-1 IIIB, but not RF – mediates ADCC – deletion of the V3 loop from gp120 does not alter ADCC activity. [Koup1991] (**ADCC**, **variant cross-recognition or cross-neutralization**)
- 15e: Cross-competes with MAbs ICR 39.13g and ICR 39.3b. [Cordell1991] (**antibody interactions**)
- 15e: Broadly neutralizing, binds multiple strains, competes with CD4 for gp120 binding, DTT reduction of env abrogates binding – more potent blocking of gp120-sCD4 binding than MAbs G3-536 and G3-537. [Ho1991b] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
969	21h (2.1H)	Env	gp120		L	HIV-1 infection	human (IgG1)

Ab type CD4BS **Research Contact** James Robinson, Tulane University, LA

References Gorny2004, Xiang2002b, Fouts1998, Parren1998a, Wyatt1998a, Parren1997c, Wyatt1997, Ugolini1997, Li1997, Fouts1997, Binley1997a, McKeating1996b, Wisnewski1996, Poignard1996a, Moore1996, Sattentau1995b, Thali1994, Bagley1994, Moore1994a, Moore1994b, Moore1993a, Wyatt1993, Ho1992, Thali1992a, Ho1991b

Keywords acute infection, antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, binding affinity, inter-clade comparisons, review, structure, variant cross-recognition or cross-neutralization.

- 21h: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 21h: UK Medical Research Council AIDS reagent: ARP3017.
- 21h: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations—375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91) was markedly reduced—IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced—2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope—another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**)
- 21h: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with [Parren1998a] [Fouts1998]. [Fouts1998, Parren1998a] (**binding affinity**)
- 21h: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**antibody binding site definition and exposure**)
- 21h: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] (**antibody binding site definition and exposure**, **structure**)
- 21h: Neutralizes TCLA strains, but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- 21h: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding. [Wyatt1997] (**antibody binding site definition and exposure**)
- 21h: Viral binding inhibition by 21h strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997] (**antibody binding site definition and exposure**)
- 21h: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 50% neutralization could not be achieved at a maximal concentration of 67 mug/ml. [Li1997] (**variant cross-recognition or cross-neutralization**)
- 21h: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 21h bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- 21h: Called 2.1H – Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 21h: 21h is V H3 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- 21h: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs. [Poignard1996a] (**antibody binding site definition and exposure**, **antibody interactions**)
- 21h: Anti-CD4 binding site MAb – reciprocal inhibition by anti-C1, -C4 and other anti-CD4 binding site antibodies – enhanced by some anti-V2 MAbs and anti-V3 MAb 5G11 – enhances binding of some anti-V3 and -V2 MAbs. [Moore1996] (**antibody interactions**)
- 21h: Binds with higher affinity to monomer than to oligomer, moderate association rate. [Sattentau1995b] (**antibody binding site definition and exposure**)
- 21h: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 15e and 17b) [Thali1994] (**variant cross-recognition or cross-neutralization**)
- 21h: Heavy chain is V HIII, VDP-35 – light chain is V_lambdaIIIa, Hum318. Compared to 15e and F105. [Bagley1994] (**antibody sequence, variable domain**)
- 21h: Competition studies with human sera from seroconverting individuals showed that anti-CD4 BS antibodies can arise very early in infection, comparable or prior to anti-V3 antibodies. [Moore1994a] (**acute infection**)
- 21h: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F, with the least reactivity to clade E. [Moore1994b] (**inter-clade comparisons**)
- 21h: Conformational, does not bind denatured gp120 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120. [Moore1993a] (**antibody binding site definition and exposure**)
- 21h: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is greater than binding to wildtype gp120. [Wyatt1993] (**antibody binding site definition and exposure**)
- 21h: Amino acid substitutions in HXB2 that inhibit binding, some shared with CD4 binding inhibition, 88, 113, 257, 368, 370, 421, 470, 480. [Thali1992a] (**antibody binding site definition and exposure**)

970	28A11/B1	Env	gp120 (SF162)		L	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Ab type CD4BS **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny2004, He2002
Keywords inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 28A11/B1: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 28A11/B1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—28A11/B1 was one of these four MAbs. [He2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

971	2G6	Env	gp120				

Ab type CD4BS **Research Contact** Herman Katinger, Inst. Appl. Microbiol. University of Agricultural Science, or Polymun Scientific Inc., Vienna, Austria
References Gorny2004, Parren1998a, Fouts1998
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization.

- 2G6: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2G6: Binds to JRFL oligomer with an affinity comparable to IgG1b12, but does not neutralize the virus, so binding of oligomer is not always predictive of neutralization – conclusions of this paper contrast with [Parren1998a] – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect [Fouts1998]. [Fouts1998, Parren1998a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)					
972	35F3/E2	Env	gp120 (SF162)		L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** CD4BS **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 35F3/E2: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 35F3/E2: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—35F3/E2 was one of these four MAbs. [He2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					
973	38G3/A9	Env	gp120 (SF162)		L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** CD4BS **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** variant cross-recognition or cross-neutralization. • 38G3/A9: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**variant cross-recognition or cross-neutralization**) • 38G3/A9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—38G3/A9 was one of these four MAbs. [He2002] (**variant cross-recognition or cross-neutralization**)					
974	428	Env	gp120			HIV-1 infection	human
		Ab type CD4BS **References** Jeffs1996, Karwowska1992a • 428: Slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. [Jeffs1996]					
975	448-D (448D)	Env	gp120		L	HIV-1 infection	human (IgG1λ)
		Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Gorny2004, Nyambi2000, Wyatt1998a, Li1997, Manca1995a, Forthal1995, Laal1994, Spear1993, McKeating1992c, Karwowska1992a **Keywords** ADCC, antibody binding site definition and exposure, antibody interactions, complement, enhancing activity, inter-clade comparisons, review, structure, variant cross-recognition or cross-neutralization. • 448-D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 448-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**) • 448-D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] (**structure**) • 448-D: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env. [Li1997] (**variant cross-recognition or cross-neutralization**) • 448-D: Virions complexed to gp120 Ab facilitate presentation of p66 RT epitopes to Th cells. [Manca1995a] • 448-D: Neutralizing activity, positive ADCC activity, and no viral enhancing activity. [Forthal1995] (**ADCC**, **enhancing activity**) • 448-D: Dissociation constant gp120 IIIB 0.029 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D. [Laal1994] (**antibody interactions**) • 448-D: Did not mediate deposition of complement component C3 on HIV infected cells. [Spear1993] (**complement**) • 448-D: Called 448D – blocks gp120-CD4 binding – substitutions at gp120 residues 88, 113, 117, 257, 368 and 370 reduce binding – epitope similar to rat MAbs 39.13g and 39.3b. [McKeating1992c] (**antibody binding site definition and exposure**) • 448-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay. [Karwowska1992a] (**antibody binding site definition and exposure**)			
976	46D2/D5	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI) **Ab type** CD4BS **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** He2002 • 44D2/D5: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—44D2/D5 could not neutralize autologous SF162, and while it was cross-reactive, it was at lower affinity. [He2002]			
977	48-16	Env	gp120		no	HIV-1 infection	human (IgGκ)
		Ab type CD4BS **References** Gorny2004, Fevrier1995 **Keywords** antibody binding site definition and exposure, binding affinity, review, variant cross-recognition or cross-neutralization. • 48-16: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database. Most neutralize TCLA strains only, 48-16 is one of four that are non-neutralizing. [Gorny2004] (**review**) • 48-16: Broadly cross-reactive, reacts outside the CD4 binding site and V3 region—competes with sera from 45 seropositive subjects—binding affinity 2–5 $\times 10^{-9}$ M. [Fevrier1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **binding affinity**)			
978	50-61A	Env	gp120		L	HIV-1 infection	human (IgGκ)
		Ab type CD4BS **References** Gorny2004, Fevrier1995 **Keywords** binding affinity, review, variant cross-recognition or cross-neutralization. • 50-61A: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 50-61A: Neutralizes lab strains LAI and SF2 – competes with sera from 45 seropositive subjects – binding affinity 2.4 x 10^{-10} M. [Fevrier1995] (**variant cross-recognition or cross-neutralization**, **binding affinity**)			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
979	5145A	Env	gp120		L	HIV-1 infection	human (IgG1)

Ab type CD4BS
References Gorny2004, He2002, Alsmadi1998, Pincus1996, Warrier1996, Pinter1993a
Keywords ADCC, antibody interactions, immunotoxin, variant cross-recognition or cross-neutralization.

- 5145A: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**variant cross-recognition or cross-neutralization**)
- 5145A: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A, 4117C and 697D were used as controls. [He2002]
- 5145A: A study of 6 anti-Env MAbs and their ability to bind or direct ADCC against target cells infected with IIIB, MN, SF-2, and RF – bound and directed lysis against all four strains. [Alsmadi1998] (**ADCC**)
- 5145A: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] (**immunotoxin**)
- 5145A: Synergistic neutralization of HIV-1 when combined with anti-V2 MAb C108G. [Warrier1996] (**antibody interactions**)
- 5145A: Potent and broadly cross-reactive neutralization of lab strains. [Pinter1993a] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
980	558-D	Env	gp120		L	HIV-1 infection	human

Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny2004, Nyambi1998, McKeating1992c
Keywords antibody binding site definition and exposure, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 558-D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 558-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 558-D did not bind to any B clade viruses, and weakly bound to clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities. [Nyambi1998] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 558-D: Blocks gp120-CD4 binding – binds a panel of mutants all except for 256 S/Y and 262 N/T, which are probably conformationally disruptive. [McKeating1992c] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
981	559/64-D (559, 559-64D)	Env	gp120 (LAI)		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny2004, Zwick2003, York2001, Hioe2001, Nyambi2000, Hioe2000, Gorny2000a, Nyambi1998, Hioe1997b, Hioe1997a, Jeffs1996, Forthal1995, Stamatatos1995, Spear1993, McKeating1992c, Karwowska1992a
Keywords ADCC, antibody binding site definition and exposure, antibody interactions, assay development, complement, enhancing activity, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 559/64D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 559/64D: called 559-64D: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 559/64-D: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4 induced or CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 559/64-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFNγ production—anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs. [Hioe2001]
- 559/64-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. [Nyambi2000] (**inter-clade comparisons**)
- 559/64-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. [Hioe2000]
- 559/64-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 559/64-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 559/64-D did not bind to any B clade viruses, and weakly bound clade A, C, and G isolates – 559/64-D, 558-D and 1202-D had similar reactivities. [Nyambi1998] (**antibody binding site definition and exposure**, **inter-clade comparisons**)
- 559/64-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**)
- 559/64-D: Used in the development of resting cell neutralization assay. [Hioe1997a] (**assay development**)
- 559/64-D: Called 559 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. [Jeffs1996] (**antibody binding site definition and exposure**)
- 559/64-D: Neutralizing activity, no ADCC activity, and no viral enhancing activity. [Forthal1995] (**ADCC**, **enhancing activity**, **variant cross-recognition or cross-neutralization**)
- 559/64-D: Called 559-64D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface. [Stamatatos1995] (**antibody binding site definition and exposure**)
- 559/64-D: Did not mediate deposition of complement component C3 on HIV infected cells. [Spear1993] (**complement**)
- 559/64-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay. [Karwowska1992a] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
982	55D5/F9	Env	gp120 (SF162)		L	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Ab type CD4BS **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny2004, He2002
Keywords review, variant cross-recognition or cross-neutralization.

- 55D5/F9: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database. Most neutralize TCLA strains only, this is one of four that are non-neutralizing. [Gorny2004] (**review**)
- 55D5/F9: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—55D5/F9 was one of these four MAbs. [He2002] (**variant cross-recognition or cross-neutralization**)

983	588-D (588)	Env	gp120		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Nyambi2000, Hioe2000, Nyambi1998, Jeffs1996, Moore1993a, Buchbinder1992, Karwowska1992a

- 588-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12. [Nyambi2000]
- 588-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. [Hioe2000]
- 588-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind weakly without clade specificity to virions, but bound well to soluble gp120 – 588-D did not bind to any B clade viruses, and weakly bound a clade A, C, and G clade isolate – 559/64-D, 558-D and 1202-D reacted had similar reactivities. [Nyambi1998]
- 588-D: Called 588 – slight, not significant increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. [Jeffs1996]
- 588-D: Weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120. [Moore1993a]
- 588-D: 4-fold increase in neutralization potency for 588-D when combined 1:1 with human MAb 447-D. [Buchbinder1992]
- 588-D: Conformational – reactive with IIIB gp120 in RIP, but not WB assay. [Karwowska1992a]

984	654-D (654-30D, 654/30D, 654-D100, 654.30D, 654)	Env	gp120 (LAI)		L	HIV-1 infection	human (IgGκ)

Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny2004, Zwick2003, Gorny2002, Verrier2001, Nyambi2000, Hioe2001, Hioe2000, Gorny2000a, Hioe1999, Stamatatos1998, Nyambi1998, Schonning1998, Gorny1998, Hioe1997b, Gorny1997, Stamatatos1997, Li1997, Stamatatos1995, Gorny1994, Laal1994, Karwowska1993
Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization.

- 654-D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 654-D: Called 654-30D. scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 654-D: Called 654: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions and the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), and MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) [Gorny2002]
- 654-D: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6—six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D, while six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281—no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 654-D: CD4BS MAbs when complexed with gp120, inhibit proliferation of gp120-specific CD4 T-cells and IFN gamma production – anti-CD4BS MAbs inhibit gp120 presentation by altering the uptake and/or processing of gp120 by the APCs, not by blocking of gp120 attachment to CD4 on the surface of APCs. [Hioe2001]
- 654-D: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12 – 654-D had the weakest binding among CD4BS MAbs, binding to only 4/26 isolates. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 654-D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – CD4BS MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – MAb 654-D strongly diminished proliferation – there is a discrepancy in isotyping this antibody, previous reports indicated IgG1kappa, while Hioe suggests it is IgG1lambda. [Hioe2000]
- 654-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 654-D: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs. [Hioe1999]
- 654-D: Called 654.30D – deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly allowed neutralization by CD4BS MAb 654.30D. [Stamatatos1998] (**antibody binding site definition and exposure**, **inter-clade comparisons**)
- 654-D: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – CD4-BS Abs tended to bind very weakly without clade specificity to virions, but bound well to soluble gp120 – 654-D bound only to JRFL. [Nyambi1998] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 654-D: Called 654-D100 – 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan. [Schonning1998] (**variant cross-recognition or cross-neutralization**)
- 654-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 654-D: Anti-CD4 BS MAb 654-30D and IgG1b12 have comparable binding affinities, neither mediates gp120-virion dissociation, but IgG1b12 can neutralize SF128A and SF162 and 654-D cannot – 654-D actually enhances infection by both viruses in primary macrophages. [Stamatatos1997] (**enhancing activity**, **binding affinity**)
- 654-D: Called 654-30D – One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env. [Li1997] (**variant cross-recognition or cross-neutralization**)
- 654-D: Called 654-30D – The binding of conformation-dependent anti-V2, anti-V3, and anti-CD4BS MAbs to monomeric and virion-associated gp120 from HIV-1 isolates with differences in cell tropism was studied – CD4BS loop epitopes are somewhat occluded in the oligomeric gp120 epitopes on the virion surface relative to the gp120 monomer as indicated by an increase in the half-maximal binding values to macrophage-tropic isolates SF162 and SF128a and to T-cell tropic SF2 – binding of anti-CD4BS MAbs to SF2 resulted in a significant amount of dissociation of gp120 from virion surface. [Stamatatos1995] (**antibody binding site definition and exposure**)
- 654-D: Mild oxidation of carbohydrate moieties inhibits binding. [Gorny1994] (**antibody binding site definition and exposure**)
- 654-D: Dissociation constant gp120 IIIB 0.008 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D – reported to be human(IgG1lambda) [Laal1994] (**antibody interactions**, **kinetics**)

985	67G6/C4	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)

Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)
Ab type CD4BS **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org
References Gorny2004, He2002
Keywords review, variant cross-recognition or cross-neutralization.

- 67G6/C4: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database. Most neutralize TCLA strains only, this MAb is one of four that are non-neutralizing. [Gorny2004] (**review**)
- 67G6/C4: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2κ MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120—6 anti-CD4BS MAbs competed with anti-CD4BS MAb 5145A, blocked sCD4 binding and were conformationally sensitive—4/6 could neutralize the autologous strain SF162, and were broadly cross-reactive with B clade R5 and X4 strains (not E clade)—67G6/C4 could not neutralize autologous SF162, and its binding was strain-specific. [He2002] (**variant cross-recognition or cross-neutralization**)

986	729-D (729-30D)	Env	gp120 (LAI)		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY
References Gorny2004, Gorny2000a, Parren1997c, Li1997, D'Souza1997, Laal1994
Keywords antibody binding site definition and exposure, antibody interactions, kinetics, review, variant cross-recognition or cross-neutralization.

- 729-D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- 729-D: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**)
- 729-D: Neutralizes TCLA strains, but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- 729-D: Called 720-30D – one of 14 human MAbs tested for ability to neutralize chimeric SHIV-vpu+, which expressed HIV-1 IIIB env. [Li1997] (**variant cross-recognition or cross-neutralization**)
- 729-D: In a multilaboratory blinded study, failed to consistently neutralize any of nine B clade primary isolates – reported here to have a lambda light chain, but originally reported in [Laal1994] to be IgG1kappa [D'Souza1997]. [D'Souza1997, Laal1994] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 729-D: Dissociation constant gp120 IIIB 0.025 – neutralizes IIIB, acts synergistically with anti-V3 MAb 447-52D. [Laal1994] (**antibody interactions**, **kinetics**)					
987	830D (830-D)	Env	gp120		L		human (IgG1κ)
		Ab type CD4BS **References** Gorny2004, Hioe2000, Wyatt1998a, Hioe1997b **Keywords** review, structure, variant cross-recognition or cross-neutralization. • 830D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 830D: Ab responses, because of their capacity to alter antigen uptake and processing, can influence helper T cell responses – anti-CD4 binding site MAbs or serum Ig from HIV+ individuals inhibited proliferative responses of gp120 specific T cells – CD4BS MAbs 654-D, 559/64-D, 588-D, 830-D, 1027-30-D, and 1202-30D strongly diminished proliferation. [Hioe2000] • 830D: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] (**structure**) • 830D: Called 830-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**)				
988	9CL	Env	gp120 (LAI)			HIV-1 infection	human
		Ab type CD4BS **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Gorny2004, Gorny2000a **Keywords** antibody binding site definition and exposure, review. • 9CL: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • 9CL: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – CD4BS MAbs 559/64-D, 654-D, 729-D, 9CL and 1331E bound with a 5-13 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**)				
989	BM12	Env	gp120		L	HIV-1 infection	human
		Ab type CD4BS **References** Kessler1995 • BM12: Broad cross-clade neutralization of primary isolates – additive effect in combination with MAb 2F5. [Kessler1995]					
990	D20	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1997, Otteken1996, Richardson1996, Broder1994, Earl1994 **Keywords** antibody binding site definition and exposure, antibody generation. • D20: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D20 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. [Sugiura1999] (**antibody binding site definition and exposure**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- D20: Used for comparison in a study of gp41 antibodies – D20 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs. [Earl1997] (**antibody binding site definition and exposure**)
- D20: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. [Otteken1996]
- D20: Human sera blocked binding in oligomeric ELISA assay to a similar extent for gp41 MAbs D20, D43, D61, and T4. [Richardson1996]
- D20: Binding completely blocked by pooled human sera. [Broder1994]
- D20: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)

991 D21 Env gp120 (IIIB) Vaccine mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Ab type CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Earl1994

- D21: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D21 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. [Sugiura1999]
- D21: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

992 D24 Env gp120 (IIIB) no Vaccine mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Ab type CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Earl1994

- D24: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D24 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999]
- D24: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

993 D25 Env gp120 (IIIB) Vaccine mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Ab type CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Earl1994

- D25: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D25 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. [Sugiura1999]
- D25: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

994 D28 Env gp120 (IIIB) no Vaccine mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Ab type CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Earl1994

- D28: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D28 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D28: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
995	D35	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • D35: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D35 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999] • D35: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
996	D39	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • D39: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D39 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. [Sugiura1999] • D39: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
997	D42	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • D42: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D42 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999] • D42: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
998	D52	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • D52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D52 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999] • D52: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
999	D53	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D53: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D53 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999] • D53: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1000	D60	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Richardson1996, Earl1994 • D60: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D60 is part of a group of MAbs labeled B-I, that had limited cross-reactivity – of seven clade B isolates BH8 and B-al were they only two that consistently reacted with B-I MAbs – B-I MAbs fully blocked CD4 binding. [Sugiura1999] • D60: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1001	DA48	Env	gp120 (BRU)			HIV-1 infection	human
		Ab type CD4BS **References** Gorny2004, Sullivan1998a, Parren1998a **Keywords** antibody binding site definition and exposure, antibody generation, binding affinity, review, variant cross-recognition or cross-neutralization. • DO8i: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**) • DA48: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab Ab fragment DA48 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism – while DA48 enhances YU2, it neutralizes HXBc2 – DA48 was obtained by panning libraries derived from bone marrow from a >15 year long term non-progressor against BRU gp120. [Sullivan1998a] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**) • DA48: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**binding affinity**)					
1002	DO8i	Env	gp120 (BRU)			HIV-1 infection	human
		Ab type CD4BS **References** Sullivan1998a, Parren1998a • DO8i – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment DO8i also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – DO8i was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against BRU gp120. [Sullivan1998a] • DO8i: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1003	F105 (F-105)	Env	gp120		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Research Contact** Marshall Posner, Boston MA

References Gorny2004, Pantophlet2003b, Zwick2003, Ohagen2003, Raja2003, Xiang2003, Poignard2003, Pantophlet2003a, Kwong2002, Cavacini2002, Liu2002, Ferrantelli2002, Zhang2002, Basmaciogullari2002, Grundner2002, Edwards2002, Xiang2002b, Chakrabarti2002, Xu2002, Yang2002, York2001, Kolchinsky2001, Si2001, Yang2000, Park2000, Fortin2000, Baba2000, Robert-Guroff2000, Oscherwitz1999a, Cavacini1999, Giraud1999, Sugiura1999, Kropelin1998, Sullivan1998a, Brand1998, Cavacini1998a, Li1998, Cavacini1998b, Wyatt1998a, Wyatt1997, Cao1997b, Li1997, D'Souza1997, Parren1997c, Chen1996, Litwin1996, Pincus1996, Wisnewski1996, McDougal1996, Wolfe1996, Jagodzinski1996, Khouri1995, Sullivan1995, Cavacini1995, Posner1995, Turbica1995, Chen1994a, Earl1994, Cavacini1994a, Cavacini1994b, Cook1994, Thali1994, Bagley1994, Marasco1993, Watkins1993, Pincus1993b, Klasse1993a, Potts1993, Montefiori1993, Wyatt1993, Cavacini1993b, Cavacini1993a, Posner1993, Moore1993a, Posner1992a, Posner1992b, Wyatt1992, Marasco1992, Thali1992a, Thali1991, Posner1991

Keywords ADCC, antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, assay development, brain/CSF, co-receptor, complement, enhancing activity, escape, immunoprophylaxis, immunotherapy, immunotoxin, inter-clade comparisons, kinetics, mother-to-infant transmission, mucosal immunity, rate of progression, review, structure, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization.

- F105: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- F105: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- F105: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)
- F105: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. F105 recognized most variants,some from each of the four individuals by gp120 immunoprecipitation. [Ohagen2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)
- F105: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. [Raja2003] (**antibody binding site definition and exposure**, **co-receptor**)
- F105: 17b: This paper describes the generation of CD4i MAb E51, that like CD4i MAb 17b, blocks CCR5 binding to sCD4-bound gp120. The substitutions E381R, F383S, R419D I420R, K421D, Q422L, I423S, and Y435S (HXB2 numbering) all severely reduce 17b and E51 binding. All but I423S also diminish CCR5 binding by more than 50%. The mutation F383S also inhibits sCD4 binding and F105 binding, and K421D inhibits F105 binding, but not sCD4. [Xiang2003] (**antibody binding site definition and exposure**)
- F105: This study examined Ab interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 to both R5X4 and R5 isolates, but had no effect on neutralization. Anti-V3 MAb B4a1 increased CD4BS MAbs IgG1b12 and F105 to R5X4 virions, but only IgG1b12 binding was increased by B4a1 to the R5 isolate, and neutralization was not impacted. [Cavacini2002] (**co-receptor**)
- F105: NIH AIDS Research and Reference Reagent Program: 857.
- F105: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished. [Pantophlet2003a] (**antibody binding site definition and exposure**)
- F105: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers. [Poignard2003] (**antibody interactions**)
- F105: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. [Liu2002] (**immunoprophylaxis**)
- F105: Review of NAbs that notes that F105 binds the CD4BS, in combination with other MAbs it can protect some macaques against SHIV infection, and that it has strong ADCC activity. [Ferrantelli2002] (**ADCC**, **antibody interactions**, **immunoprophylaxis**, **review**)
- F105: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**antibody binding site definition and exposure**)
- F105: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding—basic residues in the V3 loop and the β19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding—MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants—the affinity of ΔV1 and ΔV1-V2 mutants for F105 was comparable to the wildtype—V3 mutants did not affect F105 binding—the K421A mutation in the β19 strand dramatically reduced F105 affinity, consistent with what is known about the F105 epitope. [Basmaciogullari2002] (**antibody binding site definition and exposure**)
- F105: HIV-1 gp160δCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160δCT with a reconstituted membrane ten-fold better than the same protein on beads, while such an affinity difference was not seen with F105 and 2G12—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160δCT PLs indistinguishably from gp160δCT expressed on the cell surface. [Grundner2002] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**)
- F105: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. [Chakrabarti2002] (**vaccine antigen design**)
- F105: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. [Xu2002] (**immunoprophylaxis**, **mother-to-infant transmission**)
- F105: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002] (**vaccine antigen design**)
- F105: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001] (**antibody binding site definition and exposure**)
- F105: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to F105. [Kolchinsky2001] (**antibody binding site definition and exposure**)
- F105: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkeys yielded highly pathogenic SHIV KU-1—HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160—substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1—17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. [Si2001] (**antibody binding site definition and exposure**)
- F105: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] (**vaccine antigen design**)
- F105: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form, although F105 was an exception and cannot neutralize either form of MN – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000]
- F105: Host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab. [Fortin2000]
- F105: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the plasma half-life was 7.2 +/- 2.2 days. [Baba2000] (**immunoprophylaxis**, **mother-to-infant transmission**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge. [Robert-Guroff2000] (**immunoprophylaxis**, **mucosal immunity**, **review**)
- F105: Anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998] (**antibody interactions**)
- F105: F105 enhances viral entry of viruses carrying the YU2 envelope glycoproteins, but neutralizes HXBc2. [Sullivan1998a] (**enhancing activity**)
- F105: A comparison of 25 gp120 specific, conformation dependent MAbs was done and F105 was used for competition studies – F105 did cross-compete with multiple CD4BS specific MAbs, however most could not neutralize even the autologous NL4-3 strains. [Sugiura1999] (**antibody interactions**)
- F105: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein. [Brand1998] (**vaccine antigen design**)
- F105: The MAb F240 binds to the immunodominant region of gp41 and enhances infection in the presence of complement – reactivity of F240 is enhanced by preincubation of cells with sCD4 or anti-CD4BS MAb F105. [Cavacini1998a] (**antibody interactions**)
- F105: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998] (**antibody interactions**)
- F105: Phase I dose escalation study, single dose of 100 or 500 mg/m2 was given to 4 HIV+ patients – sustained levels, no immune response against F105, no toxicity, infused Ab retained function – there was no evidence of anti-HIV-1 activity and virus was not diminished at day 1 or 7, by culture or plasma RNA. [Cavacini1998b] (**kinetics**, **immunotherapy**)
- F105: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a] (**antibody binding site definition and exposure**, **structure**)
- F105: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding – does not bind to HXBc2 gp120 if the 19 C-term amino acids, in conjunction with C1 positions 31-93, are deleted. [Wyatt1997] (**antibody binding site definition and exposure**)
- F105: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105 or sCD4. [Cao1997b] (**antibody binding site definition and exposure**)
- F105: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – F105 could only achieve 50% neutralization alone – all Ab combinations tested showed synergistic neutralization – F105 has synergistic response with MAbs 694/98-D (anti-V3), 48d, 2F5, and 2G12, and also with HIVIG. [Li1997] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- F105: In a multilaboratory blinded study, failed to neutralize any of nine B clade primary isolates. [D'Souza1997] (**variant cross-recognition or cross-neutralization**)
- F105: Neutralizes TCLA strains, but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- F105: Intracellular co-expression of heavy and light chains of the Fab105 fragment MAb F105 was enhanced by inclusion of an internal ribosome entry site (IRES) sequence – the Fab105 IRES expression cassette was cloned into an adeno-associated virus (AAV) shuttle vector, and transduced into human lymphocytes which were able to produce and secrete the Fab105 fragments while maintaining normal growth – several primary HIV-1 patient isolates were effectively blocked. [Chen1996] (**immunotherapy**)
- F105: Binding of F105 to oligomeric gp120 occurs despite the fact it cannot neutralize primary isolates. [Litwin1996]
- F105: A panel of immunotoxins were generated by linking Env MAbs to ricin A – immunotoxins mediated cell killing, but killing was not directly proportional to binding. [Pincus1996] (**immunotoxin**)
- F105: F105 is V H4 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- F105: Neutralizes HIV-1 LAI less potently than V3 specific MAbs. [McDougal1996]
- F105: Phase I study – MAb clearance in plasma has a 13 day half-life. [Wolfe1996] (**kinetics**, **immunotherapy**)

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- F105: The sulfated polysaccharide curdlan sulfate (CRDS) binds to the Envelope of T-tropic viruses and neutralizes virus – deletion of the V3 loop results in less potent inhibition of F105 binding by CRDS – binding site of F105 described as 256-257 ST, 368-370 DPE, 421 K, and 470-484 PGGGDMRDNWRSELY. [Jagodzinski1996] (**antibody binding site definition and exposure**)
- F105: Changing heavy chain from IgG1 to IgG3 increased neutralization efficiency. [Cavacini1995]
- F105: Biotinylated F105 was used for competition studies with Ab derived from pregnant HIV-1+ women – a correlation between maternal anti-CD4 BS Abs overlapping the F105 binding site and lack of HIV-1 transmission to infants was noted. [Khouri1995] (**mother-to-infant transmission**)
- F105: Efficient neutralization of T-cell adapted lines HXBc2 and MN, no neutralization of primary isolates 89.6, ADA and YU2 – even some enhancement of infection of ADA and YU2 was observed. [Sullivan1995] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- F105: Eight patient phase Ia trial for use as an immunotherapeutic – no clinical or biochemical side effects observed, plasma levels of 10 ug/ml maintained for 21 days. [Posner1995] (**immunotherapy**)
- F105: An immunoassay for titrating CD4BS serum antibody was developed using a gp120-coated solid phase and competition with MAb F105 – 109/110 French HIV-1+ sera and 51/56 HIV-1+ African sera had detectable CD4BS Abs using this assay, demonstrating CD4 binding site conservation among diverse subtypes – CD4BS Abs were detected soon after seroconversion and persisted – 0/21 HIV-2+ sera reacted, indicating that the HIV-1 and HIV-2 CD4BS Abs are not cross-reactive. [Turbica1995] (**assay development**, **inter-clade comparisons**)
- F105: A human CD4+ T lymphocyte line was transduced to express Fab fragments of F105 – heavy and light chains are joined by an inter-chain linker – in the transduced cells infected with HIV-1, the Fab binds intracellularly to the envelope protein and inhibits HIV-1 production – secreted Fab fragments neutralize cell-free HIV-1 – combined intra- and extracellular binding activities of the expressed Fab make transduced cells resistant to HIV-1 infection and also can protect surrounding lymphocytes by secreting neutralizing antibodies. [Chen1994a, Marasco1993] (**variant cross-recognition or cross-neutralization**)
- F105: Used as a positive control for CD4 BS antibodies in a study of the influence of oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody binding site definition and exposure**)
- F105: Fab fragments show reduced capacity to neutralize IIIB, MN, and RF compared to intact IgG1, suggesting bivalent interaction may be important in binding and neutralization. [Cavacini1994a] (**variant cross-recognition or cross-neutralization**)
- F105: Administered intravenously to four cynomologus monkeys, plasma pharmacokinetics and biological activity tested. [Cavacini1994b] (**kinetics**)
- F105: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – anti-CD4 MAbs moderately inhibit gp120 binding to GalCer, possibly through steric hindrance – binding of GalCer to gp120 inhibited but did not completely block F105 binding. [Cook1994] (**brain/CSF**)
- F105: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs 48d, 21h, 15e and 17b) [Thali1994] (**antibody binding site definition and exposure**)
- F105: Comparison of MAb F105 sequences with those of MAbs 21h and 15e. [Bagley1994] (**antibody sequence, variable domain**)
- F105: A neutralization escape mutant (HXB2 A281V) was selected by growth of HXB2 in the presence of broadly neutralizing sera – F105 neutralization was not affected by this mutation. [Watkins1993] (**escape**)
- F105: Ab response in IIIB lab workers was compared to gp160 LAI vaccine recipients – F105 was used as a control – infected lab workers and some of the gp160 vaccinees had a MAb response that could inhibit gp120-CD4 binding, at lower titers than the infected lab workers. [Pincus1993b] (**vaccine-specific epitope characteristics**)
- F105: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – required >81 fold higher concentrations to neutralize the mutant than wild type. [Klasse1993a] (**antibody interactions**)
- F105: Study of synergy of neutralization and binding comparing F105 and sCD4 with the V3 MAbs: 50.1, 59.1, 83.1, and 58.2 – synergy was observed, and the data suggest that binding of one ligand (F105) can increase the binding of the second (e. g. V3 loop MAbs) due to conformational changes. [Potts1993] (**antibody interactions**)
- F105: Study of synergy between F105 and sera from vaccinated volunteers with V3-loop specific neutralization activity – 2/3 sera demonstrated neutralization synergy, and 3/3 binding/fusion-inhibition synergy. [Montefiori1993] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F105: Binding to Delta V1/2 and Delta V1/2/3 mutant glycoproteins is 2.4- and 13-fold greater, respectively, than binding to wildtype gp120. [Wyatt1993] (**antibody binding site definition and exposure**)
- F105: Serum from all asymptomatic HIV-1 positive people tested block F105 binding, but only from 27% of symptomatic individuals. [Cavacini1993b] (**rate of progression**)
- F105: Additive MN or SF2 neutralization when combined with anti-V3 MAbs 447-52D and 257-D. [Cavacini1993a] (**antibody interactions**)
- F105: No neutralization of primary isolates observed (John Moore, pers comm) (**variant cross-recognition or cross-neutralization**)
- F105: F105 binds to and neutralizes selected lab strains and 3/9 HIV-1 primary isolates – synergistic enhancement of neutralization by seropositive sera. [Posner1993] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- F105: Called F-105 – neutralizes IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120. [Moore1993a]
- F105: Significant enhancement of F105 binding to RF infected cells preincubated with V3-specific MAbs V3-2 and V3-1. [Posner1992a] (**antibody interactions**)
- F105: F105 mediates ADCC against SF2 through the CD16+ population of PBMC – does not mediate complement-dependent cytotoxicity. [Posner1992b] (**ADCC**, **complement**)
- F105: Precipitation of Delta 297-329 env glycoprotein, which has a deleted V3 loop, is much more efficient than precipitation of wild type. [Wyatt1992] (**antibody binding site definition and exposure**)
- F105: MAb cDNA sequence – V H4 V71-4 rearranged with a D H D-D fusion product of dlr4 and da4, and with J H5 – V kappa is from the Humvk325 germline gene joined with Jkappa 2. [Marasco1992] (**antibody sequence, variable domain**)
- F105: Amino acid substitutions that impair F105 neutralization inhibit gp120-CD4 interaction. [Thali1992a] (**antibody binding site definition and exposure**)
- F105: F105 neutralization escape mutants result from changes in amino acids in discontinuous regions: C2, 256-262 and C3, 386-370. [Thali1991] (**antibody binding site definition and exposure**)
- F105: First description of F105, binds topographically near the CD4-binding site – inhibits binding of free, infectious virions to uninfected HT-H9 cells, but does not react with virus adsorbed to uninfected HT-H9 cells – soluble rCD4 pre-bound to infected cells inhibits F105 binding – F105 inhibits infection of HT-H9 cells in standard neutralization assays with HIV-1 and MN strains. [Posner1991] (**antibody binding site definition and exposure**, **antibody generation**)

1004	F91 (F-91)	Env	gp120		no		

Ab type CD4BS **Research Contact** James Robinson, University of Connecticut, Storrs

References Gorny2004, Pantophlet2003b, Zwick2003, Raja2003, Pantophlet2003a, Kwong2002, Xiang2002b, Yang2002, Yang2000, Fouts1998, Binley1998, Parren1998a, Mondor1998, Fouts1997, Moore1996, Moore1994b, Moore1993a

Keywords antibody binding site definition and exposure, antibody interactions, co-receptor, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- F91: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- F91: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- F91: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)

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- F91:Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- F91: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. [Raja2003] (**co-receptor**)
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- F91: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**)
- F91: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002] (**antibody binding site definition and exposure**)
- F91: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] (**antibody binding site definition and exposure**)
- F91: CD4BS MAbs 15e, 21h, and F91 bind with even lower affinity than 205-43-1 and 205-42-15 to JRFL oligomer – conclusions of this paper contrast with [Parren1998a] [Fouts1998]. [Fouts1998, Parren1998a] (**antibody binding site definition and exposure**)
- F91: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type. [Binley1998] (**antibody binding site definition and exposure**)
- F91: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**antibody binding site definition and exposure**)
- F91: Weak inhibition of binding of Hx10 to CD4 positive or negative cells, weakly neutralizing. [Mondor1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- F91: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – F91 bound monomer, did not bind oligomer or neutralize JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- F91: Unusual pattern of reciprocal enhancement with several anti-V2 and V3 directed MAbs – reciprocal inhibition of other CD4BS MAbs. [Moore1996] (**antibody binding site definition and exposure**, **antibody interactions**)
- F91: Has strong cross-reactivity with gp120 monomers from most subtypes, A-F. [Moore1994b] (**inter-clade comparisons**)
- F91: Called F-91 – neutralizes IIIB – reactive with SF-2 gp120 – strong inhibition of HIV+ human sera binding to IIIB gp120. [Moore1993a] (**variant cross-recognition or cross-neutralization**)

1005 GP13 (ARP3054) Env gp120 L HIV-1 infection human (IgG1)

Ab type CD4BS

References Gorny2004, Vella2002, Schutten1997, Schutten1996, Wisnewski1996, Bolmstedt1996, Schutten1995b, Schutten1995a, Bagley1994, Back1993, Schutten1993

Keywords antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, assay development, binding affinity, enhancing activity, escape, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- GP13: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- GP13: UK Medical Research council AIDS reagent: ARP3054.
- GP13: Called ARP3054: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. [Vella2002] (**assay development**)
- GP13: Neutralized (50%) an SI-env chimeric virus and enhanced (>5 fold) an NSI-env chimeric virus. [Schutten1997] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- GP13: IIIB neutralizing MAbs *in vitro* fail to neutralize in a mouse model *in vivo*. [Schutten1996]
- GP13: GP13 is V H5 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- GP13: Sera were obtained from guinea pigs vaccinated either with gp160, or with gp160 lacking N-linked glycans at N406, N448, and N463 – these sera could block equally well both the CD4 BS MAb GP13 and the V3 MAb F58/H3. [Bolmstedt1996] (**antibody interactions**)
- GP13: Neutralizes T-cell adapted viruses but not the SI strain 16.2, despite high binding affinity. [Schutten1995b] (**variant cross-recognition or cross-neutralization**, **binding affinity**)
- GP13: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor. [Schutten1995a] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- GP13: Mutations in a neutralization resistant isolate obtained by passage of the IIIB isolate in chimpanzees reduced neutralization, but the escape was not as clear as seen with anti-V3 MAbs. [Back1993] (**escape**)
- GP13: Neutralized a broad range of HIV-1 strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D), 384(Y/E) [Schutten1993] (**antibody binding site definition and exposure**, **inter-clade comparisons**)

1006 GP44 Env gp120 L HIV-1 infection human (IgG1)

Ab type CD4BS

References Gorny2004, Wisnewski1996, Bagley1994, Schutten1993

Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review, variant cross-recognition or cross-neutralization.

- GP44: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- GP44: GP44 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- GP44: Exhibited a more restricted pattern of neutralizing activity than GP13 and GP68 – the following gp120 amino acid substitutions strongly inhibit binding: 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q or D) [Schutten1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

1007 GP68 Env gp120 L HIV-1 infection human (IgG1)

Ab type CD4BS

References Gorny2004, Guillon2002, Wisnewski1996, Schutten1995a, Bagley1994, Klasse1993a, Schutten1993

Keywords antibody binding site definition and exposure, antibody sequence, variable domain, enhancing activity, review, variant cross-recognition or cross-neutralization.

- GP68: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- GP68: UK Medical Research Council AIDS reagent: ARP3055.
- GP68: The affect of Ab binding on infectivity was studied by pseudotyping three related envs with different phenotypes – R5 viruses were preferentially enhanced, not X4 – the V3 region was the main determinant of Ab-mediated enhancement and modulation of the interaction between CCR5 and gp120 is critical – tests with MAbs anti-V3 391/95-D and CD4BS-specific GP68 indicate that Ab specificity did not determine whether or not infectivity was enhanced or neutralized, rather the phenotype was determined by Envelope conformation. [Guillon2002] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- GP68: GP68 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**)
- GP68: Neutralizes IIIB – only slight inhibition of SI phenotype, and strong enhancement of NSI phenotype chimeric viruses, that incorporated different envs from the same donor. [Schutten1995a] (**variant cross-recognition or cross-neutralization**)
- GP68: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – GP68 required markedly higher concentrations to neutralize the mutant than wild type. [Klasse1993a] (**antibody binding site definition and exposure**)
- GP68: Neutralized a broad range of HIV-1 lab strains from phylogenetically different subfamilies – the following gp120 amino acid substitutions strongly inhibit binding: 117(K/W), 256(S/Y), 257(T/G), 262(N/T), 368(D/R or K), 370(E/R or Q), 384(Y/E), 435(Y/H) [Schutten1993] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)

1008 HF1.7 Env gp120 L anti-idiotype mouse (IgM)

Ab type CD4BS

References Chanh1987

- HF1.7: An anti-Id antibody stimulated by anti-CD4 MAb Leu-3a binds to recombinant gp160, suggesting HF1.7 mimics CD4. [Chanh1987]

1009 HT5 (205-43-1) Env gp120 L (weak) HIV-1 infection human

Ab type CD4BS **Research Contact** Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas

References Gorny2004, Herrera2003, Grovit-Ferbas2000, Parren1998a, Fouts1998, Fouts1997, Moore1995a, Moore1994b

Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- HT5: Also called 205-43-1. This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- HT5: Called 205-43-1: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. [Grovit-Ferbas2000] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- HT5: Called 205-43-1 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. [Herrera2003] (**antibody binding site definition and exposure**, **antibody interactions**)
- HT5: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with [Parren1998a] [Fouts1998]. [Fouts1998, Parren1998a] (**antibody binding site definition and exposure**)
- HT5: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL. [Fouts1997] (**antibody binding site definition and exposure**, **antibody interactions**)
- HT5: 205-46-9 was cross-reactive across clades A-F, 205-43-1 very cross-reactive but not quite as extensive 205-46-9. [Moore1994b] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- HT5: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN. [Moore1995a] (**variant cross-recognition or cross-neutralization**)
- HT5: HT5, HT6, and HT7 are also known as 205-43-1, 205-42-15, and 205-46-9, respectively. Rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2. [Fouts1998] (**binding affinity**)

1010	HT6 (205-42-15)	Env	gp120		L (weak)	HIV-1 infection	human

Ab type CD4BS **Research Contact** Ciba-Geigy AG Basel, Switzerland, and Tanox Biosystems, Houston, Texas
References Gorny2004, Herrera2003, Parren1998a, Fouts1998, Fouts1997, Moore1995a, Moore1994b
Keywords antibody binding site definition and exposure, antibody interactions, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- HT6: Called 205-42-15: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- HT6: Called 205-42-15 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. [Herrera2003] (**antibody binding site definition and exposure**, **antibody interactions**)
- HT6: HT5 and HT6 bind JRSF oligomer but with low affinity, and are not neutralizing – conclusions of this paper contrast with [Parren1998a] [Fouts1998]. [Fouts1998, Parren1998a] (**antibody binding site definition and exposure**)
- HT6: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL. [Fouts1997] (**antibody binding site definition and exposure**, **antibody interactions**)
- HT6: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was not quite as extensively cross-reactive. [Moore1994b] (**inter-clade comparisons**)
- HT6: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only weakly neutralizes IIIB and MN. [Moore1995a] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• HT6: HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively. [Fouts1998]					
1011	HT7 (205-46-9)	Env	gp120		L (IIIB)	HIV-1 infection	human

Ab type CD4BS **Research Contact** Ciba-Geigy AG (Basel, Switzerland), and Tanox Biosystems, Houston, Texas
References Gorny2004, Herrera2003, Grovit-Ferbas2000, Parren1998a, Fouts1998, Fouts1997, Moore1995a, Moore1994b
Keywords antibody binding site definition and exposure, assay standardization, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- HT7: Also called 205-46-9. This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**)
- HT7: Called 205-46-9. To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. [Grovit-Ferbas2000] (**antibody binding site definition and exposure**)
- HT7: Called 205-46-9 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. [Herrera2003] (**antibody binding site definition and exposure**)
- HT7: Binds JRSF oligomer with high affinity, at least as high as IgG1b12, but IgG1b12 is neutralizing, H7 is not – conclusions of this paper contrast with [Parren1998a] – authors propose a model where H7 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect [Fouts1998]. [Fouts1998, Parren1998a] (**antibody binding site definition and exposure**)
- HT7: MAbs IgG1b12, HT5, HT6, and HT7 cross-compete for binding to monomeric gp120, bind equally well, inhibit gp120-sCD4 interactions, but only IgG1b12 neutralizes JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- HT7: 205-46-9 was cross-reactive across clades A-F, 205-43-1 was cross-reactive, but not quite as extensive. [Moore1994b] (**inter-clade comparisons**)
- HT7: Despite highly cross-reactive binding to many primary and T-cell adapted viral strains, only neutralizes IIIB well, with sporadic weak neutralization of other isolates. [Moore1995a] (**variant cross-recognition or cross-neutralization**)
- HT7: Called 205-46-9. HT5, HT6, and HT7 are also known as 205-43-1 , 205-42-15, and 205-46-9, respectively. Binds JRSF oligomer with high affinity as does IgG1b12, but IgG1b12 is neutralizing, 205-46-9 is not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2. [Fouts1998] (**assay standardization**)

1012	ICR 39.13g (ICR39.13g, 39.13g)	Env	gp120		L	Vaccine	rat (IgG2b)

Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120
Ab type CD4BS **Research Contact** Jackie Cordell and C. Dean
References Vella2002, Peet1998, Klasse1996, Armstrong1996a, McKeating1996b, Beretta1994, McLain1994, Klasse1993a, Thali1993, Moore1993a, McKeating1993b, McKeating1992c, McKeating1992a, Cordell1991

- ICR 39.13g: UK Medical Research Council AIDS reagent: ARP390.
- ICR 39.13g: Called ARP390/391, but no such entry was found at the UK Medical Research Council AIDS reagent web site: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. [Vella2002]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- ICR 39.13g: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – ICR 39.13g was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]
- ICR 39.13g: Variants of LAI have differing neutralization susceptibility to 39.13g. [Klasse1996]
- ICR 39.13g: Post-attachment neutralization mechanism, in contrast to MAb 39.3b. [Armstrong1996a]
- ICR 39.13g: Called 39.13g Neutralizes HXB2, but fails to neutralize chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b]
- ICR 39.13g: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to a class of conformation sensitive neutralizing MAbs – ICR 39.13g required moderately higher concentrations to neutralize the mutant than wild type. [Klasse1993a]
- ICR 39.13g: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – mediates neutralization with 2.3 molecules of IgG. [McLain1994]
- ICR 39.13g: Strongly inhibits CD4 inducible MAb 48d. [Thali1993]
- ICR 39.13g: Conformational, does not bind denatured gp120 – weak neutralization of IIIB – strong inhibition of HIV+ human sera binding to IIIB gp120. [Moore1993a]
- ICR 39.13g: Neutralization activity against HXB10, RF, SF-2 and MN strains of HIV-1. [McKeating1993b]
- ICR 39.13g: Binds to a conformational epitope involved in CD4 binding – exerts a synergistic effect in combination with V3 directed MAbs. [McKeating1992a]
- ICR 39.13g: Cross-competes with MAbs ICR 39.3b and 15e. [Cordell1991]

1013	ICR 39.3b (39.3, 39.3b, ICR39.3b)	Env	gp120		L	Vaccine	rat (IgG2b)

Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120
Ab type CD4BS **Research Contact** J. Cordell and C. Dean
References Wyatt1998a, Jeffs1996, Armstrong1996a, McLain1994, Moore1993c, Moore1993a, McKeating1992c, Cordell1991

- ICR 39.3b: UK Medical Research Council AIDS reagent: ARP391.
- ICR 39.3b: Called 39.3 – summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding. [Wyatt1998a]
- ICR 39.3b: Called 39.3b – increased binding when V1/V2 or V1/V2 and V3 were deleted from gp120. [Jeffs1996]
- ICR 39.3b: Neutralizes only if the antibody is added prior to the attachment of the virus to the cell, in contrast to 39.13g. [Armstrong1996a]
- ICR 39.3b: Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively. [McLain1994]
- ICR 39.3b: Conformational, does not bind to denatured IIIB. [Moore1993a]
- ICR 39.3b: Cross-competes with MAbs ICR 39.13g and 15e. [Cordell1991]
- ICR 39.3b: also known as 39.3, 39.3b and ICR39.3b.

1014	IgG1b12 (Fab b12, Fab 3B3, MAb IgG1b12, IgG1-b12, IgG1 b12, IgGB12, b4/12, b12, 1b12, immunoglobulin G1b12, ARP3065, IgG1 b12)	Env	gp120		L P	HIV-1 infection	human (IgG1κ)

Ab type CD4BS **Research Contact** D. Burton, Scripps Research Institute, La Jolla, CA, also J. Geltowsky and J. Pyati, R. W. Johnson Pharmaceutical Research Inst. La Jolla, CA

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Zwick2004, Zwick2003, Pantophlet2003b, Zhu2003, Veazey2003, Montefiori2003, Kitabwalla2003, Zhang2003, Wang2003, Mascola2003a, Raja2003, Hart2003, Ferrantelli2003, Dey2003, Cavacini2003, Binley2003, Herrera2003, Pantophlet2003a, Poignard2003, Lewis2002, Kwong2002, Gorry2002, Cavacini2002, Bures2002, Liu2002, Ferrantelli2002, Klasse2002, Zhang2002, Grundner2002, Edwards2002, Xiang2002b, Vella2002, Chakrabarti2002, Xu2002, Scanlan2002, Saphire2002, Yang2002, Schulke2002, Sanders2002, Golding2002b, Srivastava2002, Hezareh2001, Xu2001, Hofmann-Lehmann2001, Verrier2001, Spenlehauer2001, Zeder-Lutz2001, Poignard2001, Parren2001, Zwick2001c, Zwick2001b, Zwick2001a, York2001, Yang2001, Saphire2001b, Saphire2001a, Kolchinsky2001, Si2001, Park2000, Nyambi2000, Ly2000, Grovit-Ferbas2000, Binley1999, Beddows1999, Giraud1999, Montefiori1999, Hioe1999, Jackson1999, Crawford1999, Poignard1999, Stamatatos1998, Kropelin1998, Frankel1998, Sullivan1998a, Schonning1998, Brand1998, Parren1998b, Takefman1998, Fouts1998, Binley1998, Connor1998, Parren1998a, Mondor1998, Wyatt1998a, Valenzuela1998, Parren1997a, Parren1997b, Parren1997c, Boots1997, Burton1997, Wyatt1997, Ugolini1997, Ditzel1997, Stamatatos1997, Moore1997, Kessler II1997, Li1997, Fouts1997, Mo1997, Schutten1997, D'Souza1997, McKeating1996a, Sattentau1996, Trkola1996a, Poignard1996a, Poignard1996b, Gauduin1996, Moore1996, Yang1997c, Sullivan1995, Ditzel1995, Trkola1995, Parren1995, Moore1995b, Moore1995a, Sattentau1995a, Sattentau1995c, Kessler1995, Moore1994b, Burton1994, Roben1994, Barbas III1992, Burton1991

Keywords ADCC, antibody binding site definition and exposure, antibody generation, antibody interactions, assay development, assay standardization, binding affinity, co-receptor, complement, enhancing activity, escape, immunoprophylaxis, immunotherapy, inter-clade comparisons, kinetics, mimotopes, mother-to-infant transmission, mucosal immunity, responses in children, review, structure, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization.

- IgG1b12: 4KG5, a single-chain Fv (scFv), reacts with a conformational epitope which is formed by the V1, V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Denaturation of gp120 abolished binding of 4KG5 and Fab b12. Addtionally, binding of 4KG5 was abrogated when any of the V1, V2 or V3 loops were deleted. Of a panel of Abs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished or abroated binding: V2 loop MAbs (G3-4, G3-136), V3 loop MAbs (19b, 447-52D, hNM01, AH48, loop2, F425 B4e8, 694-88D), V3-C4 (G3-299, G3-42, G3-519, G3-537), CD4BS (b6, b3, F91, F105, 15e, L33, 1008-D, 654-30D, 559-64D, 1027-30D, Ia3, Ia7, FG39, Fbb14). MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1, V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. 4KG5 did not enhance IgG1b12 neutralization. [Zwick2003] (**antibody binding site definition and exposure**, **antibody interactions**)
- IgG1b12: This paper describes an attempt to engineer a gp120 molecule that would focus the immune response onto the IgG1b12 epitope. Four Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with seven N-linked glycosylation site sequons and this combination minimized the binding of non-neutralizing MAbs. b12 affinity was lowered, and binding of non-neutralizing MAbs was knocked out. C1 and C5 regions were then removed to eliminate the epitopes for MAbs against these regions, but these also diminished IgG1b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- IgG1b12: The HIV-1 primary isolate DH012 has preserved the epitopes for the MAbs IgG1b12, 2G12, 17b, however natural DH012 infection in chimpanzees and DH012 gp120 vaccination in guinea pigs does not give rise to Abs against these epitopes. [Zhu2003] (**vaccine-specific epitope characteristics**)
- IgG1b12: Called b12. The NAb b12 was administered locally to the vagina in macaques and could protect against subsequent vaginal infection with SHIV-162P4. This NAb model of a topical microbicide was dose dependence, and was effective for up to 2 hours after administration. [Veazey2003] (**immunoprophylaxis**, **mucosal immunity**)
- IgG1b12: AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessaton of therapy, which then declined to a low level. The polylconal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. [Montefiori2003] (**escape**)
- IgG1b12: Recombinant adeno-associated virus was used to deliver the IgG1b12 gene into mice by injection. IgG1b12 was expressed in these mice for over 6 months after the primary injection. This strategy allows for predetermined Ab specificity, and could ultimately be used with synergistic Ab combinations. [Lewis2002] (**immunoprophylaxis**, **vaccine antigen design**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: Called b6. Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. Enthalpy and entropy changes were divergent, but compensated. CD4 and MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy of binding to the gp120 monomer (mean: 26.1 kcal/mol, range 18.6-31.5), but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. The high values suggest surface burial or protein folding and ordering of amino acids upon binding. NAb 2G12 had an entropy value of -1.6. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding that is not faced by other anti-gp120 antibodies. [Kwong2002] (**antibody binding site definition and exposure**, **structure**)
- IgG1b12: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. [Kitabwalla2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**)
- IgG1b12: Called b12. The Fab m18 was selected from a human phage display library by a new method called sequential antigen panning (SAP), using a series of antigens to screen the library to pick broadly cross-reactive isolates. The ability to block cell mediated fusion by m17 was compared to Fabs X5 and b12 for a clade A, CRF01 EA, G, and 6 clade B isolates, and the inhibitory activity of m18 was slightly lower but comparable to neutralizing Fabs b12 and X5. [Zhang2003] (**inter-clade comparisons**)
- IgG1b12: Called b12. Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. [Wang2003] (**vaccine antigen design**, **review**)
- IgG1b12: This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. [Mascola2003a] (**immunoprophylaxis**, **review**)
- IgG1b12: Called IgG1 b12. IgG1b12 induces strong ADCC and CDC cytoxicity of HIV-1 infected cells. A panel of mutants in the Fc region of IgG1b12 was generated. K322A reduced ADCC binding of FcγR and abolished complement-dependent cytotoxicity (CDC) and C1q binding. L234A plus L235 in the lower hinge region of the IgG1 heavy chain abolished both FcγR and C1q binding and ADCC and CDC. These mutants did not impact IgG1b12's ability to neutralize virus. [Hezareh2001] (**ADCC**, **complement**)
- IgG1b12: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs F105, 15e, and IgG1b12 as well as their Fab fragments inhibited CD4-independent binding of the V1/V2 loop-deleted gp120 glycoproteins of R5 HIV-1 isolates ADA, YU2 and JR-FL and to CCR5 in a concentration dependent manner. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. [Raja2003] (**co-receptor**)
- IgG1b12: Called IgG1 b12. This paper is a study of the 2F5 NAb complexed to peptide ELDKWAS; the peptide was found to interact with amino acids near the base of the very long (22 residue) CDR 3H region of the Ab, although a Phe at the apex of the loop was also important. The authors suggest that particularly long CDR H3 regions may be a common feature of HIV-1 neuturalizing antibodies – there are 22 residues in 2F5's H3, 18 in IgG1b12's H3, and 22 residues in X5's H3. They express concern that because small animals like mice are be unable to elicit Ab responses with such long H3s, they may be poor model systems for HIV vaccine studies. [Zwick2004] (**antibody interactions**)
- IgG1b12: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. [Ferrantelli2003] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)

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- IgG1b12: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. [Dey2003] (**immunoprophylaxis**, **immunotherapy**)
- IgG1b12: Called 1b12. The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. CD4BS MAb IgG1b12 had no effect on B4e8 binding. [Cavacini2003] (**antibody interactions**)
- IgG1b12: This study examined Ab interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 enhanced the binding of CD4BS MAbs IgG1b12 and F105 to both R5X4 and R5 isolates, but had no effect on neutralization. Anti-V3 MAb B4a1 increased CD4BS MAbs IgG1b12 and F105 to R5X4 virions, but only IgG1b12 binding was increased by B4a1 to the R5 isolate, and neutralization was not impacted. [Cavacini2002] (**co-receptor**)
- IgG1b12: Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate-like or TCLA SHIV variants. IgG1b12 neutralized SHIV strains HXBc2, KU2, 89.6, but not 89.6P and KB9. 89.6 is a dual tropic primary isolate that is not pathogenic in macaques, 89.6P is a highly pathogenic form of 89.6 obtained after passage in macaques, and KB9 is a molecular clone of 89.6P. Neutralization resistance was cell line independent. [Crawford1999] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. IgG1b12 neutralized SOS and WT proteins comparably, and neither IgG1b12 nor the Fab b12 could neutralize well post-attachment, consistent with the notion that theb12 binding site would be blocked upon cellular binding. [Binley2003] (**vaccine antigen design**)
- IgG1b12: IgG1b12 neutralized many South African (5/8) and Malawian (4/8) clade C primary HIV-1 isolates, being more effective than 2F5 which neutralized only two Malawian and no South African isolates. 2G12 did not neutralize any of the 16 isolates. [Bures2002] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: NIH AIDS Research and Reference Reagent Program: 2640IgG1b12 was more effective than 2G12 and 2F5 in neutralizing 5/8 south african and 4/8 malawian clade C primary HIV-1 isolates in a p24 ELISA capture assay. (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: UK Medical Research Council AIDS reagent: ARP3065.
- IgG1b12: Called b12 – CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (nonneutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the nonneutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – the nonneutralizing MAbs partially competed with b12 for Env binding of the surface of Env-transfected cells – this suggests Env has two categories of binding site for CD4BS MAbs, one recognized by both b12 and nonneutralizing CD4BS MAbs, the other is recognized by only b12 – Ab-gp120 interactions based on the use of monomeric gp120 or Env-transfected cells do not predict the outcome of HIV-1 neutralization assays, and they should be interpreted with caution. [Herrera2003] (**antibody interactions**)
- IgG1b12: Called b12 – Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never in enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded – for twelve mutants, b12 neutralization sensitivity and affinity correlated, but for five mutants neutralization efficiency was maintained or increased despite a decrease in affinity suggesting that the subsitutions that influence b12 binding to the monomer are different that those that impact neutralization sensitivity to the trimer. [Pantophlet2003a] (**antibody binding site definition and exposure**, **binding affinity**)

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- IgG1b12: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, but anti-V3 Abs 447-52D and 19b, which did not neutralize JR-CSF and ADA captured amounts of p24 equal to or higher than the amounts captured by the neutralizing Ab b12. [Poignard2003] (**assay development**, **variant cross-recognition or cross-neutralization**)
- IgG1b12: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. [Liu2002] (**review**)
- IgG1b12: Review of NAbs that notes IgG1b12 is a recombinant IgG1 from a phage displayed Fab generated against gp120 from a B clade infected individual, that it binds the CD4BS, that alone or in combination with other MAbs it can protect some macaques against SHIV infection, and that it has strong ADCC activity. [Ferrantelli2002] (**review**)
- IgG1b12: A broad review of NAbs that mentions IgG1b12 as an example of a NAb that does not alter the conformation of gp120, but interferes with CD4 binding. [Klasse2002] (**review**)
- IgG1b12: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface—non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12—the MAb 17b was sCD4 inducible on gp160ΔCT PL. [Grundner2002] (**vaccine antigen design**)
- IgG1b12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- IgG1b12: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**)
- IgG1b12: Called ARP3065: Herpesvirus saimiri-immortalized CD4+ T lymphocytes (HVS T cells) were used to isolate virus and perform HIV-1 neutralization assays, and compared with a standard PBMC protocol – neutralization sensitivities to a panel of MAbs and to homologous or heterologous plasma/sera were similar for HVS T cells (CN-2 cells) and PBMCs. [Vella2002] (**assay development**)
- IgG1b12: A modified gp140 (gp140ΔCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. [Chakrabarti2002] (**vaccine antigen design**)

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- IgG1b12: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. [Xu2002] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- IgG1b12: Alanine scanning mutagenesis used in conjunction with competition and replacement studies of N-linked carbohydrates and sugars suggest that the 2G12 epitope is formed from mannose residues contributed by the glycans attached to N295 and N332, with the other N-linked carbohydrates in positions N339, N386, and N392 playing a role in maintaining conformation relevant to 2G12 binding – N295A and N332A mutants showed essentially unchanged anti-CD4BS NAb b12 binding affinities, while N339A, N386A and N392A mutants displayed significantly lowered b12 affinity, presumably due to conformational changes. [Scanlan2002] (**antibody binding site definition and exposure**)
- IgG1b12: The crystal structure of IgG1b12 is resolved and is the first structure of an intact human Ab with an ordered, full length hinge – the structure is extremely asymmetric and flexible with an antigen-binding site that has an unusually long CDR H3 region with a ten residue insertion that projects above the rest of the antigen-binding site – this loop may be required for recognition of the recessed CD4 binding site of gp120. [Saphire2002] (**structure**)
- IgG1b12: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002] (**vaccine antigen design**)
- IgG1b12: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – SOS gp140-2F5-IgG1b12 formed multiple ring structures composed of two SOS gp140 proteins bridged by two Ab molecules, while 2F5 and 2G12 formed extended chains rather than closed rings. [Schulke2002] (**vaccine antigen design**)
- IgG1b12: Deglycosylation of gp120 does not significantly affect IG1b12 binding, in contrast to MAB 2G12. [Sanders2002] (**antibody binding site definition and exposure**)
- IgG1b12: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. [Golding2002b]
- IgG1b12: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4. [Srivastava2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- IgG1b12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. [Xu2001] (**inter-clade comparisons**)
- IgG1b12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline – the most potent combination included IgG1b12, which alone does not alone neutralize SHIV89.6P. [Hofmann-Lehmann2001] (**antibody interactions**, **immunoprophylaxis**)
- IgG1b12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 M Abs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**, **co-receptor**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12. [Spenlehauer2001] (**assay development**)
- IgG1b12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers. [Zeder-Lutz2001] (**antibody interactions**)
- IgG1b12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the structure of CD4-bound gp120 reveals features that HIV has evolved to escape anti-CD4BS Abs like IgG1b12 despite profound functional constraints – CD4BS Abs must first access the CD4 binding site, deeply recessed within the gp120 core, and the Fab of an Ab molecule is "wider" than CD4, and in addition the binding site is flanked by variable and glycosylated regions. [Poignard2001] (**review**, **structure**)
- IgG1b12: Intravenous passive transfer of MAb b12 provides dose-dependent protection from infection to macaques vaginally challenged with the R5 virus SHIV(162P4) – the primary isolate HIV-1SF162 is neutralized 90% (IC90) by b12 at 2 µg/ml, and SHIV162P4, derived from HIV-1SF162, was neutralized by 90% at 2 µg/ml in PHA-activated PBMC from rhesus macaques – the 90% neutralization titers achieved in three groups of animals that were given 25-, 5-, and 1-mg/kg doses were approximately 1:400, 1:80, and 1:16, respectively – the half-life of IgG1 b12 in plasma was about 1 week, but while the peak b12 plasma concentration was immediately after the infusion, the peak vaginal fluid concentration was 7-14 days later. [Parren2001] (**immunoprophylaxis**, **kinetics**)
- IgG1b12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – whole IgG1b12 and b12 Fab fragments behaved similarly in the neutralization assays – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates. [Zwick2001c] (**antibody interactions**)
- IgG1b12: This paper primarily concerns 4E10 and Z13, MAbs that both bind proximally to the 2F5 binding site to a conserved epitope, and that neutralize some primary isolates from clades B, C, and E – broadly neutralizing MAbs 2F5, IgG1b12, and 4E10 and Z13 fail to neutralize different subsets of viruses. [Zwick2001b] (**inter-clade comparisons**)
- IgG1b12: b12 recognizes a conformational epitope that overlaps with the CD4 binding site – a phage displayed peptide library was used to identify a peptide which bound b12, called B2.1, which competes with b12 in competition assays – B2.1 has significant homology to the D loop of gp120: upper case letters indicate residues B2.1 shares with gp120, heRsymFSDlenrcI – one of the goals of defining peptide mimics to the b12 epitope is to develop an immunogen that can stimulate b12-like antibodies, but B2.1 cross-linked to phage and ovalbumin bound IgG1b12 did not elicit cross-reactive gp120 Abs in mice or rabbits. [Zwick2001a] (**antibody binding site definition and exposure**, **mimotopes**)
- IgG1b12: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding. [York2001] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Primary isolates YU2 and ADA are more resistant to IgG1b12 neutralization than HXBc2: 90% Neutralization of HXBc2 is observed with 1.25 ug of IgG1b12, while ADA and YU2 require 2.5 and 5 ug respectively to achieve 50% neutralization, and 90% neutralization could not be achieved with 10 or 20 ug of IgG1b12, respectively. [Yang2001] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: This paper describes the biological implications of the crystal structure of b12 – a remarkable feature of this antibody is a long protruding finger-like CDR H3 that can dock in the recessed CD4-binding site – a contact residues in gp120 are modeled, with numbering based on the variable loop-deleted crystal structure of gp120. [Saphire2001b] (**structure**)
- IgG1b12: This paper describes the technical aspects of the crystallization of b12 at a resolution of 2.7 angstroms with all 12 Ig domains resolved. [Saphire2001a] (**structure**)
- IgG1b12: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, except the mutation 197 S/R which resulted in a carbohydrate addition to 195 N that disrupts the IgG1b12 binding site. [Kolchinsky2001] (**antibody binding site definition and exposure**)
- IgG1b12: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. [Si2001]
- IgG1b12: Fab b12 was used – six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000]
- IgG1b12: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 CD4BS MAbs – CD4BS MAbs bound consistently to most isolates of clade D, but poorly to isolates of other clades with the exception of broadly reactive MAb IgG1b12, binding to 22 of 26 isolates tested – 8 MAbs were tested for neutralization and MAb IgG1b12 was most potent, with 90% neutralization of 3/5 isolates tested. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not enhance neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows increased infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000] (**escape**)
- IgG1b12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. [Grovit-Ferbas2000] (**vaccine antigen design**)
- IgG1b12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**vaccine antigen design**)
- IgG1b12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – at day 6 post infection, mice were given 50 mg/kg of b12, an amount that would have been protective if given up to 8 hours post-infection, and 100-fold higher than the amount required for 90% neutralization *in vitro* – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs. [Poignard1999] (**escape**, **immunotherapy**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: does not inhibit attachment of virus to cells and was used as a control of a study of neutralization by a MAb F58 based micro antibody. [Jackson1999]
- IgG1b12: A meeting summary presented results regarding neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo*. [Montefiori1999] (**review**)
- IgG1b12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – TCLA strains showed enhanced IgG1b12 neutralization sensitivity relative to PBMC-adapted lines – IgG1b12 was able to bind, with low affinity, to the rgp120 monomer HIV-1 W61D. [Beddows1999] (**co-receptor**)
- IgG1b12: The presence of leukocyte function-associated molecule 1 (LFA-1) promotes virus infectivity and hinders neutralization, and anti-LFA-1 MAbs can enhance the neutralizing effect of anti-HIV V3 MAb 447-52D and anti-HIV CD4BS MAb IgG1b12 – non-neutralizing anti-HIV CD4BS MAb 654-D did not become neutralizing in the presence of anti-LFA-1 MAbs. [Hioe1999] (**antibody interactions**)
- IgG1b12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. [Frankel1998] (**antibody interactions**, **mucosal immunity**)
- IgG1b12: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2, but not V1, diminished neutralization by CD4BS MAb IgG1b12, in contrast to 654.30D and IgGCD4. [Stamatatos1998] (**vaccine antigen design**)
- IgG1b12: anti-C1 region MAb 87-135/9 blocks gp120 interaction with CD4+ cells – blocking activity is additive when combined with antibodies which bind in the C4 region of gp120 (F105, 388/389, and b12) [Kropelin1998] (**antibody interactions**)
- IgG1b12: Fab b12 – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment b12 also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2. [Sullivan1998a]
- IgG1b12: MAbs 654-D100 and IgG1b12 neutralized viruses HIV-BRU and a mutated virus that lacks the V3 loop glycan equally effectively – in contrast, sera from guinea pigs immunized with BRU gp120 neutralize viruses more effectively that lack the V3 glycan. [Schonning1998] (**antibody binding site definition and exposure**)
- IgG1b12: Immunoprecipitation of gp120 and gp160 expressed from a rec Semliki Forest virus by F105 and IgG1b12 indicated that the SFV expressed HIV-1 Env was folded appropriately – and SVF-HIV-1 Env vaccine gave the strongest anti-HIV-1 Env response in mice, when compared to an HIV-1 Env DNA vaccine and a rgp160 protein. [Brand1998] (**vaccine antigen design**)
- IgG1b12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope. [Parren1998b] (**variant cross-recognition or cross-neutralization**, **responses in children**)
- IgG1b12: Induces Complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML. [Takefman1998] (**complement**)
- IgG1b12: Binds JRSF oligomer with high affinity, as do 205-46-9 and 2G6, but IgG1b12 is neutralizing, the other two are not – conclusions of this paper contrast with Parren98 – authors propose a model where 205-46-9 and 2G6 may inhibit CD4 binding, but cause a conformational shift which enhances CCR5 binding and thus counteracts the neutralizing effect – rank order of CD4BS antibodies oligomer binding is IgG1b12 = 2G6 = 205-46-9 > 205-43-1 = 205-42-15 > 15e = 21h = F91, and the only thing notably distinguishing about neutralizing IgG1b12 is that it depends on residues in V2. [Fouts1998] (**antibody binding site definition and exposure**)
- IgG1b12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4BS MAbs 15e, F91 and IgG1b12 bound better to the deleted protein than to wild type. [Binley1998] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. [Connor1998] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: IgG1b12, Fab b12 and 3B3 derived from b12 were all included in this study – the rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope – binding affinity of divalent IgG1b12 is 17-fold greater than monovalent Fab b12. [Parren1998a] (**binding affinity**)
- IgG1b12: Enhances binding of Hx10 to CD4 positive or negative HeLa cells, inhibits binding to CD4+ T-cell line A3.01 – neutralizes HeLa and A3.01 cell Hx10 infection. [Mondor1998]
- IgG1b12: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by CD4BS Ab is direct interference with CD4 binding – IgG1b12 is an unusual CD4BS antibody because it is particularly potent as a neutralizing antibody and it is susceptible to changes in the V1-V2 stem loop structure, and so it may disrupt an interaction between CD4 and conserved amino acids on the V1-V2 stem. [Wyatt1998a] (**structure**)
- IgG1b12: MAb was slightly more efficient at neutralization than Fab – inhibits viral binding to cells and viral entry – doesn't affect CD4-independent binding to T-cells. [Valenzuela1998]
- IgG1b12: Fab b12 is unusual in that it binds to gp140 and monomeric gp120 with similar affinities, and with a higher affinity to the native oligomer—authors propose this antibody may be exceptional because it binds the virus rather than viral debris—IgG1b12 can protect against infection prior to or shortly after challenge of hu-PBL-SCID mice with TCLA strains and primary strains, but the serum concentrations required *in vivo* were higher than for *in vitro* neutralization. [Parren1997c, Parren1997b] (**antibody binding site definition and exposure**, **immunoprophylaxis**)
- IgG1b12: Abs that recognize discontinuous epitopes can identify mimotopes from a phage peptide display library – IgG1b12 blocks CD4 binding and is the most potent neutralizing Ab – many 15 and 21-mer phage inserts were recognized, but it was not possible to derive a consensus – common features were a W and at least one acidic residue, and one sequence was found multiple times: NWPRWWEEFVDKHSS, and this peptide could compete with gp120 – two short stretches found in the phage peptides might mimic gp120 components of the epitope: positions 382-384, FFY(I), and 423-426 I(FV)I(V)NM. [Boots1997] (**mimotopes**)
- IgG1b12: In this review, the technique and potential application of Fab expression and selection in phage display libraries, and subsequent production of IgG molecules is discussed – b12 is exceptionally potent at neutralization and can successfully neutralize most B clade primary isolates, and many isolates from other subtypes as well – 3B3 was derived from b12 by selection for higher affinity using the CDR walking strategy – 3B3 has 8-fold enhancement of binding, a linear correlation was found between neutralization and affinity, and 3B3 can neutralize strains b12 cannot. [Parren1997a] (**binding affinity**, **review**)
- IgG1b12: This is a review that includes a description of IgG1b12, noting approximately equivalent affinities for sgp120 and unprocessed gp160, and somewhat enhanced affinity for the native oligomer on TCLA viruses – primary viruses have reduced affinity, but still in the useful range for neutralization – there can be complete protection in hu-PBL-SCID mice with Ab even when administered several hours after viral challenge – competes with sCD4, but unlike other CD4BS antibodies, it is sensitive to mutations in V2. [Burton1997] (**review**)
- IgG1b12: Major deletions in C1 and C5 and deletions of the V1V2 and V3 loops do not diminish binding. [Wyatt1997] (**antibody binding site definition and exposure**)
- IgG1b12: Viral binding inhibition by IgG1b12 strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- IgG1b12: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes. [Moore1997] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: 35 primary isolates were tested and all were neutralized by IgG1b12 (including 4, UG270, RW92/026, ZB20, and 301727 which been had reported as not neutralized by IgG1b12 [Trkola1995]) – IgG1b12 could neutralize even when added after the virus to the culture – selection for 400-fold increased affinity did not enhance neutralization by antibody – IgG1b12 was more potent with greater breadth than MAb 2F5 [Kessler II1997]. [Kessler II1997, Trkola1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- IgG1b12: b12 was used in its IgG1 form – of 14 human MAbs, the most potent neutralizer of SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – b12 has a synergistic response with MAbs 694/98-D (anti-V3), 2F5, and 2G12. [Li1997] (**antibody interactions**)
- IgG1b12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – IgG1b12 bound monomer, oligomer, and neutralized JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- IgG1b12: JRCSF was cultured in the presence of IgG1b12 until a 100-fold resistance to neutralization was selected – resistance was due to three changes: V2 substitution D182N and C3 substitution P365L conferred resistance, and V2 D164N was also required for a viable virus – IgG1b12 resistant virus remained sensitive to MAbs 2G12 and 2F5. [Mo1997] (**escape**)
- IgG1b12: Inhibited some SI- and NSI-env chimeric viruses but enhanced one NSI-env chimeric virus 3 fold. [Schutten1997] (**enhancing activity**, **variant cross-recognition or cross-neutralization**)
- IgG1b12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – IgG1b12 failed to neutralize only 1/9 primary isolates, although there was some variation between test sites. [D'Souza1997] (**variant cross-recognition or cross-neutralization**, **assay standardization**)
- IgG1b12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. [Sattentau1996] (**review**)
- IgG1b12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**antibody binding site definition and exposure**)
- IgG1b12: Anti-CD4BS MAbs 15e, 21h, and IgG1b12 did not cause gp120 dissociation from virus, or exposure of the gp41 epitope of MAb 50-69, in contrast to CD4i MAb 48d and anti-V3 neutralizing MAbs. [Poignard1996a] (**antibody interactions**)
- IgG1b12: Review: Unique among anti-CD4BS MAbs in terms of being potent against both lab adapted virus and primary isolates – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates. [Poignard1996b] (**review**)
- IgG1b12: Potent neutralizing *ex vivo* of virus taken directly from plasma of HIV-1 infected individuals – little correlation between neutralization sensitivity of passaged virus and plasma derived virus – more effective than MAb 19b. [Gauduin1996] (**antibody interactions**)
- IgG1b12: Saturation mutagenesis of the complementarity-determining region and optimization strategies were used to create very high affinity versions of this Fab – increased affinity was dominated by a slowing of the off rate. [Yang1997c] (**binding affinity**)
- IgG1b12: Fab b12 showed potent neutralization of T-cell-line-adapted strains, but much reduced neutralization of 3 primary isolates – 2 of the 3 primary isolates also had reduced binding affinity, but the third was as efficiently immunoprecipitated as HXBc2. [Sullivan1995] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Because Fab b12 shows reduction in binding when the V2 loop is deleted and when aa 183/184 PI/SG substitutions are made competition studies were done with Fab L78 and anti-V2 MAbs SC258 and 684-238 and they do not compete with IgG1b12. [Ditzel1995] (**antibody interactions**)
- IgG1b12: Could potently neutralize primary isolates from within clade B, but showed a slight reduction in efficacy outside of clade B. [Trkola1995] (**inter-clade comparisons**)
- IgG1b12: Review: unusual properties for anti-CD4 BS MAb: sensitive to V2 substitutions, preferential recognition of the oligomer on the cell surface. [Moore1995b] (**review**)
- IgG1b12: Called BM12 – broad cross-clade neutralization of primary isolates – additive neutralization in combination with MAb 2F5. [Kessler1995] (**antibody interactions**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- IgG1b12: Complete protection against HIV-1 infection was achieved in hu-PBL-SCID mice by passive immunization with physiologically relevant doses – pharmacokinetics showed serum half-life of 30.2 +/- 1.3 hours for Fab b12 and 7.4 +/- 0.7 days for IgG1 b12 in mice, but IgG1 half-lives in human are generally between 21-23 days. [Parren1995, Parren1997a] (**immunoprophylaxis**, **kinetics**)
- IgG1b12: Anti-CD4 binding site MAb – very potent neutralization of a number of primary isolates. [Moore1995a] (**variant cross-recognition or cross-neutralization**)
- IgG1b12: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. [Sattentau1995c] (**vaccine antigen design**)
- IgG1b12: Cross-reactive with some gp120s, (but not all), from clades A-D – not reactive with gp120 from clades E or F. [Moore1994b] (**inter-clade comparisons**)
- IgG1b12: Very potent neutralization, of primary and lab strains, at concentrations that could be achieved by passive immunization – reduced binding with A,C, and D clade viruses relative to B clade, poor reactivity with E clade – isolates that were refractive to neutralization by sera from HIV-1+ donors could be neutralized by IgG1 b12. [Burton1994] (**inter-clade comparisons**)
- IgG1b12: Anti-CD4 binding site Fab, potent neutralizing activity, greater affinity for a subpopulation of gp120 molecules suggested to be in a mature confirmation – mutations in gp120 that abrogate binding: 368 D/R or D/T, 370 E/R, and 477 D/V, of clone HXBc2 of LAI – sensitive to V1 and V2 substitutions. [Roben1994] (**antibody binding site definition and exposure**)
- IgG1b12: The original Fab fragment was derived from a combinatorial phage library from bone marrow of an HIV-1 positive individual who had been asymptomatic for six years. [Burton1991] (**antibody generation**)
- IgG1b12: Fab b12 was derived from IgG1b12, Fab 3B3 was derived from Fab b12 by random mutagenesis and selected for increased affinity to sgp120 – database note. (**antibody generation**)

1015	IgGCD4 (IgG-CD4)	Env	gp120				human (IgG)

Ab type CD4BS

References Srivastava2002, Ly2000, Stamatatos1998, Capon1989

- IgGCD4: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – Abs directed against the CD4 binding site (IgGCD4 and IgG1b12) reacted slightly more strongly with the gp120 monomer than with the oligomer, as did sCD4. [Srivastava2002]
- IgGCD4: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000]
- IgGCD4: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 slightly enhanced neutralization by CD4BS MAb IgGCD4. [Stamatatos1998]
- IgGCD4: An antibody-like immunoadhesins molecule was constructed incorporating the gp120-binding domain of CD4. [Capon1989]

1016	L28	Env	gp120		L	HIV-1 infection	human (IgG1κ)

Ab type CD4BS

References Gorny2004, Ditzel1995

Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review.

- L28: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L28: Substitutions at 257 T/R, 368 D/R, 370 E/R and 370 E/Q, 475 M/S 102 E/L and 463 N/D reduce binding – binding was enhanced by removal of the V3 loop and by substitutions 45 W/S, 298 R/G, 381 E/P, 382 F/L, 420 I/R, 435 Y/H or Y/R – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. [Ditzel1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1017	L33	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Gorny2004, Zwick2003, Ditzel1995 **Keywords** antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, review. • L33: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**) • L33: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**) • L33: binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. [Ditzel1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1018	L41	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Gorny2004, Ditzel1995 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, review. • L41: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**) • L41: Substitutions at 133 D/R, 256 S/Y, 257 T/R, 368 D/R or D/T, 370 E/Q or E/R, 384 Y/E, and 421 K/L reduce binding – paradoxically, this Fab was retrieved from the library after masking with known anti-CD4BS MAbs – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. [Ditzel1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1019	L42	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Gorny2004, Ditzel1995 **Keywords** antibody binding site definition and exposure, review. • L42: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**) • L42: Substitutions at 257 T/R, 368 D/R, 370 E/R, 266 A/E and 477 D/V reduce binding – binding was significantly enhanced by 381 E/P and 382 F/L – binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. [Ditzel1995] (**antibody binding site definition and exposure**)					
1020	L52	Env	gp120		L	HIV-1 infection	human (IgG1κ)
		Ab type CD4BS **References** Gorny2004, Ditzel1995 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, review. • L52: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L52: Binding is sensitive to deglycosylation – heavy and light chain variable region sequence is available. [Ditzel1995] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1021	L72	Env	gp120				mouse
		Ab type CD4BS **Research Contact** Dr. Hariharam, IDEC Pharmaceuticals Corp La Jolla, CA **References** Ditzel1997 • L72: Used to bind gp120 to solid phase to select MAbs from a phage selection library. [Ditzel1997]					
1022	M12	Env	gp120 (IIIB)		L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • M12: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M12 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4-3 was achieved with 21 ug/ml of M12. [Sugiura1999] • M12: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] • M12: There is a p15 gag specific MAb also named M12.					
1023	M13	Env	gp120 (IIIB)		L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • M13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M13 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – 50% neutralization of NL4-3 was achieved with 35 ug/ml of M13. [Sugiura1999] • M13: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1024	M6	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • M6: A comparison of 25 gp120 specific, conformation dependent MAbs was done – M6 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4. [Sugiura1999] • M6: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1025	MAG 116	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 116: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L – neutralizes MN, IIIB and RF. [Kang1994]					
1026	MAG 12B	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 12B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 477 D/V – weak neutralization of IIIB. [Kang1994]					
1027	MAG 29B	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 29B: Amino acid substitutions that reduce binding 10 fold: 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 386 N/Q, 421 K/L – weak neutralization of IIIB. [Kang1994]					
1028	MAG 3B	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 3B: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 381 E/P, 384 Y/E, 421 K/L, 475 M/S, 477 D/V. [Kang1994]					
1029	MAG 55 (#55)	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Moore1996, Kang1994 • MAG 55: Called #55 – binding reciprocally inhibited by other anti-CD4 binding site MAbs, and by some C1-C5 MAbs – binding enhanced by anti-V3 MAb 110.5 and anti-V2 MAbs G3-136 and G3-4 – enhances binding of many anti-V3 and -V2 MAbs. [Moore1996] • MAG 55: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 475 M/S, 477 D/V – neutralizes MN, IIIB and RF. [Kang1994]					
1030	MAG 72 (L72)	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** CD4BS **Research Contact** C. Y. Kang or Dr. Hariharam, IDEC Pharmaceuticals Corp, La Jolla, CA **References** Ditzel1997, Kang1994 • MAG 72: Called L72 – used to bind gp120 to solid phase to select MAbs from a phage selection library. [Ditzel1997] • MAG 72: Amino acid substitutions that reduce binding 10 fold: 257 T/R or A or G, 262 N/T, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 477 D/V – neutralizes MN, IIIB and RF. [Kang1994]					
1031	MAG 86	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 86: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R or Q, 384 Y/E, 421 K/L, 470 P/L, 477 D/V – neutralizes MN, IIIB and RF. [Kang1994]					
1032	MAG 96	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type CD4BS **Research Contact** C. Y. Kang, IDEC Inc **References** Kang1994 • MAG 96: Amino acid substitutions that reduce binding 10 fold: 256 S/Y, 257 T/R, 368 D/R or T, 370 E/R – weak neutralization of IIIB. [Kang1994]					
1033	MTW61D	Env	gp120 (W61D)		L	HIV-1 infection	human
		Ab type CD4BS **References** Gorny2004, Fouts1998, Sullivan1998a **Keywords** enhancing activity, review. • MTW61D: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**) • MTW61D – the HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – Fab fragment MTW61D also enhances YU2 entry, ruling out Fc interactions or Env cross-linking as a mechanism, while neutralizing HXBc2 – MTW61D was obtained by panning libraries derived from bone marrow from a long term asymptomatic donor against gp120 from primary isolate W61D. [Sullivan1998a] (**enhancing activity**)				
1034	S1-1	Env	gp120		L	HIV-1 infection	human (IgG1λ)
		Ab type CD4BS **References** Gorny2004, Wisnewski1996, Moran1993, Lake1992 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, complement, enhancing activity, review. • S1-1: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • S1-1: S1-1 is V H1 – V-region heavy chain usage was examined and a bias of enhanced V H1 and V H4, and reduced V H3, was noted among HIV infected individuals. [Wisnewski1996] (**antibody sequence, variable domain**) • S1-1: Heavy (V HI) and light (V lambdaIII) chain sequenced – no enhancing activity – similar germline sequence to MAb 86, but very different activity. [Moran1993] (**enhancing activity**, **antibody sequence, variable domain**) • S1-1: Neutralizes IIIB and MN without complement, and neutralizes RF and a clinical isolate with complement – binds to native but not denatured gp120 – inhibits sCD4-gp120 binding. [Lake1992] (**antibody binding site definition and exposure**, **complement**)				
1035	T13	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • T13: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T13 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T13 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold. [Sugiura1999] • T13: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]				
1036	T49	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • T49: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T49 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T49 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold. [Sugiura1999]				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• T49: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1037	T56	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** CD4BS **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • T56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T56 is one of three MAbs labeled group Cb, that was type-specific for BH8 – T56 fully blocked CD4 binding, and the deletion of the V3 loop enhanced binding 10-fold. [Sugiura1999] • T56: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1038	TH9	Env	gp120		L		human (IgG1κ)
		Ab type CD4BS **Research Contact** Michael Fung, Tanox Biosystem, USA **References** Gorny2004, Yang1998, D'Souza1995 **Keywords** assay development, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • TH9: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this MAb, neutralize TCLA strains only. [Gorny2004] (**review**) • TH9: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998] (**assay development**) • TH9: Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. [D'Souza1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					
1039	anti-CD4BS summary	Env	gp120				
		Ab type CD4BS **References** Moore1996, Thali1993 • Anti-CD4 binding site antibodies (CD4BS) competitively inhibit CD4 binding to monomeric gp120, and they differ in precise dependence on gp120 residues, but generally require Asp-368 and Glu-370. [Moore1996] • Shared components of MAb epitopes and the discontinuous CD4 binding regions included Thr 257, Asp 368, Glu 370, Lys 421 through Trp 427 and Asp 457. [Thali1993]					
1040	b11	Env	gp120				human
		Ab type CD4BS **References** Gorny2004, Parren1998a **Keywords** binding affinity, review. • b11: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**) • b11: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**binding affinity**)					
1041	b13	Env	gp120				human
		Ab type CD4BS **References** Gorny2004, Parren1997a, Parren1998a, Parren1995					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

Keywords binding affinity, immunoprophylaxis, review.

- b13: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**)
- b13: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**binding affinity**)
- b13: Fab b13 was used as a control in a hu-PBL SCID mouse study – animals were protected from HIV-1 SF2 infection by IgG1b12, somewhat by Fab b12, but not by b13. [Parren1995, Parren1997a] (**immunoprophylaxis**)

1042 b14 Env gp120 human

Ab type CD4BS

References Gorny2004, Parren1998a

Keywords binding affinity, review.

- b14: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**)
- b14: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**binding affinity**)

1043 b3 Env gp120 human

Ab type CD4BS

References Gorny2004, Pantophlet2003b, Zwick2003, Pantophlet2003a, Parren1998a, Parren1997c

Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- b3: This review summarizes MAbs directed and HIV-1 Env. There are 51 CD4BS MAbs and Fabs in the database; most, like this Fab, neutralize TCLA strains only. [Gorny2004] (**review**)
- b3: A gp120 molecule was design to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- b3: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)
- b3: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never in enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded. [Pantophlet2003a] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- b3: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**binding affinity**)
- b3: Neutralizes TCLA strains, but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)

1044 b6 Env gp120 L human

Ab type CD4BS **Research Contact** Dennis Burton, Scripps, San Diego, CA, USA

References Pantophlet2003b, Zwick2003, Pantophlet2003a, Poignard2003, Kwong2002, Parren1998a, Parren1997c

Keywords antibody binding site definition and exposure, antibody interactions, vaccine antigen design.

- b6: A gp120 molecule was design to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- b6: scFv 4KG5 reacts with a conformational epitope which is formed by the V1V2 and V3 loops and the bridging sheet (C4) region of gp120 and is influenced by carbohydrates. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120 JR-FL. MAbs to the following regions diminished 4KG5 binding: V2 loop, V3 loop, V3-C4 region, CD4BS. MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected by these loops. This was one of the CD4BS MAbs used. [Zwick2003] (**antibody interactions**)
- b6: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- b6: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 binding to those that affect binding of sCD4 and two non-neutralizing anti-CD4BS Abs b3 and b6 – while the epitope maps overlapped, there were some differences observed – binding of CD4 was never in enhanced, indicating it had evolved to be optimal – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded. [Pantophlet2003a]
- b6: Virion capture assays are not a good preditor of neutralization, and the presentation of epitopes using this assay seems to be different from that of functional Envelope spikes on primary isolates – F105 and b6 could efficiently block the b12-mediated capture of infectious virions in a virus capture, but did not inhibit b12 neutralization – while b12 was potent at neutralizing the three primary virions JR-CSF, ADA, and 89.6, the Abs F105, 19b, and Fab b6 were overall very poor neutralizers. [Poignard2003]
- b6: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- b6: Neutralizes TCLA strains, but not primary isolates. [Parren1997c]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1045	polyclonal	Env	gp120		no	Vaccine	mouse

Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* CD4BS, Gag, V3
Ab type CD4BS
References Truong1996

- Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly. [Truong1996]

1046	D33	Env	gp120 (IIIB)			Vaccine	mouse (IgG)

Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140
Ab type CD4BS, C-term, N-term **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD
References Sugiura1999, Earl1994

- D33: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D33 is part of a group of MAbs labeled A1 – all A1 MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, blocked CD4 binding, were sensitive to mutations in gp120 positions 368 and 370 that directly contact CD4 – D33 was unusual for the group of A1 MAbs, because while it blocked CD4 binding completely, but competed with MAbs that did not in a BIAcore assay – both the N- and C-terminal ends of gp120 are involved in D33 binding. [Sugiura1999]
- D33: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]

1047		Env	gp120		yes		human

Ab type CD4BS, CD4i, V2, V3
References Moore2001

- Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – they suggest the primary goal in vaccine efforts should be to design an immunogen that can be shown to elicit neutralizing antibodies against a significant proportion of primary isolates – assay artifacts that can result in confused interpretations are also discussed, such as Ab binding to defective spikes, which does not affect HIV-1 infectivity, but can dominant an assay signal. [Moore2001]

1048	17b (1.7b, sCD4-17b)	Env	gp120		L P (wea	HIV-1 infection	human

Ab type CD4i **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA
References Gorny2004, Pantophlet2003b, Zwick2003, Zhu2003, Ohagen2003, Xiang2003, Labrijn2003, Dey2003, Cavacini2003, Binley2003, Finnegan2002, Cavacini2002, Arthos2002, Zhang2002, Basmaciogullari2002, Grundner2002, Edwards2002, Xiang2002a, Xiang2002b, Dowd2002, Yang2002, Schulke2002, Golding2002b, Srivastava2002, Kwong2002, Poignard2001, Zhang2001a, York2001, Kolchinsky2001, Si2001, Rizzuto2000, Yang2000, Stamatatos2000, Salzwedel2000, Park2000, Ly2000, Grovit-Ferbas2000, Binley1999, Hoffman1999, Oscherwitz1999a, Stamatatos1998, Binley1998, Sullivan1998a, Sullivan1998b, Rizzuto1998, Moore1998, Wyatt1998a, Kwong1998, Parren1997c, Wyatt1997, Cao1997b, Ditzel1997, Weinberg1997, Li1997, Fouts1997, Binley1997a, Trkola1996a, Wu1996, Poignard1996a, Moore1996, Sattentau1995b, Wyatt1995, Beretta1994, Thali1994, Moore1993d, Thali1993
Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, brain/CSF, co-receptor, immunoprophylaxis, immunotherapy, inter-clade comparisons, kinetics, review, structure, vaccine antigen design, vaccine-specific epitope characteristics, variant cross-recognition or cross-neutralization.

- 17b: This review summarizes MAbs directed and HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. [Gorny2004] (**antibody binding site definition and exposure**, **review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 17b: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 17b: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a CD4i MAb that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- 17b: The HIV-1 primary isolate DH012 has preserved the epitopes for the MAbs IgG1b12, 2G12, 17b, however natural DH012 infection in chimpanzees and DH012 gp120 vaccination in guinea pigs does not give rise to Abs against these epitopes. [Zhu2003] (**vaccine-specific epitope characteristics**)
- 17b: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. 17b recognized most variants,some from each of the four individuals, by gp120 immunoprecipitation. [Ohagen2003] (**brain/CSF**, **variant cross-recognition or cross-neutralization**)
- 17b: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- 17b: This paper describes the generation of CD4i MAb E51, that like CD4i MAb 17b, blocks CCR5 binding to sCD4-bound gp120. E51 has more cross-neutralizing potency than other prototype CD4i MAbs (17b) for B and C clade isolates. E51 and 17b both neutralized HIV-1 clade B strains HXBc2 and ADA, while JR-FL and 89.6 were only neutralized by E51, not 17b. Clade C strains MCGP1.3 and SA32 were both inhibited by 17b and E51, but E51 was more potent against SA32. The substitutions E381R, F383S, R419D I420R, K421D, Q422L, I423S, and Y435S (HXB2 numbering) all severely reduce 17b and E51 binding. All but I423S also diminish CCR5 binding by more than 50%. The mutation F383S also inhibits sCD4 binding and F105 binding, and K421D inhibits F105 binding, but not sCD4. [Xiang2003] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 17b: This study shows the fragments of CD4i MAbs are better able to neutralize virus than whole IgG. Neutralization of HIV-1 R5 isolates JRFL, JR-CSF and ADA by CD4i MAbs X5, 17b, and 48d decreased with increased molecule size, the neutralizing potency of single-chain Fv (scFv) > than Fab fragments > whole Ab molecules. (With the exception of IgG 48d neutralization of HIV-1 ADA.) HIV-1 X4 isolates 89.6 and HxB2 are both relatively sensitive even to the larger IgG version. R5X4 isolate neutralization was dependent on the isolate and co-receptor usage. The CD4i MAb fragments neutralize HIV-1 subsequent to CD4 binding. The CD4i MAbs bind near the co-receptor binding sites on gp120. Co-receptors bind to the conserved beta19 strand and part of the V3 loop, regions which are masked by the V1V2 loops in the CD4-unbound state. When CD4 is bound, the co-receptor site is exposed near the membrane surface where it would be optimally accessible to co-receptors, and the smaller versions of the molecules are better able to overcome the steric hindrence. [Labrijn2003] (**antibody binding site definition and exposure**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- 17b: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. 17b was used to demonstrate that the Cluster I and II MAbs bound to gp120/gp41 complexes, not to gp41 after shedding of gp120. [Finnegan2002]

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- 17b: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. It neutralized 5/6 R5 and X4 strains from the B clade, but was only moderately protective against a D clade isolate, and did not neutralize clade A, C, E, and F isolates. [Dey2003] (**co-receptor**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **immunotherapy**, **inter-clade comparisons**)
- 17b: Called 1.7b. The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to R5X4 virus 92HT593, but only of 48d to the R5 virus 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. [Cavacini2003] (**antibody interactions**, **co-receptor**)
- 17b: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-V3 MAb B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, but only A1g8 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. Anti-gp41 MAb F240 had a synergistic effect on neutralization with CD4i MAbs 48d and 17b, but not with A1g8 for the R5X4 virus. [Cavacini2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- 17b: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. CD4i Abs 17b and X5 were weakly neutralizing in all formats, WT, SOS, and when added postbinding. [Binley2003] (**vaccine antigen design**)
- 17b: NIH AIDS Research and Reference Reagent Program: 4091.
- 17b: The two N-terminal domains of CD4, termed D1 and D2, when expressed in the absence of the remaining domains of CD4 retain the capacity to bind to gp120—coding sequences of D1D2 and Igαtp were fused to create a large, multivalent rec protein D1D2Igαtp, which, unlike CD4, does not enhance infection at sub-optimal concentrations—the MAb 17b can also enhance viral replication at sub-optimal concentrations, but D1D2-Igα inhibited the 17b enhancement of two primary isolates. [Arthos2002] (**variant cross-recognition or cross-neutralization**)
- 17b: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002]
- 17b: gp120 mutants were used to define the CXCR4 binding site using CXCR4 displayed on paramagnetic proteoliposomes (PMPLs) to reduce non-specific gp120 binding—basic residues in the V3 loop and the β19 strand (RIKQ, positions 419-422) were involved, and deletion of the V1-V2 loops allowed CD4-independent CXCR4 binding—MAbs 17b (CD4i) and F105 (CD4BS) were used to study conformational changes in the mutants—the affinity of ΔV1 and ΔV1-V2 for 17b was dramatically increased and no longer inducible in the presence of sCD4—V3 mutants R298A and R327A were not recognized by 17b except in the presence of sCD4—mutations in the β19 strand dramatically reduced 17b affinity in the presence or absence of sCD4, consistent with known 17b contact residues in this region. [Basmaciogullari2002]
- 17b: HIV-1 gp160ΔCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines—2F5 bound to gp160ΔCT with a reconstituted membrane ten-fold better than the same protein on beads—anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160ΔCT PLs indistinguishably from gp160ΔCT expressed on the cell surface—non-neutralizing MAbs C11 and A32 bound with lower affinity than NAb IgG1b12—the MAb 17b was sCD4 inducible on gp160ΔCT PL. [Grundner2002] (**vaccine antigen design**)

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- 17b: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] (**vaccine-specific epitope characteristics**)
- 17b: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. [Xiang2002a] (**antibody binding site definition and exposure**)
- 17b: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**variant cross-recognition or cross-neutralization**)
- 17b: CD4 residue Phe43 significantly contributes to the affinity of CD4-gp120 interactions – despite decreased affinities for gp120, CD4 proteins and CD4-mimetic peptides lacking a Phe side-chain enhance binding of gp120 to 17b in a manner similar to Phe-bearing ligands indicating the Phe42 interaction is not critical for CD4-induced conformational changes in gp120. [Dowd2002]
- 17b: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin—stabilized oligomer gp140Δ683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002]
- 17b: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140. [Schulke2002] (**vaccine antigen design**)
- 17b: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. [Golding2002b]
- 17b: Oligomeric gp140 (o-gp140) derived from R5 primary isolate US4 was characterized for use as a vaccine reagent – antigen capture ELISA was used to compare the antigenicity of gp120 and o-gp140 using a panel of well characterized MAbs – 17b recognized both gp120 monomer and o-gp140. [Srivastava2002]
- 17b: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – the 17b epitope is masked prior to CD4 binding by the V1-V2 loop and in contrast to sCD4, the binding of cell surface CD4 to virus does not appear to make the epitope accessible to binding by 17b to allow neutralization. [Poignard2001] (**antibody binding site definition and exposure**, **review**)

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- 17b: 17b binds to a CD4 inducible epitope which partially overlaps the CCR5 binding site – JRFL, YU2, 89.6, and HXB2 and their C1-, V1/V2-, C5 -deletion mutants were used to study how 17b binding affects gp120-CD4 interactions – 17b reduced CD4-gp120 interactions by decreasing the on-rate and increasing the off-rate of sCD4, while enhanced binding of sCD4 binding was observed for the 17b-bound, V1/V2 deleted gp120s – 17b was considered to be a surrogate for CCR5, and the authors suggest that 17b binding may shift V1/V2 into a position that interferes with CD4 binding, forcing a release. [Zhang2001a] (**antibody binding site definition and exposure**, **kinetics**)
- 17b: Abs against the V3 loop (50.1, 58.2, 59.1, 257-D, 268-D, 447-52D), CD4BS (IgG1b12, 559-64D, F105), CD4i (17b), and to gp41 (2F5, F240) each showed similar binding efficiency to Env derived from related pairs of primary and TCLA lines (primary: 168P and 320SI, and TCLA: 168C and 320SI-C3.3), but the TCLA lines were much more susceptible to neutralization suggesting that the change in TCLA lines that make them more susceptible to NAbs alters some step after binding – 17b bound at somewhat greater levels to 168C than to 168P, but this is not a general feature of 17b binding to primary versus TCLA strains. [York2001] (**variant cross-recognition or cross-neutralization**)
- 17b: Mutations in two glycosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone—these same mutations tended to increase the neutralization sensitivity of the virus, including to 17b—only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type. [Kolchinsky2001] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. [Si2001] (**variant cross-recognition or cross-neutralization**)
- 17b: Mutagenesis defines Ile-420, Lys-421, Gln-422, Pro-438, and Gly-441 to be important residues for CCR5 binding – these positions are located on two strands that connect the gp120 bridging sheet and outer domain, suggesting a mechanism for conformational shifts induced by CD4 binding to facilitate CCR5 binding. [Rizzuto2000] (**antibody binding site definition and exposure**)
- 17b: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000] (**vaccine antigen design**)
- 17b: Soluble gp140 derived from SF162, a neutralization-resistant primary isolate, and SF162AV2 a neutralization-susceptible isolate with 30 amino acids deleted from the V2 loop, were generated with or without the gp120-gp41 cleavage site intact – all forms are recognized by oligomer-specific MAb T4 and show enhanced binding of CD4i MAb 17b when sCD4 is bound – the fused forms are less efficiently recognized than the cleaved forms by polyclonal neutralizing sera from HIV-infected patients – the V3 loop is more exposed on the fused form. [Stamatatos2000] (**vaccine antigen design**)
- 17b: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion – 17b was broadly cross-reactive inhibiting sCD4 activated fusion with Env from clades A, B, C, D, E, F, and F/B. [Salzwedel2000] (**inter-clade comparisons**)
- 17b: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000] (**antibody binding site definition and exposure**)
- 17b: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000] (**variant cross-recognition or cross-neutralization**)

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- 17b: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. [Grovit-Ferbas2000] (**vaccine antigen design**)
- 17b: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**vaccine antigen design**)
- 17b: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera – the 17b epitope has significant overlap with the CCR5 coreceptor binding site. [Hoffman1999] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 17b: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d. [Stamatatos1998] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 17b: A panel of MAbs was shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type. [Binley1998] (**antibody binding site definition and exposure**)
- 17b: The HIV-1 virus YU2 entry can be enhanced by MAbs binding to the CD4BS, V3 loop, and CD4i epitopes – the activation for this enhanced entry state could be conferred on HxB2 by introducing the YU2 V3 loop, or the YU2 V3 and V1/V2 loops, and the presence of V1/V2 increased the enhancement – a similar effect is observed by sub-neutralizing concentrations of sCD4 and the effect is dependent of CCR5 – 17b enhances YU2 enhanced viral entry 10-fold, whereas HXBc2 was neutralized. [Sullivan1998a]
- 17b: sCD4 induces 17b binding in primary isolates and TCLA strains – amino acids that reduce the efficiency of binding were determined and found also to compromise syncytia formation and viral entry – V1V2 deletion or sCD4 binding can expose the 17b epitope for both HXBc2 and macrophage tropic YU2 – neutralizing potency of 17b is probably weak due to poor exposure of the epitope – 17b epitope exposure upon sCD4 binding can occur over a wide range of temperatures, consistent with the energy of CD4 binding being sufficient to drive the V1/V2 loop into a new conformation. [Sullivan1998b] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 17b: Site directed mutagenesis of a WU2 protein with the V1-V2 loops deleted revealed key residues for 17b-gp120 interaction and interaction of gp120 and CCR5 – mutations in residues that reduced 17b by 70% were R/D 419, I/R 420, Q/L 422, Y/S 435, I/S 423, K/D 121 and K/D 421– 17b can neutralize HIV-1 strains that use different chemokine receptors, supporting a common region in gp120 in chemokine-receptor interaction. [Rizzuto1998] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**)
- 17b: Moore and Binley provide a commentary on the papers by [Rizzuto1998], [Wyatt1998a] and [Kwong1998] – they point out 17b shares binding elements in gp120 with chemokine receptor molecules, and that CD4 needs to bind to gp120 first to make the 17b epitope accessible and it may be sterically blocked in the CD4 bound virus, thus making it a poor NAb for primary isolates [Moore1998]. [Kwong1998, Moore1998, Rizzuto1998, Wyatt1998a] (**review**, **structure**)

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- 17b: Summary of the implications of the crystal structure of a gp120 core bound to CD4 and 17b, combined with what is known about mutations that reduce NAb binding to gp120 – probable mechanism of neutralization is interference with chemokine receptor binding – mutations in 88N, 117K, 121K, 256S, 257T, N262, Delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 of HXBc2 (IIIB) reduce binding – the only variable residues in gp120 that contact 17b are 202T and 434M – the contact points for 17b with the crystallized incomplete gp120 are mostly in the heavy chain of the Ab, and there is a gap between 17b's light chain and the partial gp120 which may be occupied by the V3 loop in a complete gp120 molecule – the authors propose that the V2 and V3 loops may mask the CD4i Ab binding site, and that the V2 loop may be repositioned upon CD4 binding. [Wyatt1998a] (**structure**)
- 17b: 17b Fab was co-crystallized with a gp120 core and CD4, and it's binding site can be directly visualized—17b binds to the "bridging sheet" of gp120, an antiparallel beta sheet region, contacting residues from the C4 region and the V1/V2 stem—the contact area is small for an Ab-antigen interactive surface, and dominated in the Ab by the heavy chain—the center of the binding region has hydrophobic interactions, and the periphery charge interactions, acidic on 17b and basic on gp120. [Kwong1998] (**structure**)
- 17b: Neutralizes TCLA strains, but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- 17b: Binds to sgp120 efficiently, but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding – partial re-exposure if sCD4 was bound – could not bind to HXBc2 gp120 if the 19 C-term amino acids were deleted in conjunction with amino acids 31-93 in C1, but binding was restored in the presence of sCD4. [Wyatt1997] (**antibody binding site definition and exposure**)
- 17b: Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to a CD4BS MAb, F105, or sCD4. [Cao1997b] (**vaccine antigen design**)
- 17b: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d – it does not bind to 17b, distinguishing the epitopes. [Weinberg1997]
- 17b: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – 17b has synergistic response in combination with anti-V3 MAb 694/98-D. [Li1997]
- 17b: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 17b bound monomer, oligomer, and neutralized JRFL in the presence of sCD4, but if sCD4 was not present, 17b only bound monomer. [Fouts1997]
- 17b: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a]
- 17b: MIP-1α binding to CCR-5 expressing cells can be inhibited by gp120-sCD4 — binding of 17b blocks this inhibition. [Wu1996]
- 17b: Binding did not result in significant gp120 dissociation from virion, in contrast to 48d, although the gp41 epitope of MAb 50-69 was exposed. [Poignard1996a] (**antibody interactions**)
- 17b: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-V3 MAb 5G11 enhances binding, as do C1-C4 discontinuous epitopes A32 and 2/11c – enhances binding of some anti-V2 MAbs. [Moore1996] (**antibody interactions**)
- 17b: Binds with higher affinity to monomer and oligomer, slow association rate, poor neutralization of lab strain – this is in contrast to 48d, which has very different kinetics. [Sattentau1995b] (**kinetics**, **binding affinity**)
- 17b: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 17b in the presence sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 48d and A32. [Wyatt1995] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 17b: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 48d, 21h and 15e) [Thali1994] (**variant cross-recognition or cross-neutralization**)
- 17b: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b. [Moore1993d] (**variant cross-recognition or cross-neutralization**)
- 17b: Epitope is better exposed upon CD4 binding to gp120 – competes with 15e and 21h, anti-CD4 binding site MAbs – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization. [Thali1993] (**antibody binding site definition and exposure**, **antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 17b: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs. (**antibody binding site definition and exposure**)					
1049	21c	Env	gp120 (IIIB, J62)		L	HIV-1 infection	human (IgG)
		Ab type CD4i **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA **References** Gorny2004, Xiang2002b, Xiang2002a **Keywords** antibody binding site definition and exposure, antibody generation, review, vaccine antigen design. • 21c: This review summarizes MAbs directed and HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. [Gorny2004] (**review**) • 21c: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**, **vaccine antigen design**) • 21c: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. [Xiang2002a] (**antibody binding site definition and exposure**, **antibody generation**)					
1050	23e	Env	gp120 (IIIB, J62)		L	HIV-1 infection	human (IgG)
		Ab type CD4i **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA **References** Gorny2004, Xiang2002b, Xiang2002a **Keywords** antibody binding site definition and exposure, antibody generation, review, vaccine antigen design. • 23e: This review summarizes MAbs directed and HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. [Gorny2004] (**review**) • 23e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**, **vaccine antigen design**) • 23e: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. [Xiang2002a] (**antibody binding site definition and exposure**, **antibody generation**)					
1051	48d (4.8d, 4.8D)	Env	gp120		L P (wea	HIV-1 infection	human (IgG1κ)
		Ab type CD4i **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Gorny2004, Pantophlet2003b, Zwick2003, Labrijn2003, Cavacini2003, Cavacini2002, Zhang2002, Edwards2002, Xiang2002a, Xiang2002b, Yang2002, Golding2002b, Kwong2002, Verrier2001, Kolchinsky2001, Salzwedel2000, Yang2000, Park2000, Ly2000, Fortin2000, Hoffman1999, Oscherwitz1999a, Stamatatos1998, Binley1998, Yang1998, Sullivan1998b, Parren1998a, Mondor1998, Wyatt1998a, Frankel1998, Parren1997c, Wyatt1997, Ugolini1997, Lee1997, Weinberg1997, Li1997, Binley1997a, Trkola1996a, Poignard1996a, Moore1996, Sattentau1995b, Sattentau1995c, Wyatt1995, Sattentau1995a, D'Souza1995, Moore1994b, Thali1994, Moore1993d, Moore1993a, Thali1993

Keywords antibody binding site definition and exposure, antibody interactions, binding affinity, co-receptor, inter-clade comparisons, kinetics, review, structure, vaccine antigen design, variant cross-recognition or cross-neutralization.

- 48d: This review summarizes MAbs directed and HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. [Gorny2004] (**review**)
- 48d: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 48d: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a CD4i MAb that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- 48d: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- 48d: This study shows the fragments of CD4i MAbs are better able to neutralize virus than whole IgG. Neutralization of HIV-1 R5 isolates JRFL, JR-CSF and ADA by CD4i MAbs X5, 17b, and 48d decreased with increased molecule size, the neutralizing potency of single-chain Fv (scFv) > than Fab fragments > whole Ab molecules. (With the exception of IgG 48d neutralization of HIV-1 ADA being better than the Fab – for 48d, only the IgG and Fab forms were available, not the scFv.) HIV-1 X4 isolates 89.6 and HxB2 are both relatively sensitive even to the larger IgG version. R5X4 isolate neutralization was dependent on the isolate and co-receptor usage. The CD4i MAb fragments neutralize HIV-1 subsequent to CD4 binding. The CD4i MAbs bind near the co-receptor binding sites on gp120. Co-receptors bind to the conserved beta19 strand and part of the V3 loop, regions which are masked by the V1V2 loops in the CD4-unbound state. When CD4 is bound, the co-receptor site is exposed near the membrane surface where it would be optimally accessible to co-receptors, and the smaller versions of the molecules are better able to overcome the steric hindrence. [Labrijn2003] (**antibody binding site definition and exposure**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- 48d: Called 4.8d. The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 enhanced binding of CD4i MAbs 4.8d, 1.7b, and A1g8 to R5X4 virus 92HT593, but only of 48d to the R5 virus 92US660, and there was only a modest impact of the combination of B4e8 and CD4i MAbs on neutralization. [Cavacini2003] (**antibody interactions**, **co-receptor**)
- 48d: This study examined antibody interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-V3 MAb B4a1 increased binding of CD4i MAbs 48d, 17b and A1g8, but only A1g8 binding was increased by B4a1 to the R5 isolate. Additive affects on neutralizaton of the R5X4 isolate with B4a1 and CD4i MAbs was observed, presumably due to increased exposure of the CD4i binding site, but not for the R5 isolate. Anti-gp41 MAb F240 had a synergistic effect on neutralization with CD4i MAbs 48d and 17b, but not with A1g8 for the R5X4 virus. [Cavacini2002] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 48d: NIH AIDS Research and Reference Reagent Program: 1756.
- 48d: Called 4.8D – A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**variant cross-recognition or cross-neutralization**)
- 48d: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] (**co-receptor**)
- 48d: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. [Xiang2002a] (**antibody binding site definition and exposure**, **co-receptor**)
- 48d: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b]
- 48d: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002]
- 48d: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. [Golding2002b]
- 48d: Called 4.8d – A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001]
- 48d: Mutations in two glcosylation sites in the V2 region of HIV-1 ADA at positions 190 and 197 (187 DNTSYRLINCNTS 199) cause the virus to become CD4-independent and able to enter cells through CCR5 alone – these same mutations tended to increase the neutralization sensitivity of the virus, including to 48d – only the CD4i antibodies 17b and 48d showed an increased affinity of the CD4 independent viruses relative to wild-type. [Kolchinsky2001]
- 48d: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) that preserve and expose some neutralizing epitopes while occluding some non-neutralizing epitopes – CD4BS MAbs (F105 and F91) and CD4i (17b and 48d) recognized gp140-GNC4 as well as gp120 or gp140 – non-neutralizing MAbs C11, A32, 522-149, M90, and #45 bound to the gp140-GNC4 glycoprotein at reduced levels compared to gp120 – MAbs directed at the extreme termini of gp120 C1 (135/9 and 133/290) and C5 (CRA-1 and M91) bound efficiently to gp140-GNC4. [Yang2000]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 48d: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – CD4i MAbs 17b and 48d have little effect on a standard cell fusion assay but potently block sCD4 activated fusion. [Salzwedel2000] (**co-receptor**)
- 48d: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – the mutation L544P reduced binding of all MAbs against gp120 by causing conformational changes. [Park2000]
- 48d: SF162 is a neutralization-resistant HIV-1 isolate – N-linked glycosylation modifications in the V2 loop of the SF162 gp120 revealed that these sites prevent neutralization by CD4BS MAbs (IgG1b12 and IgGCD4), and protect against neutralization by V3 MAbs (447-D and 391-95D) – V2-region glycosylation site mutations did not alter neutralization resistance to V2 MAbs (G3.4 and G3.136) or CD4i MAbs (17b and 48d) – V2 glycosylation site modification allows infection of macrophages, probably due to glycosylated forms requiring fewer CCR5 molecules for viral entry. [Ly2000]
- 48d: Called 4.8D – host encoded intercellular adhesion molecule (ICAM-1) is incorporated by the HIV-1 virion and enhances viral infectivity – ICAM-1 does not modify virus sensitivity to antibodies 0.5beta or 4.8D or sCD4, but neutralizing ability of F105 was diminished in ICAM bearing virions in the presence of lymphocyte function-association antigen-1 (LFA-1) Ab. [Fortin2000]
- 48d: A CD4-independent viral variant of IIIB, IIIBx, was generated on CXCR4-expressing cells – IIIBx exhibited greater exposure of the 17b and 48d epitopes and enhanced neutralization by CD4i MAbs and by polyclonal human sera. [Hoffman1999]
- 48d: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. [Frankel1998]
- 48d: Deleting the V2 loop of neutralization-resistant HIV-1 isolate SF162 does not abrogate its replication in PBMC or macrophages, but it enhances its neutralization sensitivity to sera from patients with B clade infection up to 170-fold, and also enhances sensitivity to sera from clades A through F – deletion of V2 but not V1 enabled neutralization by CD4i MAbs 17b and 48d. [Stamatatos1998]
- 48d: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – CD4i MAbs 17b and 48d bound better to the deleted protein than to wild type. [Binley1998]
- 48d: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998]
- 48d: CD4i MAbs 17b and 48d compete with MAb CG10, and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10. [Sullivan1998b]
- 48d: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a]
- 48d: Inhibits binding of Hx10 to both CD4 positive and CD4 negative HeLa cells. [Mondor1998]
- 48d: Summary of the implications of the crystal structure of the core of gp120 bound to CD4 and 17b with what is known about mutations that reduce NAb binding – probable mechanism of neutralization of 48d is interference with chemokine receptor binding – CD4 binding increases exposure of epitope due to V2 loop movement – 88N, 117K, 121K, 256S, 257T, N262, delta V3, E370, E381, F 382, R 419, I 420, K 421, Q 422, I 423, W 427, Y 435, P 438, M 475 mutations in HXBc2 (IIIB) decrease binding. [Wyatt1998a] (**structure**)
- 48d: Neutralizes TCLA strains, but not primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- 48d: Binds efficiently to sgp120 but not soluble gp120+gp41, suggesting its gp120 epitope is blocked by gp41 binding. [Wyatt1997] (**antibody binding site definition and exposure**)
- 48d: Viral binding inhibition by 48d was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]
- 48d: Prefers CD4-gp120 complex to gp120 alone, but does not enhance fusion, in contrast to MAb CG10, in fact it inhibits syncytium formation. [Lee1997] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 48d: 48d binds to the IIIB protein and not IIIB V3 peptide, while binding to the Can0A V3 peptide, suggesting Can0A V3 is a conformer that mimics the 48d, (but not 17b), epitope. [Weinberg1997] (**antibody binding site definition and exposure**)
- 48d: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB env – all Ab combinations tested showed synergistic neutralization – 48d has synergistic response with MAbs 694/98-D (anti-V3) and F105. [Li1997] (**antibody interactions**)
- 48d: Neutralizes JR-FL – slightly inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**antibody binding site definition and exposure**, **co-receptor**)
- 48d: Binding resulted in gp120 dissociation from virion, mimicking sCD4, and exposure of the gp41 epitope of MAb 50-69, in contrast to CD4BS MAbs. [Poignard1996a] (**antibody interactions**)
- 48d: Many MAbs inhibit binding (anti-C1, -C5, -C4, -CD4BS) – anti-C1-C4 discontinuous epitope MAbs A32 and 2/11c enhance binding – reciprocal enhanced binding with some anti-V2 MAbs. [Moore1996] (**antibody interactions**)
- 48d: Binds with similar affinity to monomer and oligomer, moderate association rate, potent neutralization – this is in contrast to 17b, which has very different kinetics. [Sattentau1995b] (**antibody binding site definition and exposure**, **kinetics**, **binding affinity**)
- 48d: Formalin inactivation of virus at 0.1% formalin for 10 hours at 4 degrees was optimal for inactivation of virus while maintaining epitope integrity. [Sattentau1995c] (**vaccine antigen design**)
- 48d: Studies using a V1/V2 deletion mutant demonstrated that enhanced binding of 48d in the presence of sCD4 involves the V1/V2 loops, with more significant involvement of V2 – similar effect observed for 17b and A32. [Wyatt1995] (**vaccine antigen design**)
- 48d: Called 4.8D – Found to neutralize MN, but not JRCSF, two B subtype primary isolates, or a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. [D'Souza1995] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- 48d: Poor cross-reactivity with gp120 from most clades. [Moore1994b] (**inter-clade comparisons**)
- 48d: A mutation in gp41, 582 A/T, confers resistance to neutralization (also confers resistance to MAbs F105, 21h, 15e and 17b) [Thali1994] (**variant cross-recognition or cross-neutralization**)
- 48d: Binding of 48d is much more influenced by sequence variation among molecular clones of LAI than is binding of 17b. [Moore1993d] (**variant cross-recognition or cross-neutralization**)
- 48d: Called 4.8d – Neutralizes IIIB – reactive with SF-2 gp120 – does not inhibit HIV-1 sera from binding to IIIB gp120. [Moore1993a] (**variant cross-recognition or cross-neutralization**)
- 48d: Epitope is better exposed upon CD4 binding to gp120 – competes with ICR 39.13, 15e and 21h, anti-CD4 binding site MAbs – inhibited by anti-CD4BS MAb ICR 39.13g and linear anti-C4 MAbs G3-42 and G3-508 – 113 D/R, 252 R/W, 257 T/A or G, 370 E/D, 382 F/L, 420 I/R, 421 K/L, 433A/L, 438 P/R and 475 M/S confer decreased sensitivity to neutralization. [Thali1993] (**antibody binding site definition and exposure**, **antibody interactions**)
- 48d: 48d and 17b have similar epitopes, and the pair are unique among human and rodent MAbs.

1052	49e	Env	gp120 (IIIB, J62)		L	HIV-1 infection	human (IgG)

Ab type CD4i **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA
References Gorny2004, Xiang2002b, Xiang2002a
Keywords antibody binding site definition and exposure, antibody generation, review, vaccine antigen design.

- 49e: This review summarizes MAbs directed and HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. [Gorny2004] (**review**)
- 49e: A series of mutational changes were introduced into the YU2 gp120 that favored different conformations – 375 S/W seems to favor a conformation of gp120 closer to the CD4-bound state, and is readily bound by sCD4 and CD4i MAbs (17b, 48d, 49e, 21c and 23e) but binding of anti-CD4BS MAbs (F105, 15e, IgG1b12, 21h and F91 was markedly reduced – IgG1b12 failed to neutralize this mutant, while neutralization by 2G12 was enhanced – 2F5 did not neutralize either WT or mutant, probably due to polymorphism in the YU2 epitope – another mutant, 423 I/P, disrupted the gp120 bridging sheet, favored a different conformation and did not bind CD4, CCR5, or CD4i antibodies, but did bind to CD4BS MAbs. [Xiang2002b] (**antibody binding site definition and exposure**, **vaccine antigen design**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 49e: Five CD4i MAbs were studied, 17b, 48d and three new MAbs derived by Epstein-Barr virus transformation of PBMC from an HIV+ long term non-progressor – 23e and 21c were converted to hybridomas to increase Ab production – all compete with the well-characterized 17b CD4i MAb in an ELISA antigen capture assay – critical binding residues are mapped and the CD4i MAb epitopes were distinct but share a common element near isoleucine 420, also important for CCR5 binding, and all five can block CCR5 binding to a sCD4-gp120 complex – the MAb 48d has the epitope most similar to the CCR5 binding site. [Xiang2002a] (**antibody binding site definition and exposure**, **antibody generation**)

1053 X5 (Fab X5) Env gp120 (JRFL) P HIV-1 infection human

Ab type CD4i

References Gorny2004, Pantophlet2003b, Zwick2004, Zwick2003, Zhang2003, Labrijn2003, Binley2003, Moulard2002

Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, co-receptor, inter-clade comparisons, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- X5: This review summarizes MAbs directed and HIV-1 Env. There are six CD4 inducible MAbs and Fabs in the database. The MAb forms neutralize TCLA strains only, but the smaller Fabs and scFv fragments can neutralize primary isolates. [Gorny2004] (**review**)
- X5: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- X5: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. This is a CD4i MAb that had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- X5: The Fab m18 was selected from a human phage display library by a new method called sequential antigen panning (SAP), using a series of antigens to screen the library to pick broadly cross-reactive isolates. The ability to block cell mediated fusion by m18 was compared to Fabs X5 and b12 for a clade A, CRF01 EA, G, and 6 clade B isolates, and the inhibitory activity of m18 was slightly lower but comparable to neutralizing Fabs b12 and X5. It also showed broad cross-neutralization; 11/15 pseudotyped Envs from primary isolates from clades A-F were inhibited in an IC50 assay at concentration less than or equal to 100 ug/ml; X5 was also tested and somewhat more potent, generally requiring lower concentrations and inhibiting 13/15 primary isolates. [Zhang2003] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)
- X5: This study shows the fragments of CD4i MAbs are better able to neutralize virus than whole IgG. Neutralization of HIV-1 R5 isolates JRFL, JR-CSF and ADA by CD4i MAbs X5, 17b, and 48d decreased with increased molecule size, the neutralizing potency of single-chain Fv (scFv) > than Fab fragments > whole Ab molecules. (With the exception of IgG 48d neutralization of HIV-1 ADA.) HIV-1 X4 isolates 89.6 and HxB2 are both relatively sensitive even to the larger IgG version. R5X4 isolate neutralization was dependent on the isolate and co-receptor usage. The CD4i MAb fragments neutralize HIV-1 subsequent to CD4 binding. The CD4i MAbs bind near the co-receptor binding sites on gp120. Co-receptors bind to the conserved beta19 strand and part of the V3 loop, regions which are masked by the V1V2 loops in the CD4-unbound state. When CD4 is bound, the co-receptor site is exposed near the membrane surface where it would be optimally accessible to co-receptors, and the smaller versions of the molecules are better able to overcome the steric hindrence. [Labrijn2003] (**antibody binding site definition and exposure**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- X5: Called Fab X5. This paper is a study of the 2F5 NAb complexed to peptide ELDKWAS; the peptide was found to interact with amino acids near the base of the very long (22 residue) CDR 3H region of the Ab, although a Phe at the apex of the loop was also important. The authors suggest that particularly long CDR H3 regions may be a common feature of HIV-1 neuturalizing antibodies – there are 22 residues in 2F5's H3, 18 in b12's H3, and 22 residues in X5's H3. They express concern that because small animals like mice are be unable to elicit Ab responses with such long H3s, they may be poor model systems for HIV vaccine studies. [Zwick2004] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• X5: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. CD4i Abs X5 and 17b were weakly neutralizing in all formats, WT, SOS, and when added postbinding. [Binley2003] (**vaccine antigen design**) • X5: The human Fab X5 was selected from a phage display library derived from an HIV-1 positive donor with a highly neutralizing serum – it was selected for binding to purified gp120-CD4-coreceptor complexes – the Fab neutralizes PBMC infection by a selection of HIV-1 primary isolates from clades A, B, C, D, E, F, and G, and neutralizes R5, X4, and R5X4 isolates – it binds to a conserved epitope on gp120 induced by CD4 binding, its binding is slightly enhanced by CCR5 binding – while CD4i MAb 17b binds the CCR5 binding site, X5 also competes with Fab b12 which overlaps with the CD4 binding site, suggesting the epitope for is near both the CD4 and CCR5 binding sites. [Moulard2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)			
1054	T22	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** Env oligomer **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Otteken1996, Earl1994 • T22: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T22 is part of a group of MAbs labeled AII – all AII MAbs were broadly cross-reactive with gp160 from B-clade R5, X4, and R5X4 viruses, and could only partially blocked CD4 binding. [Sugiura1999] • T22: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp140 revealed that these anti-CD4BS MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. [Otteken1996] • T22: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1055	polyclonal	Env	gp41			Vaccine	rabbit (IgG)
		Vaccine *Vector/Type:* peptide *Adjuvant:* gp41 N-HR and C-HR helical peptides **Ab type** C-HR, N-HR, six-helix bundle **References** Golding2002b, deRosny2001 • The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter anti-C-HR Abs inability to inhibit fusion. [Golding2002b] • A panel of Abs against gp41 heptad repeats N-HR, C-HR, and self-assembled stable N-HR and C-HR six helix bundles were generated. [deRosny2001]					
1056	2A2	Env	gp41		no	HIV-1 infection	human (IgG1κ)
		Ab type N-term **References** Weissenhorn1996 • Soluble gp41(21-166) forms a rod like structure that can be visualized with electron microscopy, and 2A2 binds to one end of the rod. [Weissenhorn1996]					
1057	AC4	Env	gp120 (IIIB)		yes	Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **Ab type** N-term **References** Dickey2000 • AC4: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey2000]					
1058	AD3	Env	gp120 (IIIB)		yes	Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* gp160					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type N-term **References** Cook1994, Dickey2000 • AD3: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey2000] • AD3: There may be two Abs with this name that bind to the N-term region of gp120. [Cook1994, Dickey2000]					
1059	AD3	Env	gp120 (BH10)				mouse (IgG1)
		Ab type N-term **References** Dickey2000, Cook1994, Ugen1993 • AD3: NIH AIDS Research and Reference Reagent Program: 2342. • AD3: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994] • AD3: There may be two Abs with this name that bind to the N-term region of gp120. [Cook1994, Dickey2000]					
1060	ID6	Env	gp120 (1–193 BH10)				mouse (IgG1)
		Ab type N-term **References** Dickey2000, Cook1994, Ugen1993 • ID6: NIH AIDS Research and Reference Reagent Program: 2343. • ID6: MAbs against the glycosphingolipid GalCer block HIV infection of normally susceptible CD4 negative cells from the brain and colon – MAbs against the N-terminal half of gp120 do not inhibit gp120 binding to GalCer – binding of GalCer to gp120 does not inhibit MAb binding. [Cook1994] • ID6: There may be two Abs with this name that bind to the N-term region of gp120. [Cook1994, Dickey2000]					
1061	ID6	Env	gp120 (IIIB)		yes	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *HIV component:* gp160 **Ab type** N-term **References** Cook1994, Dickey2000 • ID6: Three MABs, ID6, AC4, and AD3 that bind to a discontinuous N-term first 204 aa of gp120 and generate ADCC were elicited through vaccination of BALBc mice with rec gp160 – these MAbs do not depend on glycosylation and are cross-reactive with viruses from clades B and CRF01(AE) [Dickey2000] • ID6: There may be two Abs with this name that bind to the N-term region of gp120. [Cook1994, Dickey2000]					
1062	11/68b	Env	gp120		L (HXB2)	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V1-V2 **Research Contact** Shotton and Dean **References** Peet1998, Shotton1995, McKeating1993b • 11/68b: UK Medical Research Council AIDS reagent: ARP3041. • 11/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind – 11/68b was not affected by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998] • 11/68b: Cross-competes with MAbs 62c, 66c, 66a, and CRA-4 – similar to MAb 62c – HXB2 neutralization escape mutant had a D/N substitution at residue 185 – non-reciprocal inhibition of binding of CRA-3 and CRA-6. [Shotton1995] • 11/68b: 435 (Y/H) in C4 does not abrogate binding (John Moore, per comm, 1996) • 11/68b: Changes at residues 183/184 (PI/SG) within V2, 435 (Y/H) in C4, abrogate binding. [McKeating1993b]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1063	62c	Env	gp120		no	Vaccine	rat (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V1-V2 **References** Shotton1995 • 62c: UK Medical Research Council AIDS reagent: ARP3075. • 62c: Cross-competes with MAbs 11/68b, 66c, 66a, and CRA-4 – same cross-competition group as MAb 11/68b – non-reciprocal inhibition of binding of CRA-3 and CRA-6 – substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – binds but does not neutralize Hx10. [Shotton1995]				
1064	CRA-6 (CRA6)	Env	gp120		no		mouse
		Ab type V1-V2 **References** Shotton1995 • CRA-6: Called CRA6 – same competition group as CRA-3. [Shotton1995]					
1065	L15	Env	gp120		P (weak)	HIV-1 infection	human (IgG1)
		Ab type V1-V2 **References** Gorny2004, Parren1997c, Ditzel1997 **Keywords** review, variant cross-recognition or cross-neutralization. • L15: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weak with limited cross-reactivity. L15 and L17 are Fabs specific for V2. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**) • L15: Does not neutralize TCLA strains but neutralizes some primary isolates weakly. [Parren1997c] • L15: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – 2 anti-V2 Fabs were obtained with very similar epitopes, L15 and L17 – deletions in V1 and V2 abolished binding, and rodent anti-V2 MAbs SC258, CRA3, G3-G4,G3-136, BAT-085, and 52-684 all compete with L15. [Ditzel1997]				
1066	T52	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** V1-V2 **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • T52: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T52 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding. [Sugiura1999] • T52: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]				
1067	T54	Env	gp120 (IIIB)		no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** V1-V2 **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • T54: A comparison of 25 gp120 specific, conformation dependent MAbs was done – T54 is one of two MAbs labeled B-II, that had limited cross-reactivity with seven clade B isolates and did not fully blocked CD4 binding – deletion of V1/V2 loops abrogated binding. [Sugiura1999] • T54: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]				
1068	polyclonal	Env	Env		yes	HIV-1 infection	human
		Ab type V1-V2 and V3-V5 **References** Gordon2000					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Primary isolates have great differences in susceptibility to neutralization – the variation in V1V2 and V3-V5 was measured by HTA in a set of viruses with a range of neutralization susceptibilities, and greater variability was uncorrelated with resistance to neutralization. [Gordon2000]					
1069	1088	Env	gp120				
		Ab type V2					
		References Berman1997					
		• 1088: Binds weakly to 2/7 isolates from breakthrough cases from a MN gp120 vaccine trial. [Berman1997]					
1070	110-B	Env	gp120		no	Vaccine	mouse
		Vaccine *Vector/Type:* HIV infected-cell lysate *Strain:* B clade BRU *HIV component:* HIV-1					
		Ab type V2 **Research Contact** Hybridolabs, Institute Pasteur, Paris, France					
		References Moore1993b					
		• 110-B: specific for BH10, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 168 K/L, 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS. [Moore1993b]					
1071	1357	Env	gp120				human (IgG1κ)
		Ab type V2 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					
		References Gorny2004, Nyambi2000, Gorny2000a, Nyambi1998					
		Keywords review.					
		• 1357: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. Anti-V2 MAbs 1357, 1361, 1393 are non-neutralizing. [Gorny2004] (**review**)					
		• 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. [Nyambi2000]					
		• 1357: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold. [Gorny2000a]					
		• 1357: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind very weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding only to subtype D MAL. [Nyambi1998]					
		• 1357: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. [Nyambi2000]					
1072	1361	Env	gp120			Vaccine	human (IgG1κ)
		Vaccine *Vector/Type:* protein *HIV component:* gp120					
		Ab type V2 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)					
		References Nyambi2000, Gorny2000a, Nyambi1998					
		• 1361: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. [Nyambi2000]					
		• 1361: Blocks binding of MAb 697-D to rgp120, and doesn't react with a protein from which V1V2 has been deleted – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V2 MAbs 697-D, 1357 and 1361 favored the monomer by approximately 2 fold. [Gorny2000a]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1361: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – V2 Abs 697-D, 1361, and 1357 tended to bind weakly with a similar pattern of specificity to virions, but bound well to soluble gp120: weak binding to 1/4 B clade viruses (CA5), and also weak binding to a subtype D virus, MAL. [Nyambi1998]					
1073	1393A	Env	gp120			HIV-1 infection	
		Ab type V2 **References** Gorny2004, Nyambi2000 **Keywords** inter-clade comparisons, review. • 1393A: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. Anti-V2 MAbs 1357, 1361, 1393A are non-neutralizing. [Gorny2004] (**review**) • 1393A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. [Nyambi2000] (**inter-clade comparisons**)					
1074	66a	Env	gp120		L (HXB2)	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V2 **References** Shotton1995 • 66a: UK Medical Research Council AIDS reagent: ARP3074. • 66a: Substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – same competition group as CRA4. [Shotton1995]					
1075	66c	Env	gp120		L (HXB2)	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V2 **References** Shotton1995 • 66c: Substitutions 176-177 FY/AT, 179-180 LD/DL, 183-184 PI/SG, and 191-193 YSL/GSS abrogate binding – same competition group as CRA4. [Shotton1995]					
1076	684-238 (52-684-238, 52-684)	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V2 **Research Contact** Gerry Robey, Abbott Laboratories **References** Ditzel1997, Moore1996, Ditzel1995, Gorny1994, Thali1993, Moore1993b • 684-238: Limited reciprocal enhancement of binding with anti-V3 and C4 region antibodies – reciprocal inhibition with V2 region antibodies. [Moore1996] • 684-238: Does not compete with IgG1b12, reciprocal inhibition with MAbs L39, L40, and L78. [Ditzel1995] • 684-238: Weakly neutralizing, IC 50 = 84 mug/ml. [Gorny1994] • 684-238: Specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177FY/AT, 179/180LD/DL, 183/184PI/SG, and 192-194YSL/GSS. [Moore1993b]					
1077	830A	Env	gp120			HIV-1 infection	
		Ab type V2 **References** Gorny2004, Nyambi2000 **Keywords** inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 830A: This broad review of anti-Envelope MAbs notes that V2 MAbs are generally weakly neutralizing at best, and somewhat strain specific. 830A neutralizes SF162. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 830A: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 anti-V2 MAbs, which showed weak and sporadic binding, with the most frequent binding to C and D clades. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					
1078	CRA-3 (CRA3)	Env	gp120		no	Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V2 **Research Contact** Mark Page, NIBSC AIDS reagent project, Potters Bar, Herts, UK **References** Ditzel1997, Moore1996, Shotton1995, Thali1993, Moore1993b, Moore1993a • CRA-3: UK Medical Research Council AIDS reagent: ARP324. • CRA-3: Called CRA3 – Same competition group as CRA6. [Shotton1995] • CRA-3: Many MAbs enhance binding, including some anti-C5, C1, V4, and C4 MAbs – enhances binding of only a small number of anti-V3 loop MAbs. [Moore1996] • CRA-3: specific for BH10 or HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS – epitope probably involves stem of V1/V2 loop structure. [Moore1993b] • CRA-3: Conformational, does not bind well to denatured gp120. [Moore1993a]					
1079	CRA-4 (CRA4)	Env	gp120		L (HXB2)	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120 **Ab type** V2 **Research Contact** Mark Page, NIBS, MRC AIDS reagent repository, ARP 325 **References** Moore1996, Shotton1995, Thali1993, Moore1993b, Moore1993a, McKeating1993b • CRA-4: UK Medical Research Council AIDS reagent: ARP325. • CRA-4: The only MAbs that enhanced binding were anti-V3 MAb 5G11 and anti-C1 MAb 135/9 binding – reciprocal inhibition of anti-V2 MAbs. [Moore1996] • CRA-4: Cross-competes with MAbs 11/68b, 62c, 66c, 66a – similar to 66c and 66a – non-reciprocal inhibition by MAbs 12b, 60b and CRA-6. [Shotton1995] • CRA-4: Specific for BH10 and HXB2, does not bind to MN, RF, or SF-2 gp120 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS. [Moore1993b] • CRA-4: Conformational, does not bind well to denatured gp120. [Moore1993a] • CRA-4: Changes at residues 191/192/193 (YSL/GSS) within V2, 435 (Y/H) in C4, abrogate binding – type-specific neutralization. [McKeating1993b]					
1080	L17	Env	gp120				human
		Ab type V2 **References** Gorny2004, Kwong2002, Parren1998a, Ditzel1997 **Keywords** antibody binding site definition and exposure, binding affinity, review, variant cross-recognition or cross-neutralization. • L17: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L15 and L17 are Fabs specific for V2. [Gorny2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L17: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**) • L17: The rank order of Fab binding affinity to monomeric gp120 (Loop 2 > 3B3 > b12 = DO8i > b11 > b3 > b14 > b13 > DO142-10 > DA48 > L17) was markedly different than Fab binding affinity to the mature oligomeric form (3B3 > b12 > DO142-10 > Loop 2 > b11 > L17 > b6 > DO8i > b14 > DA48 > b3 > b13) and binding to oligomeric form and neutralization were correlated for both Fabs and MAbs – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**binding affinity**)			
1081	SC258 (52-581-SC258)	Env	gp120		L	Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** V2 **Research Contact** Gerry Robey, Abbott Laboratories **References** He2002, Ditzel1997, Trkola1996a, Moore1996, Ditzel1995, Moore1994b, Yoshiyama1994, Gorny1994, Thali1993, Moore1993b • SC258: Transgenic mice carrying human genes allowing production of fully human MAbs were used to rapidly create a panel of anti-HIV gp120 MAb producing hybridomas by immunization with HIV SF162 gp120 – the previously described human MAbs 5145A(CD4BS) , 4117C (plus others, V3) and 697D (and SC258, V2) were used as controls. [He2002] • SC258: Does not inhibit gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study – listed as not neutralizing. [Trkola1996a] • SC258: Several MAbs binding to various gp120 epitopes enhance binding, but the only MAb that SC258 enhanced binding of was anti-CD4 binding site MAb F91 – reciprocal inhibition with V2 region antibodies. [Moore1996] • SC258: Does not compete with IgG1b12 – reciprocal inhibition with MAbs L39, L40, and L78. [Ditzel1995] • SC258: Very poor reactivity with gp120 molecules outside of clade B. [Moore1994b] • SC258: HIV-1 RF V2 substitutions 177 Y/H and 179 L/P in the V2 loop of RF reduce affinity – 177 Y/H inhibits SC258 neutralization. [Yoshiyama1994] • SC258: Called 52-581-SC258 – binds to BH10, MN, and RF gp120 – neutralizes BH10 – binding inhibited by deletion of the V2 loop, and the following amino acid substitutions: 176/177 FY/AT, 179/180 LD/DL, 183/184 PI/SG, and 192-194 YSL/GSS. [Moore1993b]			
1082	L25	Env	gp120		L (weak)	HIV-1 infection	human (IgG1)
		Ab type V2-CD4BS **References** Gorny2004, Parren1997c, Ditzel1997, Ditzel1995 **Keywords** antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization. • L25: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for a complex binding site involving V2 and elements of the sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. [Gorny2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**) • L25: Neutralizes TCLA strains weakly, but not primary isolates. [Parren1997c] • L25: gp120 immobilized on solid phase by capture with anti-CD4 BS MAb L72 was used for selection of Fabs – a single anti-V2-CD4 BS Fab was obtained with with sensitivity to substitutions in the V2 and CD4 BS regions – rodent anti-V2 MAb SC258 competes with L25. [Ditzel1997]			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1083	L39	Env	gp120		no	HIV-1 infection	human (IgG1κ)

Ab type V2-CD4BS
References Gorny2004, Ditzel1995
Keywords antibody binding site definition and exposure, review, variant cross-recognition or cross-neutralization.

- L39: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for a complex binding site involving V2 and elements of the sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. [Gorny2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)
- L39: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L39 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available. [Ditzel1995]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1084	L40	Env	gp120		no	HIV-1 infection	human (IgG1κ)

Ab type V2-CD4BS
References Gorny2004, Ditzel1995
Keywords antibody binding site definition and exposure, responses in children, variant cross-recognition or cross-neutralization.

- L40: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for a complex binding site involving V2 and elements of the sCD4 binding site regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. [Gorny2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **responses in children**)
- L40: This Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop (similar patterns were observed for L40 and L78 gp120 amino acid substitutions enhancing or reducing binding) – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – binding only partially affected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available. [Ditzel1995]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1085	L78	Env	gp120		L	HIV-1 infection	human (IgG1κ)

Ab type V2-CD4BS
References Gorny2004, Kwong2002, Ditzel1995
Keywords antibody binding site definition and exposure, antibody sequence, variable domain, review, variant cross-recognition or cross-neutralization.

- L78: In a review of Envelope binding MAbs in this database, V2-specific MAbs in are noted have some ability to neutralize HIV-1, but generally weakly with limited cross-reactivity. L25, L39, L40 and L78 are Fabs specific for V2 that are also associated with sCD4 bindingsite regions; among these only L25 and L78 mediate weak neutralization of some TCLA strains. [Gorny2004] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **review**)
- L78: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• L78: Substitutions at V2: (152/153 GE/SM, 183/184 PI/SG, 191/193 YL/GS), 262 N/T, V3 (314 G/W), CD4BS (257 T/R, 368 D/R, 370 E/R) inhibit binding, and some C4 and C5 substitutions enhance binding – this Fab does not inhibit sCD4 binding, but is inhibited by sCD4, probably due to conformational changes – it is competed by anti-V2 MAbs, and sensitive to amino acid substitutions in the V3 loop – does not compete with CD4BS MAbs, but is sensitive to amino acid changes at positions 368 and 370 – Fab neutralizes MN and LAI – binding unaffected by deglycosylation – reciprocal inhibition with V2 MAbs SC258 and 684-238 – heavy and light chain variable region sequence is available. [Ditzel1995] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **antibody sequence, variable domain**)					
1086		Env	gp120			HIV-1 infection	human
		Ab type V3 **References** Gilljam1999 • Sera from individuals with infections of HIV-1 subtype A-E were tested against purifed proteins from primary PBMC cultures. Sera reactivity tended not to be strongly related to subtype, rather probably reflected the sum of reactivities to conserved and variable regions in the proteins. V3 peptide comparisons showed some preference for within subtype binding. [Gilljam1999]					
1087	110.J	Env	gp120				
		Ab type V3 **Research Contact** F. Traincard, Pasteur Institute, France **References** Moore1996, Thali1993 • 110.J: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – and reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs. [Moore1996] • 110.J: Inhibits sCD4-inducible anti-CD4 binding site MAb 48d. [Thali1993]					
1088	1334-D (1334, 1334D)	Env	gp120 (HIV451)	TRTSV		HIV-1 infection	human (IgG1κ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Gorny2000a, Zolla-Pazner1999b, Zolla-Pazner1999a **Keywords** antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization. • 1334-D: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 1334-D: Called 1334D – A panel of 47 human MAbs was tested against 26 HIV-1 group M primary isolates from clades A through H – 19 V3 MAbs were tested, and of 494 combinations, 44% displayed some viral binding – V3 MAbs tended to have the most cross-reactive binding to clade A, B, C, and D isolates, less to E, F, G, and H – 1334D showed intermediate cross-reactivity. [Nyambi2000] (**inter-clade comparisons**) • 1334-D: Called 1334 – binds to V3 peptides from MN, SF2, NY5, RF, and CDC4 strains as well as x-reactivity with peptides from A, C, D, F, G, and H subtypes – was suggested to be IgG1lambda here – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, though anti-V3 and CD4BS MAbs reacted better with the oligomer and V2 and C5 tended to favor the monomer – V3 MAbs 447-52D, 838-D, and 1334 bound with a 7-10 fold preference for the oligomer. [Gorny2000a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**) • 1334-D: MAb peptide-reactivity pattern clustered with immunological related MAbs: 1334, 419, 504, 447, 453 and 537 – the core amino acids GP tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**) • 1334-D: This MAb was selected using oligomeric gp160 from HIV451. [Zolla-Pazner1999a] (**antibody generation**)					
1089	2182	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)
		Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Gorny2002					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 2182: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary islates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. [Gorny2004] (**review**, **inter-clade comparisons**)
- 2182: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2182 bound to 8/16 of the diverse isolates, not to any clade C or CRF01. [Gorny2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

1090	2191	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Gorny2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 2191: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary islates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- 2191: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2191 bound to 10/16 of the diverse isolates, not to any clade D or CRF01. [Gorny2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

1091	2219	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References Gorny2004, Gorny2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 2219: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary islates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**, **inter-clade comparisons**)
- 2219: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2219 bound to 13/16 of the diverse isolates. [Gorny2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

1092	2412	Env	gp120 (V3 loop) (JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Gorny2002
Keywords antibody binding site definition and exposure, antibody generation, inter-clade comparisons, review, variant cross-recognition or cross-neutralization.

- 2412: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary islates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. [Gorny2004] (**antibody binding site definition and exposure**, **review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2412: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2412 bound to 7/16 of the diverse isolates, and did not bind to any of the clade C, D or CRF01 viruses. [Gorny2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

1093	2442	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Gorny2002
Keywords antibody binding site definition and exposure, antibody generation, review, variant cross-recognition or cross-neutralization.

- 2442: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary islates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)
- 2442: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2442 bound to 13/16 of the diverse isolates. [Gorny2002] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **review**)

1094	2456	Env	(JRCSF)		P	HIV-1 infection	human (IgG1λ)

Ab type V3 **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Gorny2002
Keywords review.

- 2456: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. The set that can cross-neutralize primary isolates (2182, 2191, 2219, 2412, 2442, 2456) bind V3 but are conformationally senstitive, suggesting some structural conservation despite sequence variation. These MAbs have distinct epitopes relative to 447-52D, a MAb directed at the tip of the V3 loop that also can neutralize many primary islates. Inter-clade cross-neutralization by these anti-V3 MAbs is reduced. [Gorny2004] (**review**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2456: Conformation-dependent anti-V3 loop Abs may be more cross-reactive, so six new V3 MAbs were generated from cells of asymptomatic HIV-1-infected individuals by selection of heterhybridomas using a V3-fusion protein (V3-fp), the HIV-1 JRCSF V3 loop inserted into a truncated murine leukemia virus gp70 – the six new MAbs all bind to the tip of the V3 loop and cross-compete with the MAb 447-52D and are conformationally sensitive – MAbs showed cross-clade binding to native, intact virions of clades A(N=2), B(N=4), and F(N=2), limited binding to C(N=3) and D(N=3), and did not bind to CRF01(subtype E, N=2) – the strength binding was highly correlated with percent neutralization using the ghost cell or PHA blast assay – five well-characterized MAbs were used as controls: anti-V3 447-52D (anti-V3 MAb for competition and neutralization studies), 654 (anti-CD4BS used as a conformation-sensitive MAb control), 1331A (anti-C5 used as a linear binding site MAb control), MAb 246 (anti-gp41 MAb that bound to primary isolates of all clades) – 5/6 MAbs were derived from individuals infected in the US, presumably with clade B, and one, 2182, was derived from an individual who was infected abroad with clade A who is presently living in New York city – 2412 and 2456 were produced from cells obtained from the same individual, while the other MAbs were each generated from different subjects – 2456 bound to 12/16 of the diverse isolates. [Gorny2002]

1095 39F Env gp120 no

Ab type V3 **Research Contact** James Robinson, Tulane University, New Orleans, LA, USA
References Kwong2002, Grundner2002, Yang2002
Keywords antibody binding site definition and exposure.

- 39F: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, and not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, except the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol. High values suggest surface burial or protein folding and ordering of amino acids. Variable loop MAbs (L17, L78, 19b, 39F, Ag1211, D0142, and G3-2999) MAbs that bind to the N and C termini (211/c, A32, L100, P35, and C11) do not have dramatic entropy changes. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- 39F: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface. [Grundner2002]
- 39F: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002]

1096 55/68b Env gp120 (300–315)

Ab type V3
References Peet1998

- 55/68b: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/68b binding was abrogated by V3 serine substitutions in the V3 loop – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]

1097 5G11 Env gp120

Ab type V3 **Research Contact** S. Nigida and L. Arthur, NCI, Frederick, MD USA

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Moore1996					
		• 5G11: Binds to conformation sensitive epitope in the V3 loop – reciprocal inhibition of other V3 loop MAbs – reciprocal enhancement of some C1-C5 MAbs (unusual for an anti-V3 MAb) and CD4 binding site MAbs – and enhances binding of V2 MAbs. [Moore1996]					
1098	6.1	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)					
		Ab type V3 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					
		References Gorny2004, He2002					
		Keywords review.					
		• 6.1: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 6.1 was non-neutralizing. [Gorny2004] (**review**)					
		• 6.1: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162. [He2002]					
1099	6.7	Env	gp120 (SF162)		no	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)					
		Ab type V3 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					
		References Gorny2004, He2002					
		Keywords antibody binding site definition and exposure, antibody generation, review.					
		• 6.7: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. 6.7 was non-neutralizing. [Gorny2004] (**review**)					
		• 6.7: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162. [He2002] (**antibody binding site definition and exposure**, **antibody generation**)					
1100	8.27.3	Env	gp120 (SF162)		L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)					
		Ab type V3 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org					
		References Gorny2004, He2002					
		Keywords review, variant cross-recognition or cross-neutralization.					
		• 8.27.3: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, like 8.27.3; a subset can also neutralize some primary isolates. [Gorny2004] (**variant cross-recognition or cross-neutralization**, **review**)					
		• 8.27.3: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 1/4 V3 MAbs, 8.27.3, bound a discontinuous epitope that was broadly cross-reactive with B clade R5 and X4 strains (not E clade) and could neutralize autologous strain SF162. [He2002]					
1101	8E11/A8	Env	gp120 (SF162)		L	Vaccine	transgenic mouse (IgG2κ)
		Vaccine *Vector/Type:* protein *Strain:* B clade SF162 *HIV component:* gp120 *Adjuvant:* Ribi adjuvant (MPL+TDM) (RIBI)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V3 **Research Contact** Dr. Abraham Pinter, Public Health Research Institute, Newark, NJ, pinter@phri.org **References** Gorny2004, He2002 **Keywords** antibody binding site definition and exposure, antibody generation, autologous responses, review. • 8E11/A8: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 8E11/A8: Transgenic mice (strain XenoMouse G2) carrying human genes allowing production of fully human IgG2kappa MAbs were used to rapidly create a panel of anti-HIV gp120 MAb-producing hybridomas by immunization with HIV SF162 gp120 – 3/4 V3 MAbs bound a similar linear epitope between positions 11-30 of the MN V3 loop (8E11/A8, 6.1, and 6.7), but only 8E11/A8 could weakly neutralize autologous strain SF162. [He2002] (**antibody binding site definition and exposure**, **antibody generation**, **autologous responses**)			
1102	9305	Env	gp120		L		mouse
		Ab type V3 **Research Contact** Du Pont, Wilmington DE **References** McDougal1996					
1103	AG1121 (1121)	Env	gp120		L		
		Ab type V3 **Research Contact** AGMED, Inc, Bedford, MA, USA or ImmunoDiagnostics, Inc, Woburn, MA, USA **References** Si2001, Cao1997b, Sullivan1995 • AG1121: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. [Si2001] • AG1121: Called 1121 – Virus with the V1-V2 loop deleted was viable and more susceptible to neutralization by CD4i MAb 17b, and anti-V3 MAbs 1121, 9284, and 110.4, but not to and CD4BS MAb F105 or sCD4. [Cao1997b] • AG1121: Recognizes monomeric gp120 from T-cell adapted line HXBc2 and primary isolate 89.6 equally well, but 89.6 was three-fold less sensitive to neutralization by AG1121 than HXBc2. [Sullivan1995]			
1104	D47	Env	gp120 (IIIB)			Vaccine	mouse
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* Env **Ab type** V3 **Research Contact** Patricia Earl, NIAID, NIH **References** Salzwedel2000, Earl1997, Wyatt1997, Otteken1996, Richardson1996, Earl1994 **Keywords** antibody binding site definition and exposure, antibody generation, variant cross-recognition or cross-neutralization. • D47: sCD4 can activate fusion between effector cells expressing Env and target cells expressing coreceptor (CCR5 or CXCR4) alone without CD4 – V3 MAb D47 is strain specific and can inhibit sCD4 mediated infection, but only of the closely related LAV Env, while anti-CD4i MAbs were broadly cross-neutralizing. [Salzwedel2000] (**variant cross-recognition or cross-neutralization**) • D47: Used for comparison in a study of gp41 antibodies – D47 binds to a greater extent to cell surface expressed Env than any of 38 conformation dependent anti-gp41 MAbs. [Earl1997] • D47: Binds both gp120 and soluble gp120+gp41 complex efficiently, suggesting its gp120 epitope is not blocked by gp41 binding. [Wyatt1997] (**antibody binding site definition and exposure**) • D47: Pulse label experiments of MAb binding to noncleavable gp160 revealed that this anti-V3 MAb bound immediately and binding stayed constant through chase period. [Otteken1996] • D47: Used for capture of oligomeric Env for antigen capture ELISA – binding of this antibody to oligomeric Env IIIB was not blocked by human sera from the US, consistent with a low prevalence of IIIB-like V3 strains. [Richardson1996] (**antibody binding site definition and exposure**)			

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• D47: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994] (**antibody generation**)					
1105	F5.5	Env	gp120 (IIIB)				mouse
		Ab type V3 **Research Contact** Hybridolabs, Institute Pasteur **References** Altmeyer1999 • F5.5: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. [Altmeyer1999]					
1106	G3-1472	Env	gp120				
		Ab type V3 **Research Contact** M. Fung **References** Moore1996 • G3-1472: Binds to carboxy-terminal side of the V3 loop – reciprocal binding inhibition with other anti-V3 and anti-C4 MAbs – reciprocal enhanced binding of some anti-V2 MAbs and anti-CD4 binding site MAbs – binding inhibited by anti-C4 MAbs. [Moore1996]					
1107	K24	Env	gp120 (IIIB)				mouse
		Ab type V3 **Research Contact** Hybridolabs, Institute Pasteur **References** Altmeyer1999 • K24: A Semliki Forest virus (SFV) expression system carrying BX08 env was used to study the conformation of gp120 env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface-expressed Env was recognized only by the conformation-dependent antibodies and not by anti-V3 antibodies. [Altmeyer1999]					
1108	TH1	Env	gp120		L (MN, J		human (IgG1λ)
		Ab type V3 **Research Contact** Michael Fung, Tanox Biosystem, USA **References** Gorny2004, Yang1998, D'Souza1995 **Keywords** assay development, review, variant cross-recognition or cross-neutralization. • TH1: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. TH1 neutralizes some TCLA strains. [Gorny2004] (**review**) • TH1: A neutralization assay was developed based on hemi-nested PCR amplification of the LTR (HNPCR) – LTR-HNPCR consistently revealed HIV DNA and was shown to be a rapid, specific and reliable neutralization assay based on tests with 6 MAbs and 5 isolates. [Yang1998] (**assay development**) • TH1: Found to neutralize MN and JRCSF, but not two B subtype primary isolates, nor a D subtype primary isolate, by most labs in a multi-laboratory study involving 11 labs. [D'Souza1995] (**variant cross-recognition or cross-neutralization**)					
1109	anti-gp120/V3	Env	gp120			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* A clade 94UG018 *HIV component:* Gag, gp120, Nef, Pol **Ab type** V3 **Research Contact** Intracel Co **References** Buonaguro2001 • Anti-V3: HIV-1 pr55 gag-based virus-like particles (VLP) carrying Nef and Pol open reading frames as well as gp120 of the clade A isolate 94UG018 were created using a Baculovirus expression system to package additional ORFS into the VLP – anti-V3 and anti-p24 antibodies were used to assess the expression levels and Gag and gp120-TM were found to be expressed at comparable levels on the VLP. [Buonaguro2001]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1110	polyclonal	Env	gp120		no	Vaccine	mouse

Vaccine *Vector/Type:* protein, virus-like particle (VLP) *Strain:* B clade LAI *HIV component:* CD4BS, Gag, V3
Ab type V3
References Truong1996

- Antibodies raised against recombinant anti-p55 virus-like particles with the p24 region 196-226 deleted, bearing inserts of either the V3 or the CD4BS regions of gp120 were studied – no neutralizing responses, weak Env, and strong Gag responses were elicited – the major homology region (MHR) and proximal sequences was found to be required for capsid assembly. [Truong1996]

1111	polyclonal	Env	gp120		yes	Vaccine	human

Vaccine *Vector/Type:* canarypox prime with recombinant protein boost *Strain:* B clade LAI, B clade MN, B clade SF2 *HIV component:* Gag, gp120, gp41, Pol *Adjuvant:* MF59
Ab type V3
References Verrier2000

- Serum Abs elicited by this vaccine reacted with V3 peptides from clades B, C, and F, reacted weakly with V3 peptides from clades A, D, G, and H, and did not react with V3 peptides from clades E and O – neutralizing activity against 5 of 14 primary isolates tested was observed, including one B clade X4 virus, two dualtropic B clade viruses (from clade B) and one clade B and one clade C R5 virus. [Verrier2000]

1112	polyclonal	Env	gp120 (303–325)		no	in vitro stimulation or selectio	human (IgM)

Ab type V3
References Sidorova1999

- Polyspecific anti-MN-24 antibodies were raised through V3 peptide, MN-24 stimulation of human cells, followed by EBV transformation: they react with homologous and heterologous peptides and may be autoantibodies. [Sidorova1999]

1113	polyclonal	Env					human

Ab type V3
References Guevara2002

- Viral RNA in serum and high titers of subtype C consensus V3 peptide binding Abs were the best independent predictors of mother to infant transmission of HIV-1 subtype C – NAb to subtype B HIV-1(MN) was also correlated. [Guevara2002]

1114	polyclonal	Env			L	Vaccine	mouse (IgA)

Vaccine *Vector/Type:* HIV-1 captured on concavalin A-immobilized polystyrene nanospheres, Con A-NS *Strain:* B clade IIIB *HIV component:* gp120, heat-inactivated virus *Adjuvant:* concavalin A-immobilized polystyrene nanospheres
Ab type V3
References Kawamura2002

- Vaginal fluids were collected after intravaginal immunization of BALB/c mice and analyzed for their anti-HIV-1 antibody levels using a IIIB-V3 ELISA and IIIB neutralization assay – HIV-1 specific IgG was undetectable but anti-HIV IgA antibody response was identified in the vaginal fluids of immunized mice with HIV concavalin A-immobilized polystyrene nanosheres. [Kawamura2002]

1115	polyclonal	Env			L	Vaccine	human (IgA, IgG1, IgG2a)

Vaccine *Vector/Type:* peptide *Strain:* B clade 89.6P, B clade MN *HIV component:* Env *Adjuvant:* aluminum hydroxide, Cholera toxin (CT), GM-CSF, IL-12, IL-18, IL-1alpha
Ab type V3

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Bradney2002					
		• The cytokine-adjuvant combination IL-1alpha, IL-12 and IL-18 were found to stimulate potent mucosal antibody responses upon intranasal immunization of mice – cholera toxin is the most widely used adjuvant, but is not safe for use in humans. [Bradney2002]					
1116	polyclonal	Env				Vaccine	mouse
		Vaccine *Vector/Type:* peptide *Strain:* multiple epitope immunogen *HIV component:* V3 *Adjuvant:* Complete Freund's Adjuvant (CFA)					
		Ab type V3					
		References Hewer2002					
		• A synthetic peptide immunogen designated a multiple epitope immmunogen (MEI) was generated by synthesizing peptides with mixtures of frequently found amino acids (>10%) from the C subtypes allowed in the synthetic peptide – when injected into mice, the C subtype MEI induced antibodies that recognized the immunogen and whole virus as an antigen in ELIZAs – sera from eight HIV positive South Africans recognized the MEI peptide in ELISA tests. [Hewer2002]					
1117	11/75a/21/41	Env	gp120				
		Ab type V3 discontinuous					
		References Peet1998, McKeating1992a					
		• 11/75a/21/41: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, but anti-V3 MAb 11/75a/21/41 binding was dramatically diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]					
1118	41.1 (ICR41.1i, ICR41)	Env	gp120 (HXB10)		L (HXB2)	Vaccine	rat (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* gp120					
		Ab type V3 discontinuous **Research Contact** J. Cordell, Institute for Cancer Research, Sutton, Surrey, UK					
		References Ugolini1997, Jeffs1996, Armstrong1996b, Armstrong1996a, McLain1994, Klasse1993a, McKeating1993b, McKeating1992a, Reitz1988					
		• 41.1: Viral binding inhibition by 41.1 was weakly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997]					
		• 41.1: Deletion of the V1V2 regions did not affect anti-V3 Abs ability to bind when compared to intact rec gp120. [Jeffs1996]					
		• 41.1: Called ICR41.1i – Neutralization occurs by blocking a post-fusion internalization event, in contrast to MAb F58. [Armstrong1996b]					
		• 41.1: Called ICR41.1i – IgG2c? – Neutralization was affected if the Ab was added after the virus bound to the host cells at 24 degrees C or below. [Armstrong1996a]					
		• 41.1: Called ICR41.1i – Kinetics of neutralization studied – no lag for 39.3b, while ICR 39.13g and ICR 41.1i have lags of 5 and 15 min respectively – neutralization mediated by 3 molecules of IgG per virion – most efficient at neutralization of the three MAbs studied – acts with multi-hit kinetics. [McLain1994]					
		• 41.1: The gp41 mutation 582(Ala to Thr) results in conformational changes in gp120 that confer neutralization resistance to conformationally sensitive neutralizing MAbs – neutralization efficiency of 41.1 is not affected. [Klasse1993a, Reitz1988]					
1119	55/45a/1l	Env	gp120				
		Ab type V3 discontinuous					
		References Peet1998					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 55/45a/11: The most variable amino acids in the V3 loop were replaced with serines to make the immunodominant V3 loop less immunogenic – these changes did not affect the ability of sCD4 or MAbs to V1/V2, C1 and C4 to bind, and anti-V3 MAb 55/45a/11 binding was only marginally diminished by V3 serine substitutions – mice injected with serine substituted gp120 had a reduced response relative to wildtype, and no enhanced immunogenicity of conserved regions. [Peet1998]					
1120	1108	Env	Env			HIV-1 infection	human (IgG1λ)
		Ab type V3 mimotope **References** Gorny2004, Zolla-Pazner1999b, Zolla-Pazner1999a **Keywords** antibody binding site definition and exposure, antibody generation, mimotopes, review. • 1108: This review provides summaries of Abs that bind to HIV-1 Env. There are many V3 MAbs, many neutralize some TCLA strains, and a subset can also neutralize some primary isolates. [Gorny2004] (**review**) • 1108: The sequence of peptide 987, used to select MAb 1108, is ADGAWRSVHLGPGRGSGSGMGK. [Zolla-Pazner1999a] (**antibody binding site definition and exposure**, **antibody generation**) • 1108: Selected with peptide 987, a mimotope of anti-V3 MAb 447-D – MAb peptide reactivity pattern clustered with immunological related MAbs: 1108, 386, 268, 311, 257, 694.8 – the amino acids HI tended to be critical for reactivity in this group. [Zolla-Pazner1999b] (**antibody binding site definition and exposure**, **antibody generation**, **mimotopes**)					
1121	polyclonal	Env				HIV-1 infection	human (IgA, IgG)
		Ab type V3, V4 **References** Skott1999 • IgA and IgG from 45 HIV+ individuals was studied – people with low CD4+ cell counts had decreased levels IgA in saliva – sera and saliva IgA was primarily directed toward Env – peptide ELISA studies indicated that teh dominant IgA epitopes were the V4 region (aa 385-409) and the C-term part of the V3 loop (aa 325-344), while the IgG response was directed towards the tip of the loop (aa 308-325) [Skott1999]					
1122	polyclonal	Env	gp120 (IIIB)			Vaccine	rabbit
		Vaccine *Vector/Type:* peptide *Strain:* B clade MN *HIV component:* gp120 *Adjuvant:* Cholera toxin (CT) **Ab type** V3-C4 **References** Zinckgraf1999 • Nasal mucosal immunization and boosting of HIV peptide and was superior for inducing serum IgG and vaginal secretory IgA compared to nasal immunization and vaginal boosting – vaginal immunization and boosting resulted low serum IgG and vaginal IgA and a high vaginal IgG response. [Zinckgraf1999]					
1123	D27	Env	gp120 (IIIB)			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140 **Ab type** V3 **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Otteken1996, Earl1994 • D27: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D27 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D27 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding. [Sugiura1999] • D27: Pulse label experiments of 4 MAbs (D20, D27, T20, and T22) binding to noncleavable gp160 revealed that these anti-CD4 MAbs bound with a delay, and that the epitope formed with a t 1/2 of about 10 minutes. [Otteken1996] • D27: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1124	D56	Env	gp120 (IIIB)		L	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade IIIB *HIV component:* oligomeric gp140					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Ab type V3 **Research Contact** P. Earl, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD **References** Sugiura1999, Earl1994 • D56: A comparison of 25 gp120 specific, conformation dependent MAbs was done – D56 is one of two MAbs labeled group Ca, that was type-specific for BH8 – D56 fully blocked CD4 binding, and the deletion of the V3 loop abrogated binding – 12.5 ug/ml of D56 was required to achieve 50% neutralization of HIV-1 NL4-3. [Sugiura1999] • D56: Generated during a study of the influence of the oligomeric structure of Env in determining the repertoire of the Ab response. [Earl1994]					
1125	2G12 (c2G12)	Env	gp120		L P	HIV-1 infection	human (IgG1κ)

Ab type carbohydrates at glycosylation residues in C2, C3, C4, and V4 **Research Contact** Herman Katinger, Inst. Appl. Microbiol. or Polymun Scientific Inc., Vienna, Austria,

References Gorny2004, Pantophlet2003b, Zwick2003, Wolbank2003, Ohagen2003, Montefiori2003, Louis2003, Kitabwalla2003, Raja2003, Singh2003, Wang2003, Richman2003, Mascola2003a, Hart2003, Ferrantelli2003, Dey2003, Cavacini2003, Binley2003, Abrahamyan2003, Albu2003, Herrera2003, Pantophlet2003a, Stiegler2002, Kwong2002, Gorry2002, Cavacini2002, Bures2002, Liu2002, Ferrantelli2002, Zhang2002, Mascola2002, Grundner2002, Edwards2002, Armbruster2002, Chakrabarti2002, Xu2002, Yang2002, Schulke2002, Scanlan2002, Sanders2002, Golding2002b, Savarino2001, Xu2001, Hofmann-Lehmann2001, Spenlehauer2001, Stiegler2001, Verrier2001, Zeder-Lutz2001, Poignard2001, Moore2001, Barnett2001, Zwick2001c, Mascola2001, Si2001, Park2000, Grovit-Ferbas2000, Baba2000, Robert-Guroff2000, Binley1999, Mascola2000, Mascola1999, Parren1999, Poignard1999, Crawford1999, Altmeyer1999, Beddows1999, Montefiori1999, Schonning1998, Kunert1998, Frankel1998, Wyatt1998b, Li1998, Parren1998b, Takefman1998, Fouts1998, Trkola1998, Binley1998, Connor1998, Sullivan1998b, Parren1998a, Mondor1998, Wyatt1998a, Andrus1998, Parren1997c, Burton1997, Ugolini1997, Mascola1997, Moore1997, Li1997, Fouts1997, Binley1997a, Mo1997, D'Souza1997, Sattentau1996, Trkola1996a, Poignard1996b, Moore1996, Trkola1996b, McKeating1996a, McKeating1996b, Moore1995b, Trkola1995, Buchacher1994

Keywords acute infection, antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, assay development, autologous responses, brain/CSF, co-receptor, complement, escape, immunoprophylaxis, immunotherapy, inter-clade comparisons, isotype switch, kinetics, mother-to-infant transmission, mucosal immunity, review, vaccine antigen design, variant cross-recognition or cross-neutralization.

- 2G12: This paper is a reviw of anti-HIV-1 Envelope antibodies. This unique epitope is formed from carbohydrates. The mechanism of MAb neutralization is thought to be steric inhibition of CCR5 binding. 2G12 neutralizes many TCLA strains and about 40% of primary isolates tested. [Gorny2004] (**review**)
- 2G12: A gp120 molecule was designed to focus the immune response onto the IgG1b12 epitope. Ala substitutions that enhance the binding of IgG1b12 and reduce the binding of non-neutralizing MAbs were combined with additional N-linked glycosylation site sequons inhibiting binding of non-neutralizing MAbs; b12 bound to the mutated gp120. C1 and C5 were also removed, but this compromised b12 binding. [Pantophlet2003b] (**vaccine antigen design**)
- 2G12: scFv 4KG5 reacts with a conformational epitope. Of a panel of MAbs tested, only NAb b12 enhanced 4KG5 binding to gp120. MAbs to the V2 loop, V3 loop, V3-C4 region, and CD4BS diminished binding, while MAbs directed against C1, CD4i, C5 regions didn't impact 4KG5 binding. These results suggest that the orientation or dynamics of the V1/V2 and V3 loops restricts CD4BS access on the envelope spike, and IgG1b12 can uniquely remain unaffected. 2G12 had no impact on 4KG5 binding. [Zwick2003] (**antibody interactions**)
- 2G12: The broadly neutralizing antibodies 2F5 and 2G12 were class-switched from IgG to IgA and IgM isotypes. Neutralizing potency was increased with valence for 2G12 so the IgM form was most potent, but for 2F5 the IgG form was most potent. Eight primary isolates were tested including two subtype A isolates. The polymeric IgM and IgA Abs, but not the corresponding IgGs, could interfere with HIV-1 entry across a mucosal epithelial layer, although they were limited in a standard neutralization assay. All isotypes could interact with activated human sera, presumably through complement, to inhibit HIV replication. [Wolbank2003] (**complement**, **isotype switch**, **variant cross-recognition or cross-neutralization**, **mucosal immunity**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: The antiviral response to intravenously administered MAbs 2F5 and 2G12 was evaluated in 7 HAART-naïve asymptomatic HIV-1 infected patients during a treatment period of 28 days. MAb therapy reduced plasma HIV RNA in 3/7 patients during the treatment period, and transiently reduced viral load in two more. CD4 counts were up in 3/7 through day 28, and transiently increased in three more. Vigorous complement activation was observed after 48/56 Ab infusions. Virus derived from 2/7 patients could be neutralized by 2G12, and escape from 2G12 was observed in both cases after infusion; one year after the infusion, isolates were again sensitive to 2G12. [Stiegler2002] (**complement**, **variant cross-recognition or cross-neutralization**, **escape**, **immunotherapy**)
- 2G12: Env genes derived from uncultured brain biopsy samples from four HIV-1 infected patients with late-stage AIDS were compared to env genes from PBMC samples. Brain isolates did not differ in the total number or positions of N-glycosylation sites, patterns of coreceptor usage, or ability to be recognized by gp160 and gp41 MAbs. 2G12 was the only MAb tested to recognize all blood and brain isolates from all four patients by gp120 immunoprecipitation. [Ohagen2003] (**variant cross-recognition or cross-neutralization**)
- 2G12: AC10 is a subject who was given treatment early after infection, and had a viral rebound after cessaton of therapy, which then declined to a low level. The polylconal sera from AC10 could potently neutralize the rebound virus, and NAb escape followed with a neutralizing response against the escape variant and subsequent escape from that response. Viral loads remained low in this subject despite escape. The rebound isolate that was potently neutralized by autologous sera was not particularly neutralization sensitive, as it resisted neutralization by sCD4 and MAbs IgG1b12, 2G12 and 2F5, and was only moderately sensitive to sera from other HIV+ individuals that had high titers of NAbs to TCLA strains. [Montefiori2003] (**acute infection**, **escape**)
- 2G12: Polyclonal Abs raised against soluble trivalently linked N35CCG-N13 and N34CCG, the internal trimeric core of the coiled-coil ectodomain, inhibit HIV-1 Env-mediated cell fusion at levels comparable to 2G12. [Louis2003] (**vaccine antigen design**)
- 2G12: Thermodynamics of binding to gp120 was measured using isothermal titration calorimetry for sCD4, 17b, b12, 48d, F105, 2G12 and C11 to intact YU2 and the HXBc2 core. The free energy of binding was similar, except for 2G12, which might not have bound well to the carbohydrate additions on the Drosophila expressed core. Enthalpy and entropy changes were divergent, but compensated. Not only CD4 but MAb ligands induced thermodynamic changes in gp120 that were independent of whether the core or the full gp120 protein was used. Non-neutralizing CD4BS and CD4i MAbs (17b, 48d, 1.5e, b6, F105 and F91) had large entropy contributions to free energy (mean: 26.1 kcal/mol) of binding to the gp120 monomer, but the potent CD4BS neutralizing MAb b6 had a much smaller value of 5.7 kcal/mol, The high values suggest surface burial or protein folding an ordering of amino acids. 2G12 had an entropy value of -1.6. These results suggest that while the trimeric Env complex has four surfaces, a non-neutralizing face (occluded on the oligomer), a variable face, a neutralizing face and a silent face (protected by carbohydrate masking), gp120 monomers further protect receptor binding sites by conformational or entropic masking, requiring a large energy handicap for Ab binding not faced by other anti-gp120 Abs. [Kwong2002] (**antibody binding site definition and exposure**)
- 2G12: MAbs IgG1b12, 2G12, 2F5 and 4E10 were tested for their ability to neutralize two primary HIV-1 clade A isolates (UG/92/031 and UG/92/037) and two primary HIV-1 clade D isolates (UG/92/001 and UG/92/005). 4E10 demonstrated the most potent cross-neutralization activity. Quadruple administration of MAbs IgG1b12, 2G12, 2F5, and 4E10 induced strong synergistic neutralization of 4 clade A isolates (UG/92/031, UG/92/037, RW/92/020 and RW/92/025) as well as 5 clade D isolates (UG/92/001,UG/9/005, /93/086/RUG/94/108, UG/94/114). The authors note this combination of 4 MAbs neutralizes primary HIV A, B, C, and D isolates. [Kitabwalla2003] (**antibody interactions**, **immunoprophylaxis**, **variant cross-recognition or cross-neutralization**, **mother-to-infant transmission**, **inter-clade comparisons**)
- 2G12: This paper shows that binding of CD4BS MAbs to Env blocks the conformational shift that allows co-receptor CCR5 binding and CD4-independent mediated cell fusion. CD4BS MAbs IgG1b12, F91 and F105 and their Fab counterparts (except for C11, used as a negative control) inhibited CD4-independent JR-FL and YU-2 gp120-CCR5 binding to CCR5-expressing Cf2Th cells and syncytium formation. The carbohydrated binding MAb 2G12 also inhibited CD4-independent syncytium formation. [Raja2003] (**co-receptor**)
- 2G12: To begin to design vaccine antigens that can mimic the carbohydrate structure, the gp120 peptide 336-342 was synthesized with Man(9), Man(6), and Man(5) moieties attached. [Singh2003] (**vaccine antigen design**)

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- 2G12: Review of current neutralizing antibody-based HIV vaccine candidates and strategies of vaccine design. Strategies for targeting of the epitopes for NAbs 2F5, 2G12, 4E10, b12, and Z13 are described. They have shown that both N-glycans, at 295N and 332N are required for 2G12 binding, emphasizing the oligosaccharide cluster nature of the epitope, and suggest the uniqueness of the target structure may not result in autoimmune reactions. [Wang2003] (**vaccine antigen design**, **review**)
- 2G12: Most plasma samples of patients from early infection had NAb responses to early autologous viruses, and NAbs against heterologous strains tended to be delayed. Serial plasma samples were tested against serial isolates, and neutralization escape was shown to be rapid and continuous throughout infection. Autologous neutralization-susceptible and resistant viruses from four patients were tested for susceptability to neutralizing Ab responses using MAbs 2G12, IgG1b12 and 2F5. No correlation was established, all viruses tested were susceptible to at least one of the neutralizing MAbs. Two patients that did not have an autologous NAb response also did not evolve changes in susceptibility to these MAbs, while one patient with a pattern of autologous neutralization and escape acquired a 2G12 sensitive virus at month 6, and lost IgG1b12 sensitivity at month 21. [Richman2003] (**autologous responses**, **acute infection**, **escape**)
- 2G12: This review dicusses the importance and function of protective antibody responses in animal model studies in the context of effective vaccine development. SHIV models have shown protection using high levels of MAbs can prevent infection, and partial protection that can influence disease course can be obtained from modest levels of NAbs. SHIV challenges studies conducted with infusions of combinations of MAbs b12, 2G12, and 2F5 are reviewed. [Mascola2003a] (**immunoprophylaxis**, **review**)
- 2G12: This study investigates the effects of glycosylation inhibitors on the binding between HIV-1 gp120 and mannose-binding lectin (MBL). Mannosidase I inhibitor deoxymannojirimycin (dMM) inhibits formation of complex and hybrid N-linked saccharides and yields virus with more mannose residues. dMM added during viral production significantly enhanced the binding 2F5 and 2G12, but not IgG1b12 in a viral capture assay. [Hart2003] (**antibody binding site definition and exposure**)
- 2G12: UK1-br and MACS2-br are R5 isolates derived from brain tissue samples from AIDS patients with dementia and HIV-1 encephalitis; both are neurotropic, but only UK1-br induced neuronal apoptosis and high levels of syncytium formation in macrophages. UK1-br Env had a greater affinity for CCR5 than MACS-br, and required low levels of CCR5 and CD4 for cell-to-cell fusion and single round infection. PBMC infected with UK1-br and MACS2-br virus isolates were resistant to neutralization by MAb 2G12. UK1-br was more sensitive than MACS2-br to IgG1b12, 2F5 and CD4-IgG2 neutralization. [Gorry2002] (**brain/CSF**, **co-receptor**)
- 2G12: Four newborn macaques were challenged with pathogenic SHIV 89.6 and given post exposure prophylaxis using a combination of NAbs 2F5, 2G12, 4E10 and IgG1b12. 2/4 treated animals did not show signs of infection, and 2/4 macaques maintained normal CD4+ T cell counts and had a lower delayed peak viremia compared to the controls. [Ferrantelli2003] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: A sCD4-17b single chain chimera was made that can bind to the CD4 binding site, then bind and block co-receptor interaction. This chimeric protein is a very potent neutralizing agent, more potent than IgG1b12, 2G12 or 2F5 against Ba-L infection of CCR5-MAGI cells. It has potential for prophylaxis or therapy. [Dey2003] (**co-receptor**)
- 2G12:The MAb B4e8 binds to the base of the V3 loop, neutralizes multiple primary isolates and was studied for interaction with other MAbs. B4e8 and 2G12 enhanced each others binding, and gave synergistic neutralization. B4e8 could neutralize R5X4 virus 92HT593 better than 2G12, while 2G12 was better at neutralizing R5 virus 92US660. [Cavacini2003] (**antibody interactions**)
- 2G12: This study examined Ab interactions, binding and neutralization with a B clade R5 isolate (92US660) and R5X4 isolate (92HT593). Abs generally bound and neutralized the R5X4 isolate better than the R5 isolate. Anti-gp41 MAb F240 did not affect binding of 2G12 to either R5X4 and R5 isolates, and anti-V3 MAb B4a1 increased 2G12 binding to R5X4 virions but not R5. Neutralization with B4al and 2G12 was additive for the R5X4 virus, and was enhanced for the R5 virus. [Cavacini2002] (**antibody interactions**, **co-receptor**, **variant cross-recognition or cross-neutralization**)
- 2G12: Neutralization assays with rsCD4, MAbs, and serum samples from SHIV-infected macaques and HIV-1 infected individuals were used to characterize the antigenic properties of the env glycoprotein of six primary isolate-like or TCLA SHIV variants. 2G12 neutralized the five SHIV strains tested, HXBc2, KU2, 89.6, 89.6P and KB9, in MT-2 cells. [Crawford1999] (**variant cross-recognition or cross-neutralization**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: The SOS mutant envelope protein introduces a covalent disulfide bond between gp120 surface and gp41 transmembrane proteins into the R5 isolate JR-FL by adding cysteines at residues 501 and 605. Pseudovirions bearing this protein bind to CD4 and co-receptor bearing cells, but do not fuse until treatment with a reducing agent, and are arrested prior to fusion after CD4 and co-receptor engagement. 2G12 is able to neutralize both the wildtype and SOS protein comparably, but 2G12 could not neutralize SOS when added post-attachment. [Binley2003] (**vaccine antigen design**)
- 2G12: IgG1b12 neutralized many South African (5/8) and Malawian (4/8) clade C primary HIV-1 isolates, being more effective than 2F5 which neutralized only two Malawian and no South African isolates. 2G12 did not neutralize any of the 16 isolates. [Bures2002] (**inter-clade comparisons**)
- 2G12: SOS-Env is a mutant protein engineered to have a disulfid bond between gp120 and gp41. Cells expressing SOS-Env due not fuse with target cells expressing CD4 and CCR5, although the fusion process proceeds to an intermediate state associated with CD4 and co-receptors, prior to the formation of the six helix bundle that allows fusion.2G12 was used to monitor surface expression of SOS-Env compared to wildtype. [Abrahamyan2003] (**co-receptor**, **vaccine antigen design**)
- 2G12: 2G12 was used as a positive control to test for a NAb activity in mice intranasally immunized with gp120 or gp140 with IL-12 and Cholera Toxin B. [Albu2003]
- 2G12: NIH AIDS Research and Reference Reagent Program: 1476.
- 2G12: UK Medical Research council AIDS reagent: ARP3030.
- 2G12: CD4BS MAbs b12 (neutralizing) and 205-42-15, 204-43-1, 205-46-9 (non-neutralizing) all cross-competed for binding to monomeric gp120, indicating the topological proximity of their epitopes, however, the non-neutralizing CD4BS MAbs did not interfere with the neutralization activity of MAb b12 – 2G12 was used to normalize and as a control in these experiments. [Herrera2003] (**antibody interactions**)
- 2G12: Alanine scanning mutagenesis was used to compare substitutions that affected anti-CD4BS NAb b12 – rec gp120s were engineered to contain combinations of Alanine substitutions that enhanced b12 binding, and while binding of b12 to these gp120 monomers was generally maintained or increased, binding by five non-neutralizing anti-CD4bs MAbs (b3, b6, F105, 15e, and F91) was reduced or completely abolished – 2G12 binding was largely unperturbed, indicating these proteins were not grossly misfolded. [Pantophlet2003a] (**antibody binding site definition and exposure**)
- 2G12: Review of NAbs that discusses mechanisms of neutralization, passive transfer of NAbs and protection in animal studies, and vaccine strategies. [Liu2002] (**review**)
- 2G12: Review of NAbs that notes 2G12 alone or in combination with other MAbs can protect some macaques against SHIV infection, that it has strong ADCC activity, and that it is safe and well tolerated in humans. [Ferrantelli2002] (**immunoprophylaxis**)
- 2G12: A rare mutation in the neutralization sensitive R2-strain in the proximal limb of the V3 region caused Env to become sensitive to neutralization by MAbs directed against the CD4 binding site (CD4BS), CD4-induced (CD4i) epitopes, soluble CD4 (sCD4), and HNS2, a broadly neutralizing sera – 2/12 anti-V3 MAbs tested (19b and 694/98-D) neutralized R2, as did 2/3 anti-CD4BS MAbs (15e and IgG1b12), 2/2 CD4i MAbs (17b and 4.8D), and 2G12 and 2F5 – thus multiple epitopes on R2 are functional targets for neutralization and the neutralization sensitivity profile of R2 is intermediate between the highly sensitive MN-TCLA strain and the typically resistant MN-primary strain. [Zhang2002] (**antibody binding site definition and exposure**)
- 2G12: Rhesus macaques were better protected from vaginal challenge with SHIV89.6D (MAb 2G12, 2/4; MAbs 2F5/2G12, 2/5; and HIVIG/2F5/2G12, 4/5 infected) than from intravenous challenge (MAb 2G12, 0/3; MAbs 2F5/2G12, 1/3; and HIVIG/2F5/2G12, 3/6 infected)– the animals that were infected by vaginal challenge after Ab infusion had low or undetectable viral RNA levels and modest CD4 T-cell decline. [Mascola2002] (**immunoprophylaxis**, **mucosal immunity**)
- 2G12: HIV-1 gp160deltaCT (cytoplasmic tail-deleted) proteoliposomes (PLs) containing native, trimeric envelope glycoproteins from R5 strains YU2 and JRFL, and X4 strain HXBc2, were made in a physiologic membrane setting as candidate immunogens for HIV vaccines – 2F5 bound to gp160deltaCT with a reconstituted membrane ten-fold better than the same protein on beads, while such an affinity difference was not seen with F105 and 2G12 – anti-CD4BS MAbs IgG1b12 and F105, A32 (C1-C4), C11 (C1-C5), and 39F (V3) MAbs bound gp160deltaCT PLs indistinguishably from gp160deltaCT expressed on the cell surface. [Grundner2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)

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- 2G12: Truncation of the gp41 cytoplasmic domain of X4, R5, and X4R5 viruses forces a conformation that more closely resembles the CD4 bound state of the external Envelope, enhancing binding of CD4i MAbs 17b and 48d and of CD4BS MAbs F105, b12, and in most cases of glycosylation site dependent MAb 2G12 and the anti-gp41 MAb 246D – in contrast, binding of the anti-V2 MAb 697D and the anti-V3 MAb 694/98D were not affected – viruses bearing the truncation were more sensitive to neutralization by MAbs 48d, b12, and 2G12 – the anti-C5 MAb 1331A was used to track levels of cell surface expression of the mutated proteins. [Edwards2002] (**antibody binding site definition and exposure**)
- 2G12: A modified gp140 (gp140deltaCFI), with C-term mutations intended to mimic a fusion intermediate and stabilize trimer formation, retained antigenic conformational determinants as defined by binding to CD4 and to MAbs 2F5, 2G12, F105, and b12, and enhanced humoral immunity without diminishing the CTL response in mice injected with a DNA vaccine. [Chakrabarti2002] (**vaccine antigen design**)
- 2G12: Passive immunization of neonate macaques with a combination of F105+2G12+2F5 conferred complete protection against oral challenge with SHIV-vpu+ or – the combination b12+2G12+2F5 conferred partial protection against SHIV89.6 – such combinations may be useful for prophylaxis at birth and against milk born transmission – the synergistic combination of IgG1b12, 2G12, 2F5, and 4E10 neutralized a collection of HIV clade C primary isolates. [Xu2002] (**antibody interactions**, **immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: Uncleaved soluble gp140 (YU2 strain, R5 primary isolate) can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif or using a T4 trimeric motif derived from T4 bacteriophage fibritin – stabilized oligomer gp140 delta683(-FT) showed strong preferential recognition by NAbs IgG1b12 and 2G12 relative to the gp120 monomer, in contrast to poorly neutralizing MAbs F105, F91, 17b, 48d, and 39F which showed reduced levels of binding, and MAbs C11, A32, and 30D which did not bind the stabilized oligomer. [Yang2002] (**antibody binding site definition and exposure**)
- 2G12: Ab binding characteristics of SOS gp140 were tested using SPR and RIPA – SOS gp140 is gp120-gp41 bound by a disulfide bond – NAbs 2G12, 2F5, IgG1b12, CD4 inducible 17b, and 19b bound to SOS gp140 better than uncleaved gp140 (gp140unc) and gp120 – non-neutralizing MAbs 2.2B (binds to gp41 in gp140unc) and 23A (binds gp120) did not bind SOS gp140 – 2G12 complexes with SOS gp140 or with gp120 had a very unusual linear structure. [Schulke2002] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 2G12: Alanine scanning mutagenesis used in conjunction with competition and replacement studies of N-linked carbohydrates and sugars suggest that the 2G12 epitope is formed from mannose residues contributed by the glycans attached to N295 and N332, with the other N-linked carbohydrates in positions N339, N386, and N392 playing a role in maintaining conformation relevant to 2G12 binding – N295A and N332A mutants showed essentially unchanged anti-CD4BS NAb b12 binding affinities, while N339A, N386A and N392A mutants displayed significantly lowered b12 affinity, presumably due to conformational changes. [Scanlan2002] (**antibody binding site definition and exposure**)
- 2G12: The 2G12 epitope is composed of carbohydrates involving high-mannose and hybrid glycans of residues 295, 332, and 392, with peripheral glycans from 386 and 448 contributing on either flank, and with little direct gp120 protein surface involvement – these mannose residues are proximal to each other near the chemokine receptor binding surface. [Sanders2002] (**antibody binding site definition and exposure**)
- 2G12: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – the preincubation 31.5 C step did not alter the inhibitory activity of neutralizing Abs anti-gp41 2F5, or anti-gp120 2G12, IG1b12, 48d, and 17b. [Golding2002b] (**antibody binding site definition and exposure**)
- 2G12: A phase I trial in seven HIV+ individuals was conducted with MAbs 2F5 and 2G12 – no clinical or laboratory abnormalities were observed throughout the study – eight infusions were administered over a 4-week period (total dose 14 g) – the elimination half-life ($t\_1/2$) was calculated to be 7.94 (range, 3.46–8.31) days for 2F5 and 16.48 (range, 12.84–24.85) days for 2G12. [Armbruster2002] (**kinetics**, **immunotherapy**)
- 2G12: Chloroquine reduces the HIV-1-infectivity of H9 IIIB cells, apparently through altering the conformation of envelope – there is a reduction of reactivity of 2G12 to its epitope in chloroquine treated cultures. [Savarino2001] (**antibody binding site definition and exposure**)
- 2G12: Twenty HIV clade C isolates from five different countries were susceptible to neutralization by anti-clade B MAbs in a synergistic quadruple combination of mAbs IgG1b12, 2G12, 2F5, and 4E10. [Xu2001] (**antibody interactions**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: A combination of MAbs IgG1b12, 2F5, and 2G12 was given postnatally to four neonates macaques that were then challenged with highly pathogenic SHIV89.6P – one of the four infants remained uninfected after oral challenge, two infants had no or a delayed CD4(+) T-cell decline. [Hofmann-Lehmann2001] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**)
- 2G12: A luciferase-reporter gene-expressing T-cell line was developed to facilitate neutralization and drug-sensitivity assays – luciferase and p24 antigen neutralization titer end points were found comparable using NAb from sera from HIV+ donors, and MAbs 2F5, 2G12 and IgG1b12. [Spenlehauer2001] (**assay development**)
- 2G12: Neutralizing synergy between MAbs 1b12, 2G12 and 2F5 was studied using surface plasmon resonance to determine the binding kinetics for these three MAbs with respect to monomeric and oligomeric Env protein gp160 IIIB – the 2G12 epitope is highly accessible on both monomeric and oligomeric Envs, 1b12 is highly accessible on monomers but not oligomers, and 2F5 on neither form – binding of 2G12 exposes the 2F5 epitope on gp160 oligomers – 2G12-gp160 oligomer interactions were best fitted to a two state model, with the first complex having a high association constant and fast dissociation, stabilized by conformational changes induced by the binding of a second MAb. [Zeder-Lutz2001] (**antibody binding site definition and exposure**, **antibody interactions**, **kinetics**)
- 2G12: Structural aspects of the interaction of neutralizing Abs with HIV-1 Env are reviewed – Env essentially has three faces, one is largely inaccessible on the native trimer, and two that exposed but have low immunogenicity on primary viruses – neutralization is suggested to occur by inhibition of the interaction between gp120 and the target cell membrane receptors as a result of steric hindrance and it is noted that the attachment of approximately 70 IgG molecules per virion is required for neutralization, which is equivalent to about one IgG molecule per spike – the 2G12, 17b and b12 epitopes are discussed in detail – although it is potently neutralizing, 2G12 does not interfere with CD4 and coreceptor binding, and this Ab specificity is uncommon in sera from HIV-1-infected individuals. [Poignard2001] (**antibody binding site definition and exposure**, **review**)
- 2G12: Moore and colleagues review structural aspects of gp120 and how they relate to antigenic domains, and review the data concerning the lack of a clear relationship between genetic subtype and serotype – an exception exists for human MAb 2G12, which does not recognize CRF01 envelopes because of an unusual additional disulfide bond in the V4 loop region that appears to be unique to the subtype E, CRF01 gp120 protein. [Moore2001] (**antibody binding site definition and exposure**, **review**)
- 2G12: SF162DeltaV2 is a virus that has a 30 amino acids deletion in the V2 loop that does not abrogate its infectivity but renders it highly susceptible to neutralization – when incorporated into a codon-optimized DNA vaccine with a CMV promoter and delivered by gene gun, SF162DeltaV2 gave higher neutralizing Ab titers against SF162 than did SF162 itself, and Abs that cross-neutralized non-homologous primary isolates were obtained only when SF162DeltaV2, but not intact SF162, was used as the immunogen – Control MAbs 2F5 and 2G12 could neutralize all of the following primary isolates: 91US056(R5), 92US714(R5), 92US660(R5), 92HT593(R5X4), and BZ167(R5X4), while after the first protein boost, the sera from two SF162DeltaV2 immunized macaques could neutralize 91US056(R5), 92US714(R5), 92US660(R5) and ADA(R5), but not 92HT593(R5X4) or 92US657(R5) – the pattern of cross-recognition shifted after the second boost. [Barnett2001] (**vaccine antigen design**)
- 2G12: Review of studies in macaques that have shown immune control of pathogenic SHIV viremia, improved clinical outcome, and protection, and the implications of the observations for HIV vaccines. [Mascola2001] (**review**)
- 2G12: Neutralization synergy between anti-HIV NAbs b12, 2G12, 2F5, and 4E10 was studied – a classic fixed-ratio method was used, as well as a method where one Ab was fixed at a low neutralization titer and the other was varied – using primary isolates, a two-four fold enhancement of neutralization was observed with MAb pairs, and a ten-fold enhancement with a quadruple Ab combination – no synergy was observed with any MAb pair in the neutralization of TCLA strain HXB2 – there was no evidence for cooperativity of binding between b12 and 2G12 to envelope spikes expressed on the cell surface of TCLA or primary isolates. [Zwick2001c] (**antibody interactions**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: SHIV-HXBc2 is a neutralization sensitive non-pathogenic virus, and several *in vivo* passages through monkey's yielded highly pathogenic SHIV KU-1 – HXBc2 and the KU-1 clone HXBc2P3.2 differ in 12 amino acids in gp160 – substitutions in both gp120 and gp41 reduced the ability of sCD4, IgG1b12, F105 and AG1121 to Env achieve saturation and full occupancy, and neutralize KU-1 – 17b and 2F5 also bound less efficiently to HXBc2P3.2, although 2G12 was able to bind both comparably. [Si2001]
- 2G12: Six mutations in MN change the virus from a high-infectivity neutralization resistant phenotype to low-infectivity neutralization sensitive – V3, CD4BS, and CD4i MAbs are 20-100 fold more efficient at neutralizing the sensitive form – 2G12 was an exception and could not neutralize MN in either form. [Park2000]
- 2G12: To determine the antigenicity of virus killed by thermal and chemical inactivation, retention of conformation-dependent neutralization epitopes was examined, and exposure of CD4BS epitopes was found to be enhanced (MAbs IgG1b12, 205-46-9, and 205-43-1) – binding to 2G12 and 447-52D epitopes was essentially unaltered – the 17b CD4i epitope was also exposed. [Grovit-Ferbas2000] (**vaccine antigen design**)
- 2G12: A triple combination of 2F5, F105 and 2G12 effectively neutralized perinatal infection of macaque infants when challenged with SHIV-vpu+ – the mean plasma half-life was 14.0 +/- 7.9 days, the longest of the three Abs. [Baba2000] (**immunoprophylaxis**, **mother-to-infant transmission**)
- 2G12: A mini-review of observations of passive administration of IgG NAbs conferring protection against intervenous or vaginal SHIV challenge, that considers why IgG MAbs might protect against mucosal challenge. [Robert-Guroff2000] (**immunoprophylaxis**, **mucosal immunity**, **review**)
- 2G12: The MAbs with the broadest neutralizing activity, IgG1b12, 2G12 and 2F5, all have high affinity for the native trimer, indicating that they were raised in an immune response to the oligomer on the virion surface rather than dissociated subunits – a disulfide linked gp120-gp41 (SOS gp140) was created to mimic the native conformation of Env and explore its potential as an immunogen – SOS gp140 is recognized by NAbs IgG1b12, 2G12, and CD4-IgG2, and also by anti-V3 MAbs 19b and 83.1 – SOSgp140 is not recognized by C4 region MAbs that neutralize only TCLA strains, G3-42 and G3-519 – nor did it bind C11, 23A, and M90, MAbs that bind to gp120 C1 and C5, where it interacts with gp41 – MAbs that bind CD4 inducible epitopes, 17b and A32 were very strongly induced by CD4 in SOS gp140 – anti-gp41 MAbs that bind in the region that interacts with gp120, 7B2, 2.2B, T4, T15G1 and 4D4, did not bind to SOSgp140, in contrast to 2F5, which binds to the only gp41 epitope that is well exposed in native gp120-gp41 complexes. [Binley1999] (**antibody binding site definition and exposure**, **vaccine antigen design**)
- 2G12: Because HIV-1 is most often transmitted across mucosal surfaces, the ability of passive transfer of infused HIVIG/2F5/2G12 to protect against mucosal exposure of macaques to pathogenic SHIV 89.6PD was studied – HIVIG/2F5/2G12 protected 4/5 animals against vaginal challenge, 2F5/2G12 combined protected 2/5 animals, and 2G12 alone protected 2/4 animals – in contrast, Mascola and co-workers had previously shown single MAbs could not protect against intervenous challenge – Ab treated animals that got infected through vaginal innoculation had low viral loads and only modest declines in CD4 counts – the infused Abs were detected in the nasal, vaginal, and oral mucosa. [Mascola2000] (**immunoprophylaxis**, **mucosal immunity**)
- 2G12: Combinations of HIVIG, 2F5, 2G12 were administered in passive-transfer experiments 24 hours prior to challenge with pathogenic SHIV 89.6PD – 3/6 animals given HIVIG/2F5/2G12 were completely protected, the others had reduced viremia and normal CD4 counts – 1/3 monkeys given 2F5/2G12 showed transient infection, the other two had reduced viral load – all monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia, although animals that got HIVIG or 2G12 had a less profound CD4 T cell decline. [Mascola1999] (**antibody interactions**)
- 2G12: Review of the neutralizing Ab response to HIV-1. [Parren1999] (**review**)
- 2G12: Hu-PBL-SCID mice were infected with HIV-1s JRCSF and SF162 to study the effect of NAbs on an established infection – no significant differences in the initial rate of decrease in viral load or the plateau levels of viral RNA between the b12 treated and control mice were seen – in most of the Ab treated mice b12 escape mutants were observed with varying patterns of mutations – a combination of b12, 2G12 and 2F5 protected 1/3 mice, and an isolate from one of the other two was resistant to neutralization by all three MAbs. [Poignard1999] (**antibody interactions**, **escape**)
- 2G12: A Semliki Forest virus (SFV) expression system carrying BX08 Env was used to study the conformation of gp120 Env – intracytoplasmic gp120 was recognized by the anti-V3 MAbs K24 and F5.5, while gp120 at the plasma membrane was detected only by conformation dependent MAbs 2G12, 670-D and 694/98D and not V3 MAbs – expression in rat brain also showed that surface expressed Env was recognized only by the conformation-dependent Abs and not by anti-V3 Abs. [Altmeyer1999]
- 2G12: rgp120 derived from a R5X4 subtype B virus was used to vaccinate healthy volunteers and the resulting sera were compared with sera from HIV-1 positive subjects and neutralizing MAbs – 2G12 was able to bind with low affinity to the rgp120 monomer HIV-1 W61D. [Beddows1999]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: A meeting summary presented results regarding neutralization –MAbs 2G12 and 2F5 tested for their ability to neutralize primary isolate infection of genetically engineered cell lines (cMAGI and others, presented by T. Matthews, A. Trkola, J. Bradac) – an advantage of such cells lines over PBMCs is that markers (X-Gal) can be added for staining to simplify the assay – the consensus of the meeting was that these engineered cell lines did not improve the sensitivity of detection of primary isolate neutralization – D. Burton and J. Mascola presented results concerning passive immunization and protection of hu-PBL-SCID mice and macaques, respectively, and both found combinations of MAbs that were able to achieve 99% neutralization *in vitro* corresponded to efficacy *in vivo*. [Montefiori1999] (**review**)
- 2G12: Infection of dendritic cells cultured from CD14+ blood cells or from cadaveric human skin was blocked by neutralizing MAbs IgG1b12, or 2F5 and 2G12 delivered together, but not by control non-neutralizing anti-gp120 MAb 4.8D, indicating that NAbs could interrupt early mucosal transmission events. [Frankel1998] (**mucosal immunity**)
- 2G12: In a study of the influence of the glycan at position 306 of the V3 loop on MAb recognition, 2G12 was found to neutralize an HIV-BRU mutant virus that lacks the V3 loop glycan and has a mutation at the tip of the loop more efficiently than it neutralizes HIV-BRU. [Schonning1998] (**antibody binding site definition and exposure**)
- 2G12: The complete V, J and D(H) domain was sequenced – unlike non-neutralizing anti-gp41 MAb 3D6, five neutralizing MAbs (2F5, 2G12, 1B1, 1F7, and 3D5) showed extensive somatic mutations giving evidence of persistent antigenic pressure over long periods – 2G12 D(H) has the best homology to a D(H) segment between D3-22 and D4-23, a region not usually considered for heavy-chain rearrangement because it lacks associated recombination signals in the flanking regions, Kunert *et al.* suggest this may be why Abs that compete with 2G12 are rare. [Kunert1998] (**antibody sequence, variable domain**)
- 2G12: Review of the antigenic and receptor binding-domains of gp120 in relation to the structure of the molecule – MAbs are discussed by category (anti-V2, anti-V3, CD4i, CD4BS...), however as 2G12 binds to a rarely immunogenic region, and it is dependent on glycosylation, it was discussed individually. [Wyatt1998b] (**review**)
- 2G12: Neutralization synergy was observed when the MAbs 694/98-D (V3), 2F5 (gp41), and 2G12 (gp120 discontinuous) were used in combination, and even greater neutralizing potential was seen with the addition of a fourth MAb, F105 (CD4 BS) [Li1998] (**antibody interactions**)
- 2G12: MAbs 2G12, 2F5 and b12 are broadly neutralizing, as are some human polyconal sera, but this paper describes a set of primary isolates that are resistant to all three MAbs and 2 broadly neutralizing sera – results indicate that resistance levels of pediatric isolates might be higher than adult isolates – resistance in general did not seem to be conferred by a loss of binding affinity for gp120 or gp41, rather by a more global perturbation of oligomeric Envelope. [Parren1998b] (**variant cross-recognition or cross-neutralization**)
- 2G12: Induces complement-mediated lysis in MN but not primary isolates – primary isolates are refractive to CML. [Takefman1998] (**complement**, **variant cross-recognition or cross-neutralization**)
- 2G12: Notes that 2G12 and 2F5, potent neutralizing antibodies, were identified by screening for cell surface (oligomeric Envelope) reactivity. [Fouts1998] (**antibody binding site definition and exposure**)
- 2G12: A wide range of neutralizing titers was observed that was independent of co-receptor usage. [Trkola1998] (**co-receptor**, **variant cross-recognition or cross-neutralization**)
- 2G12: A panel of MAbs were shown to bind with similar or greater affinity and similar competition profiles to a deglycosylated or variable loop deleted core gp120 protein (Delta V1, V2, and V3), thus such a core protein produces a structure closely approximating full length folded monomer – MAb 2G12 was the only exception to this, showing reduced binding efficiency. [Binley1998] (**antibody binding site definition and exposure**)
- 2G12: Does not compete with binding of MAb generated in response to gp120-CD4 complex, CG10. [Sullivan1998b] (**antibody interactions**)
- 2G12: Ab from gp120 vaccinated individuals prior to infection, who subsequently became HIV infected, could not achieve 90% neutralization of the primary virus by which the individuals were ultimately infected – these viruses were not particularly refractive to neutralization, as determined by their susceptibility to neutralization by MAbs 2G12, IgG1b12, 2F5 and 447-52D. [Connor1998]
- 2G12: Enhances Hx10 binding to CD4 positive or negative HeLa cells, but inhibited binding to CD4+ T-cell line A3.01 – neutralizes Hx10 infection of the HeLa cells. [Mondor1998]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 2G12: Summary of the implications of the crystal structure of gp120 combined with what is known about mutations that reduce NAb binding – probable mechanism of neutralization by 2G12 is unknown, but dependent on proper glycosylation and 2G12 is predicted to be oriented toward the target cell when bound, so neutralization may be due to steric hindrance – mutations in positions N 295, T 297, S 334, N 386, N 392 and N 397 HXBc2 (IIIB) decrease 2G12 binding, and the binding region is 25 angstroms from the CD4 binding site – probably the Ab binds in part to carbohydrates, which may account for both its broad reactivity and the scarcity of Abs in the same competition group. [Wyatt1998a] (**antibody binding site definition and exposure**)
- 2G12: The MAb and Fab binding to the oligomeric form of gp120 and neutralization were highly correlated – authors suggest that neutralization is determined by the fraction of Ab sites occupied on a virion irrespective of the epitope. [Parren1998a] (**antibody binding site definition and exposure**)
- 2G12: Post-exposure prophylaxis was effective when MAb 694/98-D was delivered 15 min post-exposure to HIV-1 LAI in hu-PBL-SCID mice, but declined to 50% if delivered 60 min post-exposure, and similar time constraints have been observed for HIVIG, 2F5 and 2G12, in contrast to MAb BAT123 that could protect when delivered 4 hours post infection. [Andrus1998] (**immunoprophylaxis**)
- 2G12: Neutralizes TCLA strains and primary isolates. [Parren1997c] (**variant cross-recognition or cross-neutralization**)
- 2G12: Review that discusses this MAb – reacts with residues at the base of the V3 loop and V4, and most of the changes that reduce binding are glycosylation sites – it is not clear whether the binding site is peptidic or direct carbohydrate. [Burton1997] (**antibody binding site definition and exposure**, **review**)
- 2G12: Viral binding inhibition by 2G12 was strongly correlated with neutralization (all other neutralizing MAbs tested showed some correlation except 2F5) [Ugolini1997] (**antibody binding site definition and exposure**)
- 2G12: Using concentrations of Abs achievable *in vivo*, the triple combination of 2F5, 2G12 and HIVIG was found to be synergistic to have the greatest breadth and magnitude of response against 15 clade B primary isolates. [Mascola1997] (**antibody interactions**, **variant cross-recognition or cross-neutralization**)
- 2G12: Review: MAbs 2F5, 2G12 and IgG1b12 have potential for use in combination with CD4-IgG2 as an immunotherapeutic or immunoprophylactic – homologous MAbs to these are rare in humans and vaccine strategies should consider including constructs that may enhance exposure of these MAbs' epitopes. [Moore1997] (**immunoprophylaxis**, **immunotherapy**, **review**)
- 2G12: One of 14 human MAbs tested for ability to neutralize a chimeric SHIV-vpu+, which expressed HIV-1 IIIB Env – 2G12 was a strong neutralizer of SHIV-vpu+ – all Ab combinations tested showed synergistic neutralization – 2G12 has synergistic response with MAbs 694/98-D (anti-V3), 2F5, F105, and b12. [Li1997] (**antibody interactions**)
- 2G12: Study shows neutralization is not predicted by MAb binding to JRFL monomeric gp120, but is associated with oligomeric Env binding – 2G12 bound monomer, and weakly bound oligomer and neutralized JRFL. [Fouts1997] (**antibody binding site definition and exposure**)
- 2G12: A JRCSF variant that was selected for IgG1b12 resistance remained sensitive to MAbs 2G12 and 2F5, for combination therapy. [Mo1997] (**escape**)
- 2G12: In a multilab evaluation of monoclonal antibodies, only IgG1b12, 2G12, and 2F5 could neutralize at least half of the 9 primary test isolates at a concentration of < 25 mug per ml for 90% viral inhibition – neutralized 6 of 9 primary isolates. [D'Souza1997] (**variant cross-recognition or cross-neutralization**)
- 2G12: Review: Only four epitopes have been described which can stimulate a useful neutralizing response to a broad spectrum of primary isolates, represented by the binding sites of MAbs: 447-52-D, 2G12, Fab b12, and 2F5. [Sattentau1996] (**review**)
- 2G12: Neutralizes primary isolates, HXB2, and chimeric virus with gp120 from primary isolates in an HXB2 background. [McKeating1996b] (**variant cross-recognition or cross-neutralization**)
- 2G12: Neutralizes JR-FL – inhibits gp120 interaction with CCR-5 in a MIP-1beta-CCR-5 competition study. [Trkola1996a] (**co-receptor**)
- 2G12: Review: exceptional capacity to neutralize primary isolates in terms of both breadth and potency – one of three MAbs (IgG1b12, 2G12, and 2F5) generally accepted as having significant potency against primary isolates. [Poignard1996b] (**variant cross-recognition or cross-neutralization**, **review**)
- 2G12: Review: binding site is distinct from CD4BS MAbs epitope and is unique among known gp120 MAbs, human or rodent. [Moore1995b] (**review**)
- 2G12: Binding weakly enhanced by some anti-C1, -C4, -V3, and CD4 binding site MAbs – unusual in that 2G12 binding neither enhanced or inhibited the binding of other MAbs included in the study. [Moore1996] (**antibody interactions**)
- 2G12: Conformationally sensitive epitope destroyed by mutations altering the N-linked glycosylation sites near the base of the V3 loop and the amino-terminal flank of the V4 loop. [Trkola1996b] (**antibody binding site definition and exposure**)
- 2G12: Highly potent Cross-clade neutralizing activity. [Trkola1995] (**inter-clade comparisons**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2G12: Human MAb generated by electrofusion of PBL from HIV-1+ volunteers with CB-F7 cells. [Buchacher1994] (**antibody generation**)					
1126	1367	Env	gp41			HIV-1 infection	human (IgG1λ)
		Ab type cluster I **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Nyambi2000, Gorny2000a, Gorny2000b, Nyambi1998 **Keywords** antibody binding site definition and exposure, inter-clade comparisons, review. • 1367: One of 24 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster I region (aa 579 - 604). Only one of these has any neutralizing potential, clone 3. [Gorny2004] (**review**) • 1367: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 5 cluster I anti-gp41 MAbs which showed good cross clade reactivity – 1367 weakly bound to the majority of isolates – no neutralizing activity was observed when tested with 5 isolates, but 1367 did not bind well to these isolates. [Nyambi2000] (**inter-clade comparisons**) • 1367: Binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**) • 1367: A cluster I epitope that binds to rgp41 567-647, recognizes a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41 – this MAb doesn't react with either of the peptides N51 or C43 individually – MAbs 50-69 and 1367 had similar properties. [Gorny2000b] (**antibody binding site definition and exposure**) • 1367: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade. [Nyambi1998] (**inter-clade comparisons**)					
1127	126-6 (SZ-126.6)	Env	gp41 (HXB2)		no	HIV-1 infection	human (IgG2κ)
		Ab type cluster II **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu), NYU Med Center, NY, NY **References** Gorny2004, Finnegan2002, Nyambi2000, Gorny2000b, Hioe1997b, Earl1997, Binley1996, Chen1995, Eddleston1993, Xu1991, Robinson1991, Robinson1990b **Keywords** antibody binding site definition and exposure, enhancing activity, inter-clade comparisons, kinetics, review, variant cross-recognition or cross-neutralization. • 126-6: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • 126-6: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I MAbs 50-69, F240, 240-D,3D6, and 246-D recognize a nonhelical hydrophobic region, positions 598-604, that forms a disulfide loop in the six-helix bundle. Cluster II MAbs 98-6 and 126-6 recognized residues 644-663 of gp41, a portion of the second heptad repeat. These MAbs were found to behave similarly, so 50-69 and 98-6 were used as representatives. Exposure of cluster I and cluster II epitopes required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor. Binding to CD4 exposed hidden cluster I and II epitopes. The MAbs were found to bind to gp120/gp41 complexes, not to gp41 after shedding of gp120, and were localized to at fusing-cell interfaces. Kinetic and binding results indicate that these MAbs are exposed in transitional structures during the fusion process, possibly the prehairpin intermediate prior to co-receptor binding, although other intermediate structures may be involved. They do not bind once syncytia begin to show extensive cyotplasmic mixing. These MAbs failed to inhibit fusion. The NAb 2F5 has a very different behavior in this study. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**) • 126-6: NIH AIDS Research and Reference Reagent Program: 1243. • 126-6: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs. [Nyambi2000] (**variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

- 126-6: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone – MAb 126-6 was biotinylated and used as a probe to determine that anti-gp41 MAb 50-69 bound the fusogenic form of the protein in liquid phase. [Gorny2000b] (**antibody binding site definition and exposure**)
- 126-6: Discontinuous epitope recognizing residues between 649-668 – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding. [Binley1996] (**antibody binding site definition and exposure**)
- 126-6: One of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. [Chen1995] (**antibody binding site definition and exposure**)
- 126-6: Called SZ-126.6. [Eddleston1993]
- 126-6: Specific for a conformational epitope. [Xu1991] (**antibody binding site definition and exposure**)
- 126-6: No enhancing or neutralizing activity. [Robinson1991] (**enhancing activity**)
- 126-6: No enhancing activity for HIV-1 IIIB. [Robinson1990b] (**enhancing activity**)

1128 1342 Env gp41 no HIV-1 infection human (IgG1λ)

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References Gorny2004, Nyambi2000, Gorny2000a, Gorny2000b, Nyambi1998
Keywords antibody binding site definition and exposure, inter-clade comparisons, review.

- 1342: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**)
- 1342: 26 HIV-1 group M isolates (clades A to H) were tested for binding to 47 MAbs, including 6 cluster II anti-gp41 MAbs – of these 2F5, 167-D, 126-6, and 1281 bound across clades, but usually weakly, while 98-6 and 1342 had poor cross reactivity – Clade D isolates bound most consistently to cluster II MAbs – no neutralizing activity was observed when tested with 5 isolates, but 1342 did not bind to these isolates. [Nyambi2000] (**inter-clade comparisons**)
- 1342: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**)
- 1342: This cluster II MAb is a conformational epitope that binds in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. [Gorny2000b] (**antibody binding site definition and exposure**)
- 1342: Using a whole virion-ELISA method, 18 human MAbs were tested for their ability to bind to a panel of 9 viruses from clades A, B, D, F, G, and H – anti-gp41 Abs 98-6, 1367 and 1342 were not able to bind detectably with any of the viruses from any clade. [Nyambi1998] (**inter-clade comparisons**)

1129 1379 Env gp41 HIV-1 infection human (IgG1λ)

Ab type cluster II **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center)
References Gorny2004, Gorny2000a, Gorny2000b
Keywords antibody binding site definition and exposure, review.

- 1379: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**)
- 1379: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1379: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. [Gorny2000b] (**antibody binding site definition and exposure**)					
1130	Fab D11 (D11)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, review. • Fab D11: Called D11. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab D11: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1131	Fab D5 (D5)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, review. • Fab D5: Called D5. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab D5: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1132	Fab G1	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, review. • Fab G1: Called G1. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab G1: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1133	Fab M10	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Parren1997c, Binley1996 • Fab M10: Does not bind to MN native oligomer, but does bind to both LAI and MN rgp120 and rgp140. [Parren1997c] • Fab M10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996]					
1134	Fab M12 (M12)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody sequence, variable domain, review. • Fab M12: Called M12. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Fab M12: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody sequence, variable domain**)					
1135	Fab M15	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** review. • Fab M15: Called M15. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab M15: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996]					
1136	Fab S10 (S10)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review. • Fab S10: Called S10. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab S10: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)					
1137	Fab S6 (S6)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody interactions, antibody sequence, variable domain, review. • Fab S6: Called S6. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab S6: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody interactions**, **antibody sequence, variable domain**)					
1138	Fab S8 (S8)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, review. • Fab S8: Called S8. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab S8: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **antibody sequence, variable domain**)					
1139	Fab S9 (S9)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody interactions, antibody sequence, variable domain, review. • Fab S9: Called S9. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Fab S9: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody interactions**, **antibody sequence, variable domain**)					
1140	Fab T3 (T3)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster II **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review. • Fab T3: Called T3. One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Fab T3: Binds to cluster II region – competes with MAbs 126-6, Md-1 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)					
1141	Md-1 (MD-1)	Env	gp41		no		human (IgG1λ)
		Ab type cluster II **Research Contact** R. A. Myers State of Maryland Dept. of Health **References** Gorny2004, Binley1996, Chen1995, Myers1993 **Keywords** antibody binding site definition and exposure, review. • Md-1: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • Md-1: NIH AIDS Research and Reference Reagent Program: 1223. • Md-1: Discontinuous epitope recognizing residues between 563-672, does not recognize cluster I disulfide bridge region – reacts almost exclusively with trimers and tetramers on WB – designated cluster II – Fabs D5, D11, G1, T3, M12, M15, S6, S8, S9, S10 block binding. [Binley1996] (**antibody binding site definition and exposure**) • Md-1: Called MD-1 – one of several anti-gp41 MAbs that bind to a gp41-maltose binding fusion protein designed to study the leucine zipper domain of gp41, showing that the construct has retained aspects of normal gp41 conformation. [Chen1995] (**antibody binding site definition and exposure**) • Md-1: Called MD-1 – discontinuous epitope that binds in the N-terminal region – reacts exclusively with oligomer. [Myers1993] (**antibody binding site definition and exposure**)					
1142	1281 (1281-D)	Env	gp41			HIV-1 infection	human (IgG1λ)
		Ab type cluster II, six-helix bundle **Research Contact** Susan Zolla-Pazner (Zollas01@mcrcr6.med.nyu) (NYU Med. Center) **References** Gorny2004, Follis2002, Golding2002b, Verrier2001, Gorny2000a, Gorny2000b, Hioe1997b **Keywords** antibody binding site definition and exposure, antibody interactions, review, variant cross-recognition or cross-neutralization. • 1281: One of 19 MAbs and Fabs in this database that bind to the highly immunogenic gp41 cluster II region (aa 644-663); none have neutralizing activity. [Gorny2004] (**review**) • 1281: Alanine mutations were introduced into the N- and C-terminal α-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**) • 1281: The fusion process was slowed by using a suboptimal temperature (31.5 C) to re-evaluate the potential of Abs targeting fusion intermediates to block HIV entry – preincubation of E/T cells at 31.5 C enabled polyclonal anti-N-HR Ab and anti-six-helix bundle Abs to inhibit fusion, indicating six-helix bundles form prior to fusion – 98-6 binds to a C-HR hairpin epitope and blocks fusion when added to a 2 hour E/T preincubation at 31.5 C, but if added after 1 hour, doesn't inhibit – this is in contrast to six-helix bundle Abs 167-D and 1281 that inhibit more efficiently when added after one hour of incubation. [Golding2002b] (**antibody binding site definition and exposure**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 1281: A panel of 12 MAbs was used to identify those that could neutralize the dual-tropic primary isolate HIV-1 89.6 – six gave significant neutralization at 2 to 10 ug/ml: 2F5, 50-69, IgG1b12, 447-52D, 2G12, and 670-D six did not have neutralizing activity: 654-D, 4.8D, 450-D, 246-D, 98-6, and 1281 – no synergy, only additive effects were seen for pairwise combinations of MAbs, and antagonism was noted between gp41 MAbs 50-69 and 98-6, as well as 98-6 and 2F5. [Verrier2001] (**antibody interactions**) • 1281: Binds within the region gp41 647-682 – binding of panel of 21 MAbs to soluble oligomeric gp140 versus gp41 or gp120 monomers was compared – no MAb was oligomer specific, but gp41 MAb 50-69 bound with a 5 fold preference for the oligomer, while other gp41 MAbs (1367, 98-6, 167-D, 1281, 1342, and 1379) did not show a preference. [Gorny2000a] (**antibody binding site definition and exposure**, **variant cross-recognition or cross-neutralization**) • 1281: This cluster II MAb binds to a conformational epitope in the region 644-663 – like most cluster II MAbs (126-6, 167-D, 1281, 1342, and 1379 all reacted similarly) it binds to a peptide N51-C43 complex trimer of heterodimers that approximates the core of the fusogenic form of gp41, but not to C43 nor to N51 alone. [Gorny2000b] (**antibody binding site definition and exposure**) • 1281: Called 1281-D: Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997b] (**variant cross-recognition or cross-neutralization**)			
1143	Fab A9 (A9)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review. • Fab A9: Called A9. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. [Gorny2004] (**review**) • Fab A9: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)				
1144	Fab G15 (G15)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review. • Fab G15: Called G15. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. [Gorny2004] (**review**) • Fab G15: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)				
1145	Fab G5	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)
		Ab type cluster III **References** Gorny2004, Binley1996 **Keywords** antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review. • Fab G5: Called G5. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. [Gorny2004] (**review**) • Fab G5: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)				

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1146	Fab L1 (L1)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)

Ab type cluster III
References Gorny2004, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.

- Fab L1: Called L1. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. [Gorny2004] (**review**)
- Fab L1: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1147	Fab L11 (L11)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)

Ab type cluster III
References Gorny2004, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.

- Fab L11: Called L11. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. [Gorny2004] (**review**)
- Fab L11: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1148	Fab L2 (L2)	Env	gp41 (LAI)		no	HIV-1 infection	human (IgG1κ)

Ab type cluster III **Research Contact** P. Perrin and D. Burton (Scripps Research Institute, La Jolla, California
References Gorny2004, Earl1997, Binley1996
Keywords antibody binding site definition and exposure, antibody generation, antibody sequence, variable domain, review.

- Fab L2: Called L2. One of six Fabs in this database that bind to the gp41 cluster III region (a conformational epitope involving aa 619-648); none have neutralizing activity. [Gorny2004] (**review**)
- Fab L2: Binds to cluster III region – competes with MAb Md-1, but not MAbs 126-6 and D50 – conformation sensitive – variable regions sequenced. [Binley1996] (**antibody binding site definition and exposure**, **antibody generation**, **antibody sequence, variable domain**)

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1149	Chessie 8	Env	gp41				mouse (IgG)

Ab type cytoplasmic domain **Research Contact** G. Lewis
References Smith-Franklin2002, Rovinski1995, Poumbourios1995, Lewis1991

- Chessie 8: This Ab was used in an *in vitro* study demonstrating that HIV-1 antibody and Fcgamma receptors can trap virus on the surface of follicular dendritic cells (FDC)'s and extend the period of infectivity – blocking the FDC-Fcgamma receptor killing the FDC cell reduced their ability to maintain infectivity, and FDC cells seemed to stabilize viral particles and decrease gp120 shedding. [Smith-Franklin2002]
- Chessie 8: Used to precipitate gp160 in immunoblots in a study examining the feasibility of using unprocessed gp160 glycoprotein as an immunogen. [Rovinski1995]

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1150	8F101	Env	gp120			Vaccine	mouse (IgG)

Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120
Ab type gp120-CD4 complex
References Finnegan2002, DeVico1995
Keywords antibody binding site definition and exposure, antibody generation, kinetics.

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 8F101: Anti-gp41 MAbs were tested in a cell-cell fusion system to investigate the antigenic changes in gp41 during binding and fusion. Cluster I and Cluster II MAbs required CD4 expression on HIV HXB2 Env expressing HeLa target cells, but not the CXCR4 co-receptor, binding to a fusion intermediate. 8F101 selectively stains gp120-CD4 complexes after dissociation from gp41, and did not stain cells arrested earlier than 30 min of co-culture, but 8F101 and cluster I and II MAbs co-localized at fusing cell interfaces at 30 min coculture. After extended co-culture, only 8F101 bound. [Finnegan2002] (**antibody binding site definition and exposure**, **kinetics**) • 8F101: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans. [DeVico1995] (**antibody generation**)				
1151	8F102	Env	gp120			Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade HXB2 *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** DeVico1995 • 8F102: MAbs specifically reactive to crosslinked gp120 and CD4 were derived (8F101, 8F102) – conformation dependent – competition studies indicate the epitope is immunogenic in infected humans. [DeVico1995]					
1152	CG-10 (CG10)	Env	gp120 (IIIB)		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *Strain:* B clade IIIB *HIV component:* gp120 **Ab type** gp120-CD4 complex **Research Contact** Jonathan Gershoni, Tel Aviv University, Isreal **References** Oscherwitz1999a, Sullivan1998b, Rizzuto1998, Lee1997, Wu1996, Gershoni1993 • CG-10: Called CG10 – CD4BS MAb 15e competes with CG-10 binding, probably due to the disruption of CD4-gp120 by 15e – CD4i MAbs 17b and 48d compete and the binding sites may overlap – MAb A32 enhances binding of 17b, 48d and CG10 – MAbs C11, 2G12 and 212A do not affect CG10 binding – CG-10 can bind gp120 with V1/V2 and V3 deleted – HXBc2 mutations Delta 119-205, 314 G/W, 432 K/A, 183,184 PI/SG decrease CG-10 recognition, HXBc2 mutations Delta 298-327 (V3), 384 Y/E, 298 R/G, 435 Y/S enhance recognition – the CD4 contribution to the CG10 epitope maps to the CD4 CDR2-like loop – CG10 can neutralize HIV-1 in the presence of sCD4 even though it does not do so in the context of cell surface CD4 binding to gp120. [Sullivan1998b] • CG-10: Called CG10 – disrupts gp120-CCR5 interaction and competes with MAb 17b –binds near the conserved bridging sheet of gp120 – mutations in positions K/D 121, T/D 123, K/D 207, K/D 421, Q/L 422, Y/S 435, M/A 434, K/A 432 and I/S 423 result in a 70% reduction in CG10 binding. [Rizzuto1998] • CG-10: Called CG10 – Promotes envelope mediated cell fusion between CD4+ cells and cells infected with either T-cell and macrophage tropic viruses – infection of HeLa CD4+ (MAGI) cells by HIV-1 LAI, ELI1, and ELI2 strains was increased two-to four-fold in the presence of CG10. [Lee1997] • CG-10: Called CG10 – MIP-1alpha binding to CCR-5 expressing cells can be inhibited by gp120-sCD4, and MAb CG10 does not block this inhibition. [Wu1996] • CG-10: Reacts exclusively with sCD4-gp120 complex, not with sCD4 or gp120 alone. [Gershoni1993]					
1153	CG-25	Env	gp120		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** Gershoni1993 • CG-25: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120. [Gershoni1993]					
1154	CG-4 (CG4)	Env	gp120		no	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **Research Contact** Jonathan Gershoni, Tel Aviv University, Isreal **References** Gershoni1993					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• CG-4: Reacts with gp120 and sCD4-gp120 complex, not with sCD4. [Gershoni1993]					
1155	CG-76	Env	gp120		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** Gershoni1993 • CG-76: Reacts equally well with sCD4-gp120 and sCD4, but not with purified gp120. [Gershoni1993]					
1156	CG-9	Env	gp120		L	Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* sCD4-gp120 complex *HIV component:* gp120 **Ab type** gp120-CD4 complex **References** Gershoni1993 • CG-9: Reacts preferentially with sCD4-gp120, also with sCD4, not with gp120. [Gershoni1993]					
1157	105-518	Env	gp41 (608–637 HAM112, O group)			Vaccine	mouse (IgG1κ)
		Vaccine *Vector/Type:* protein *Strain:* O group HAM112 *HIV component:* gp160 **Ab type** immunodominant region **References** Scheffel1999 • 101-518: Overlapping peptides based on group O HAM112 Env were tested for MAb reactivity. [Scheffel1999]					
1158	31A1	Env	gp41		no	in vitro stimulation or selectio	human (IgMκ/λ)
		Ab type p24+gp41 **References** Pollock1989 • 31A1: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41. [Pollock1989]					
1159	39A64	Env	gp41		no	in vitro stimulation or selectio	human (IgMκ/λ)
		Ab type p24+gp41 **References** Pollock1989 • 39A64: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41. [Pollock1989]					
1160	39B86	Env	gp41		no	in vitro stimulation or selectio	human (IgMκ/λ)
		Ab type p24+gp41 **References** Pollock1989 • 39B86: Denatured virus was used for *in vitro* stimulation to generate Abs – Reacts with both p24 and gp41. [Pollock1989]					
1161	9303	Env	gp41		no		mouse
		Ab type p24+gp41 **Research Contact** Du Pont **References** McDougal1996					
1162	NC-1	Env	gp41 (IIIB)			Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* peptide *Strain:* B clade IIIB *HIV component:* gp41 **Ab type** six-helix bundle **Research Contact** S. Jiang, New York Blood Center, NY, NY					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)

References deRosny2004, Follis2002, Yang2002, Yang2000, Jiang1998

Keywords antibody binding site definition and exposure, antibody generation, antibody interactions, inter-clade comparisons, variant cross-recognition or cross-neutralization.

- NC-1: The MAb 2F5 binds to the C-heptad and is neutralizing, but the MAb D50 binds to the C-heptad and is not neutralizing. 2F5 binds preferentially to native gp41 prior to receptor activation. Trapped fusion-intermediates suggest 2F5 remains present shortly after gp120 triggering by CD4, but may be lost by the time the six-helix bundle is formed. 2F5 neutralization seems to block a later step of the fusion process, but it does not inhibit binding of NC-1, a MAb specific for the six-helix bundle, so it does not prevent formation of the six-helix bundle. The results are most consistent with 2F5 inhibiting a post-fusion-intermediate step. [deRosny2004] (**antibody binding site definition and exposure**, **antibody interactions**)
- NC-1: Alanine mutations were introduced into the N- and C-terminal alpha-helices of gp41 to destabilize interhelical packing interactions in order to study their inhibitory effect on viral infectivity. These mutations were shown to inhibit viral replication though affecting the conformational transition to the fusion-active form of gp41, and allow increased inhibition by gp41 peptides. 2F5 senstivity is increased in the mutated viruses, presumably because 2F5s neutralization activity is focused on the transition to the fusion active state. No other gp41 MAb against tested, including NC-1, 50-69D, 1281, 98-6D, 246-D and F240, neutralized the parental or the fusion-deficient mutated viruses. [Follis2002] (**antibody binding site definition and exposure**)
- NC-1: Uncleaved soluble gp140 can be stabilized in an oligomer by fusion with a C-term trimeric GCN4 motif (gp140delta683(-/GCN4)) or using a T4 trimeric motif derived from T4 bacteriophage fibritin (gp140delta683(-/FT)) – NC-1 binds to 15% of the GCN4 motif trimers, but this was significantly reduced for the T4 fibritin stabilized structures, indicating little is in the six-helix bundle, fusogenic conformation. [Yang2002] (**antibody binding site definition and exposure**)
- NC-1: A combination of gp41 fusion with the GNC4 trimeric sequences and disruption of the YU2 gp120-gp41 cleavage site resulted in stable gp140 trimers (gp140-GNC4) – approximately 16% of the gp140(-GNC4) stabilized trimer recognized by pooled sera was precipitated by NC-1, indicating that at a fraction assumes a fusogenic gp41 six-helix bundle conformation – gp140(-) monomers were not able to bind to the NC-1, nor was gp130(-/GCN4) glycoprotein, consistent with the expectation that the absence of C34 helices would preclude formation of the six-helix bundle. [Yang2000] (**antibody binding site definition and exposure**)
- NC-1: Ab elicited in response to immunization with N36(L6)C34, a peptide that folds into a six helix bundle like gp41 – NC-1 binds to the surface of HIV-1 infected cells only in the presence of sCD4, recognizing the fusogenic core structure – binding affinity was decreased by point mutations that disrupt core formation and abolish membrane fusion activity, (I573P and I573A) – NC-1 can recognize discontinuous epitopes from B clade isolate SC, but not E clade strain N243, O group strain GAB, or HIV-2 ROD. [Jiang1998] (**antibody binding site definition and exposure**, **antibody generation**, **variant cross-recognition or cross-neutralization**, **inter-clade comparisons**)

IV-C-17 Nef Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1163	4H4	Nef (1–33)	Nef (1–33 IIIB)	MGGKWSKSSVVGWPTVRERMRRAPT-VRERMRRAEPAADGVGAA		Vaccine	human (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade IIIB *HIV component:* Nef **References** Otake1994 • 4H4: This MAb, elicited by vaccination with a Nef fusion protein, could not detect Nef protein on the cell surface – C-term anti-Nef Abs could. [Otake1994]					
1164	polyclonal	Nef (9–24)	Nef (9–24)	SVIGWLTVRERMRRAE	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* B clade BRU *HIV component:* Nef **References** Tahtinen2001 • BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes – DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly – Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses – the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice – three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef – Rev- or-Tat immunized mice did not generate an Ab response. [Tahtinen2001]					
1165	13/042	Nef (11–20)	Nef (11–24 BH10)	VGWPTVRERM		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Schneider1991 • 13/042: Epitope mapped by overlapping decapeptides – core: TVRERM. [Schneider1991]					
1166	13/035	Nef (15–24)	Nef (11–24 BH10)	TVRERMRRAE		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Schneider1991 • 13/035: Epitope mapped by overlapping decapeptides – core: TVRERM. [Schneider1991]					
1167	A6	Nef (18–26)	Nef (18–26 NL-432)	ERMRRAEPA?		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Otake1997 **Keywords** antibody binding site definition and exposure, antibody generation. • A6: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. A6 bound to the peptide spanning amino acids 18-26; we inferred the amino acids from the positions in the NL-43 strain. A6 also bound to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					
1168	A7	Nef (28–45)	Nef (28–45 NL-432)	DGVGAVSRDLEKHGAITS?		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Otake1997 **Keywords** antibody binding site definition and exposure, antibody generation. • A7: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. A7 bound to the peptide spanning amino acids 28-45; we inferred the amino acids from the positions in the NL-43 strain. A7 did not bind to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1169	25/03	Nef (30–43)	Nef (30–43 BH10)	VGAASRDLEKHGAI		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Maksiutov2002, Schneider1991 • 25/03: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • 25/03: Epitope mapped by overlapping decapeptides – core: ASRDLEK. [Schneider1991]					
1170	26/76	Nef (30–43)	Nef (30–43 BH10)	VGAASRDLEKHGAI		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Maksiutov2002, Schneider1991 • 26/76: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • 26/76: Epitope mapped by overlapping decapeptides – core: SRDLEK. [Schneider1991]					
1171	3F2	Nef (31–40)	Nef (31–40 BRU)	GAASRDLEKH		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Maksiutov2002, Ranki1995, Saito1994, Ovod1992 • 3F2: UK Medical Research Council AIDS reagent: EVA3067.1. • 3F2: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • 3F2: Faintly cross-reactive with astrocytes of uninfected control samples. [Ranki1995] • 3F2: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992]					
1172	3D12	Nef (31–50)	Nef (31–50 BRU)	GAASRDLEKHGAITSSNTAA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Maksiutov2002, Ranki1995, Saito1994, Ovod1992 • 3D12: UK Medical Research Council AIDS reagent: EVA3067.2. • 3D12: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • 3D12: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. [Ranki1995] • 3D12: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissues. [Saito1994] • 3D12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992] • 3D12: There is an anti-RT MAb that also has this name (see.					
1173	polyclonal	Nef (33–65)	Nef (dis 32–64 LAI, BRU)	ASRDLEKHGAITSSNTAATNAACAW-LEAQEEEE		HIV-1 infection, Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein, PLG microparticle *Strain:* B clade BRU, B clade LAI *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG **References** Maksiutov2002, Moureau2002 • This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes. [Moureau2002]					
1174	polyclonal	Nef (49–64)	Nef (49–64)	AATNAACAWLEAQEEE	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* B clade BRU *HIV component:* Nef					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Tahtinen2001 • BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes – DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly – Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses – the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice – three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef – Rev- or-Tat immunized mice did not generate an Ab response. [Tahtinen2001]					
1175	3G12	Nef (51–71)	Nef (51–71 BRU)	TNAACAWLEAQEEEEVGFPVT		Vaccine	mouse (IgG2a)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Ovod1992 • 3G12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992]					
1176	13/058	Nef (60–73)	Nef (60–73 BH10)	AQEEEEVGFPVTPQ		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Schneider1991 • 13/058: Epitope mapped by overlapping decapeptides – core: EEVGFP. [Schneider1991]					
1177	26/028	Nef (60–73)	Nef (60–73 BH10)	AQEEEEVGFPVTPQ		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Schneider1991 • 26/028: Epitope mapped by overlapping decapeptides – core: EEVGFPV. [Schneider1991]					
1178	2E3	Nef (61–80)	Nef (61–80 BRU)	QEEEEVGFPVTPQVPLRPMT		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Nilsen1996, Ovod1992 • 2E3: Two isomorphic forms of Nef were identified, 2E3 reacted with the p24 but not p27 form, and was strain specific (MN and BRU reactive, not IIIB or RF) [Ovod1992] • 2E3: There are two MAbs with the name 2E3 – the other one binds to integrase. [Nilsen1996]					
1179	polyclonal	Nef (66–97)	Nef (dis 66–97 LAI)	VGFPVTPQVPLRPMTYKAAVDLSHF-LKEKGGL	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* B clade LAI *HIV component:* Nef *Adjuvant:* QS21 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 10/28, proliferative in 11/14, and CTL in 13/24 (54%) of testable volunteers – 10/28 had Ab responses to this peptide (N1), 11/24 had proliferative responses, and CTL responses were detected. [Pialoux2001]					
1180	AM5C6	Nef (82–92 + 78–92)	Nef (28–43 BH10)	DGVGAASRDLEKHGAI+KAAVDLSH-FLK		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Maksiutov2002, Schneider1991 • AM5C6: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • AM5C6: Epitope mapped by overlapping decapeptides – core: SRDL – also reacts with Nef(78-92) [Schneider1991]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1181	AM5C6	Nef (82–92 + 78–92)	Nef (28–43 BH10)	DGVGAASRDLEKHGAI+KAAVDLSH-FLK		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Maksiutov2002, Schneider1991 • AM5C6: This epitope is similar to a fragment of the human protein vascular endothelial growth factor C, AEPDAGEATAYASKDLE. [Maksiutov2002] • AM5C6: Epitope mapped by overlapping decapeptides – core: KAAVDL – also reacts with Nef(28-43) [Schneider1991]					
1182	F14.11	Nef (83–88)	Nef (83–88)	AAVDLS		Vaccine	mouse (IgG2aκ)
		Vaccine *Vector/Type:* peptide *HIV component:* Nef **References** Chang1998, De Santis1991 • F14.11: Used as a control in a study of Nef-specific single chain Abs constructed from AG11 and EH1. [Chang1998] • F14.11: The MAb was made to a six aa region of Nef that is similar to a region found in thymosin alpha 1 protein – the MAb binds to the natural Nef protein. [De Santis1991]					
1183	31/03	Nef (83–103)	Nef (82–103 BH10)	AAVDLSHFLKEKGGLEGLIHS		Vaccine	mouse
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Schneider1991 • 31/03: Epitope mapped by overlapping decapeptides – mapping suggests complex epitope in this region. [Schneider1991]					
1184	F4	Nef (115–126)	Nef (115–126 NL-432)	YHTQGYFPDWQN?		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef **References** Otake1997 **Keywords** antibody binding site definition and exposure, antibody generation. • F4: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F4 bound to the peptide spanning amino acids 115-126; we inferred the amino acids from the positions in the NL-43 strain. A6 also bound to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					
1185	F2	Nef (115–136)	Nef (115–137 NL-432)	YHTQGYFPDWQNYTPGPGVRYP?		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Otake1997 **Keywords** antibody binding site definition and exposure, antibody generation. • F2: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F2 bound to the peptide spanning amino acids 115-137; we inferred the amino acids from the positions in the NL-43 strain. F2 also bound to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					
1186	polyclonal	Nef (117–147)	Nef (dis 117–147 LAI)	TQGYFPDWQNYTPGPGVRYPLTFGW-CYKLVP	no	Vaccine	human (IgG)
		Vaccine *Vector/Type:* lipopeptide *Strain:* B clade LAI *HIV component:* Nef *Adjuvant:* QS21 **References** Pialoux2001 • 28 subjects were vaccinated with six HIV-1 peptides that were selected to be particularly rich in CTL epitopes, presented in lipopeptides with or without adjuvant QS21 – HIV-specific Ab responses were detected in 25/28, proliferative in 3/24, and CTL in 13/24 (54%) of testable volunteers – 20/28 had antibody responses to this particular peptide (N2), 3/24 had proliferative responses, and CTL responses were detected. [Pialoux2001]					
1187	polyclonal	Nef (118–133)	Nef (118–133)	QGYFPDWQNYTPGPGV	no	Vaccine	mouse (IgG)
		Vaccine *Vector/Type:* DNA *Strain:* B clade BRU *HIV component:* Nef					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		References Tahtinen2001					
		• BALB/c mice were immunized with a pBN-vector expressing HIV-1 nef, rev, or tat genes—DNA loaded onto gold microparticles was delivered using a gene gun, and DNA dissolved in saline was given intradermally or intramuscularly—Nef gene gun immunized mice showed the strongest and most long-lasting (6 months) Ab, CTL and proliferative responses—the highest IgG1/IgG2a ratio was observed in the gene gun immunized mice—three Ab binding sites were found in Nef using peptide mapping, although some sera reacted only to complete Nef—Rev- or Tat-immunized mice did not generate an Ab response. [Tahtinen2001]					
1188	polyclonal	Nef (119–168)	Nef (dis 118–167 LAI, BRU)	GYFPDWQNYTPGPGVRYPLTFGWCY-KLVPVEPDKVEEANKGENTSLLHPV		HIV-1 infection, Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein, PLG microparticle *Strain:* B clade BRU, B clade LAI *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG					
		References Maksiutov2002, Moureau2002					
		• This epitope is similar to a fragment of the human protein Bone-derived growth factor, PLEPAKLEE, and to Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. [Maksiutov2002]					
		• Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes. [Moureau2002]					
1189	F3	Nef (128–137)	Nef (128–137 NL-432)	TPGPGVRYPL?		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)					
		References Kawai2003, Otake1997					
		Keywords antibody binding site definition and exposure, antibody generation, complement.					
		• F3: Used as a control for Nef binding in a study designed to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Human heavy chain, mouse light chain anti-Nef IgM were obtained. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. [Kawai2003] (**complement**)					
		• F3: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F3 bound to the peptide spanning amino acids 128-137; we inferred the amino acids from the positions in the NL-43 strain. F3 also bound to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					
1190	F8	Nef (128–137)	Nef (128–137 NL-432)	TPGPGVRYPL?		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)					
		References Otake1997					
		Keywords antibody binding site definition and exposure, antibody generation.					
		• F8: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. F8 bound to the peptide spanning amino acids 128-137; we inferred the amino acids from the positions in the NL-43 strain. F8 also bound to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					
1191	F1	Nef (148–157)	Nef (148–157 IIIB)	VEPDKVEEAN			mouse (IgM)
		References Fujii1996b, Fujii1996c, Otake1994, Fujii1993					
		• F1: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells. [Fujii1996b]					
		• F1: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1. [Fujii1996c]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• F1: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells. [Fujii1993, Otake1994]					
1192	2F2	Nef (151–170)	Nef (151–170 BRU)	DKVEEANKGENTSLLHPVSL		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *HIV component:* Nef **References** Maksiutov2002, Ranki1995, Saito1994, Ovod1992 • 2F2: UK Medical Research Council AIDS reagent: EVA3067.3. • 2F2: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. [Maksiutov2002] • 2F2: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. [Ranki1995] • 2F2: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue. [Saito1994] • 2F2: Strain specific (MN and BRU reactive, not IIIB or RF) [Ovod1992]					
1193	E9	Nef (158–181)	Nef (158–206 IIIB)	KGENTSLLHPVSLHGMDDPEREVL			mouse (IgM)
		References Maksiutov2002, Fujii1996b, Fujii1996c, Otake1994, Fujii1993 • E9: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. [Maksiutov2002] • E9: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1. [Fujii1996c] • E9: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells. [Fujii1996b] • E9: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells. [Fujii1993, Otake1994]					
1194	3E6	Nef (161–180)	Nef (161–180 BRU)	NTSLLHPVSLHGMDDPEREV		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Maksiutov2002, Ranki1995, Saito1994, Ovod1992 • 3E6: UK Medical Research Council AIDS reagent: EVA3067.4. • 3E6: This epitope is similar to a fragment of the human protein Hematopoietic progenitor cell antigen CD34, TSLHPVSQHG. [Maksiutov2002] • 3E6: Faintly cross-reactive with astrocytes of uninfected control samples. [Ranki1995] • 3E6: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992]					
1195	E5	Nef (170–181)	Nef (170–181)	LHGMDDPEREVL?		Vaccine	mouse (IgM)
		Vaccine *Vector/Type:* protein *Strain:* B clade NL43 *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA) **References** Otake1997 **Keywords** antibody binding site definition and exposure, antibody generation. • E5: BALB/c mice were immunized with Nef protein to create a series of anti-Nef antibodies. E5 bound to the peptide spanning amino acids 170-181; we inferred the amino acids from the positions in the NL-43 strain. E5 also bound to the complete Nef protein. [Otake1997] (**antibody binding site definition and exposure**, **antibody generation**)					
1196	2A3	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Ovod1992 • 2A3: Reacted with Nef from different HIV-1 strains (BRU, IIIB, MN, but not RF) [Ovod1992]					
1197	2E4	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Ovod1992					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• 2EA: Reacted with Nef from different HIV-1 strains (BRU, IIIB, MN but not RF) [Ovod1992]					
1198	2H12	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Ranki1995, Saito1994, Ovod1992 • 2H12: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. [Ranki1995] • 2H12: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue. [Saito1994] • 2H12: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992]					
1199	3A2	Nef (171–190)	Nef (171–190 BRU)	HGMDDPEREVLEWRFDSRLA		Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein *Strain:* B clade BRU *HIV component:* Nef **References** Ranki1995, Saito1994, Ovod1992 • 3A2: UK Medical Research Council AIDS reagent: EVA3067.5. • 3A2: One of four antibodies used in combination to show HIV Nef protein expressed in astrocytes from 7/14 brain samples from HIV+ individuals – Nef expression associated with dementia. [Ranki1995] • 3A2: Over-expression of Nef in astrocytes from postmortem pediatric CNS tissue. [Saito1994] • 3A2: Reacted with Nef from different HIV-1 strains (BRU, IIIB, RF, MN) [Ovod1992]					
1200	NF1A1	Nef (173–206)	Nef (173–206)	MDDPEREVLEWRFDSRLAFHHVARE-LHPEYFKNC			mouse
		References Kaminchik1990 • NF1A1: Recognizes the Nef protein of the two isolates BH10 and LAV1 – low affinity. [Kaminchik1990]					
1201	polyclonal	Nef (186–206)	Nef (dis 185–205 LAI, BRU)	DSRLAFHHVARELHPEYFKNC		HIV-1 infection, Vaccine	mouse (IgG1)
		Vaccine *Vector/Type:* protein, PLG microparticle *Strain:* B clade BRU, B clade LAI *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA), PLG **References** Moureau2002 • Nef encapsulated in poly(DL-lactide-co-glycolide) (PLG) had a more prolonged Ab response than Nef in PBS or in Freund's adjuvant (CFA), still strong after 7 months – the response was predominantly IgG1, a Th2 immune response – three linear epitopes, Nef 32-64, 118-167, and 185-205, were frequently recognized by the sera of mice immunized with NefPLG or Nef-CFA, but not after immunization with Nef in PBS, which seemed to preferentially stimulate an Ab response to conformational epitopes. [Moureau2002]					
1202	E7	Nef (192–206)	Nef (192–206 IIIB)	HHVARELHPEYFKNC			mouse (IgM)
		References Fujii1996d, Fujii1996b, Fujii1996a, Fujii1996c, Otake1994, Fujii1993 • E7: Soluble Nef inhibits proliferation of CD4+ cells, and Nef cross-linking by MAbs may induce anti-CD4 cytocidal activity – sera from HIV+ individuals contain soluble Nef, thus this may be important for immune dysfunction and disease progression. [Fujii1996d] • E7: A carboxy-terminal domain of Nef on the cell surface induces cytolysis of CD4+ T cells. [Fujii1996b] • E7: Nef forms a homomeric oligomerizing structure, and using E7 and membrane immunofluorescence or immunoelectron microscopy, was shown to clusters on the surface of HIV-1 infected CD4+ cells. [Fujii1996a] • E7: Insect cells expressing myristylated Nef proteins on their cell surface can induce cytolysis of unstimulated CD4+ cells – this response is not due to MHC restricted CTL activity – the cell surface of Nef expressing insect cells carry Nef that can be recognized by MAbs E7 and E9 but not F1. [Fujii1996c] • E7: The C-term end of Nef is accessible to Abs at the cell surface – stained IIIB/M10, but not MN/M10, cells. [Fujii1993, Otake1994]					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1203	AE6	Nef (194–206)	Nef (LAI)	VARELHPEYFKNC		Vaccine	mouse (IgG1κ)

Vaccine *Vector/Type:* protein *HIV component:* Nef
Ab type C-term **Research Contact** Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada
References Chang1998

- AE6: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1. [Chang1998]

1204	AG11	Nef (194–206)	Nef (LAI)	VARELHPEYFKNC		Vaccine	mouse (IgG1κ)

Vaccine *Vector/Type:* protein *HIV component:* Nef
Ab type C-term **Research Contact** Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada
References Chang1998

- AG11: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 and subcloned into a eukaryotic expression vector with a green fluorescent protein marker to allow intracellular expression – the single chain Abs bind Nef intracellularly and may be useful to better understand the role of Nef and as a gene therapy model. [Chang1998]

1205	EH1	Nef (194–206)	Nef (SF2)	MARELHPEYYKDC		Vaccine	mouse (IgG1κ)

Vaccine *Vector/Type:* protein *HIV component:* Nef
Ab type C-term **Research Contact** Frank Jirik, Centre for Molecular Med and Therapeutics, U. B. C., Vancouver, B. C. Canada
References Chang1998

- EH1: The light and heavy chains of three MAbs (AG11, AE6, EH1) specific to C-terminus of NEF were cloned and variable regions sequenced – the complementarity determining regions (CDR) of AG11 and AE6 were highly related (95.1% at the DNA level) and bound LAI Nef, but not SF2 Nef – EH1 bound to SF2 and LAI and cross-competed AG11 and AE6 but had a distinctive CDR (57.9% similar to AG11) – single chain Abs were constructed from AG11 and EH1 and subcloned into a eukaryotic expression vector with a green fluorescent protein marker to allow intracellular expression – the single chain Abs bind Nef intracellularly and may be useful to better understand the role of Nef and as a gene therapy model. [Chang1998]

1206	3B4B	Nef	Nef			Vaccine	transgenic mouse (IgM)

Vaccine *Vector/Type:* protein *HIV component:* Nef *Adjuvant:* Incomplete Freund's Adjuvant (IFA)
References Kawai2003
Keywords antibody generation, complement.

- 3B4B: The goal of this study was to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Two human heavy chain, mouse light chain anti-Nef IgM were obtained, 3B4B and 3H3E; 3B4B was able to stain MOLT4/IIIB cells with greater intensity. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. [Kawai2003] (**antibody generation**, **complement**)

1207	3H3E	Nef	Nef			Vaccine	transgenic mouse (IgM)

Vaccine *Vector/Type:* protein *HIV component:* Nef *Adjuvant:* Complete Freund's Adjuvant (CFA)
References Kawai2003

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		Keywords antibody generation, complement. • 3H3E: The goal of this study was to elicit anti-Nef IgM human Abs in trans-chromosome mice that carry human chromosomes responsible for Ig production. These mice were immunized with recombinant Nef protein. Two human heavy chain, mouse light chain anti-Nef IgM were obtained, 3B4B and 3H3E; 3B4B was able to stain MOLT4/IIIB cells with greater intensity. The hope was that these human IgM anti-Nef chimeric Abs would activate complement mediated cytolysis; C3 deposition was induced but not at high enough levels to induce lysis. [Kawai2003] (**antibody generation**, **complement**)					
1208	6.1	Nef	Nef (JRCSF)				mouse
		References Ranki1995 • 6.1: NIAID Repository number 1123. [Ranki1995] • 6.1: Raised against CNS primary isolates, stains astrocytes more densely than other Nef MAbs – Nef expression associated with dementia. [Ranki1995]					
1209	NF2B2	Nef	Nef (20–78 BH10)			Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* Nef **References** Kaminchik1990 • NF2B2: NIH AIDS Research and Reference Reagent Program: 456. • NF2B2: Recognizes the Nef protein of the two isolates BH10 and LAV1. [Kaminchik1990]					
1210	NF3A3	Nef	Nef (20–78 BH10)			Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* Nef **References** Kaminchik1990 • NF3A3: Recognizes the Nef protein of the two isolates BH10 and LAV1 – low affinity. [Kaminchik1990]					
1211	NF8B4	Nef	Nef (BH10)			Vaccine	mouse
		Vaccine *Vector/Type:* protein *Strain:* B clade BH10 *HIV component:* Nef **References** Kaminchik1990 • NF8B4: Does not recognize Nef CNBr cleavage products – recognizes intact BH10 Nef but not LAV1 Nef. [Kaminchik1990]					
1212	polyclonal	Nef	Nef			Vaccine	macaque (IgG)
		Vaccine *Vector/Type:* protein *Strain:* B clade LAI, SIV *HIV component:* gp120, Nef, Tat *Adjuvant:* AS02A (oil-in-water emulsion, 3D-monophosphoryl lipid A, QS21), AS06 (CpG, aluminum hydroxide) **References** Voss2003 **Keywords** adjuvant comparison, variant cross-recognition or cross-neutralization. • Monkeys were immunized with different combinations of gp120/NefTat/SIV-Tat three times over a three-month time period and intravenously challenged with SHIV 89.6P four weeks after the last immunzation. Vaccination induced anti-Tat, -Nef and -gp120 Ab responses which decreased until challenge. Neutralizing Ab responses against HIV-1 MN and HIV-1 W61D were observed. Vaccination with the combination of all three proteins reduced viral load and kept animals from a CD4+ T cell decline, preventing AIDS for more than 2.5 years. The adjuvant AS02A elicited NAbs and protected from disease, while AS06 did not. gp120 alone or TatNef/SIV-Tat without gp120 could not protect from disease. [Voss2003] (**adjuvant comparison**, **variant cross-recognition or cross-neutralization**)					
1213	AE6	Nef	Nef				mouse
		Ab type C-term **Research Contact** James Hoxie, Div of AIDS, NIAID, NIH **References** Tornatore1994, Greenway1994 • AE6: NIH AIDS Research and Reference Reagent Program: 709.					

IV-C-18 HIV-1 Antibodies

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
1214		HIV-1				HIV-1 infection	
		References Goepfert2003 **Keywords** review. • A general review of anti-HIV human immune responses and the implications of these responses for vaccines, summarizing neutralizing antibodies, CD4+ and CD8+ T cell responses. A general overview of methods used to study these responses is presented. [Goepfert2003] (**review**)					
1215	polyclonal	HIV-1				HIV-1 infection	human
		References Fournier2002b • Purified B lymphocytes secret only a fraction of Ig and anti-HIV-1 Ab compared with unfractionated cells because monocytes and natural killer cells enhance both secretions by cell-to-cell contacts, involving adhesion and CD27, CD80 costimulatory molecules and IL-6 – cell-to-cell contacts and soluble factors induce maturation of activated B cells *in vitro* to allow prolonged survival and terminal differentiation. [Fournier2002b]					
1216	polyclonal	HIV-1				HIV-1 infection	human
		References Fournier2002a • An early and sustained fall in plasma viral load to below detection was observed in 17 HAART responders while HIV-1 RNA remained detectable in 13 incomplete responders – HIV-1 specific Ab secretion decreased in parallel with plasma viral load – HIV-1 specific Abs became negative in only six responders, and was correlated with greater increases of CD4 T-cell counts and higher levels of HIV-specific IgA secretion at baseline – persistent immune activation may be due to residual HIV antigen. [Fournier2002a]					
1217	polyclonal	HIV-1				HIV-1 infection	human
		References Subbramanian2002 • Sera from 39 patients were used to study the relative prevalence of neutralizing Abs (NAbs), ADCC-Abs and enhancing Abs – 69% of the sera were positive for NAbs but only 39% could neutralize in the presence of complement – 60% had ADCC Abs – 72% mediated the enhancement of infection in the presence of complement. [Subbramanian2002]					
1218	polyclonal	HIV-1				HIV-1 infection	human (IgA, IgG1)
		References Battle-Miller2002 • In a study of HIV-1 infected women, ADCC Abs were detected in 16% (12/51) of cervicovaginal fluids, and 56% (25/45) of serum samples – 3 women had ADCC in cervical lavage fluids, but not sera, suggesting local production. [Battle-Miller2002]					
1219	polyclonal	HIV-1				HIV-1 infection	human (IgA1, IgA2, IgM)
		References Wu2002 • IgA1 accounted for the majority of anti-HIV-1 IgA in the saliva in HIV-1 infected individuals – there was no anti-gp41 IgA in saliva, in contrast to plasma – lower levels of IgA and IgM were found in saliva than in plasma. [Wu2002]					
1220	polyclonal	HIV-1			P	HIV-1 infection	human
		References Hioe1997a					

No.	MAb ID	HXB2 Location	Author's Location	Sequence	Neutralizing	Immunogen	Species(Isotype)
		• Four primary isolates showed distinct patterns of sensitivity to neutralization by polyclonal sera or plasma and MAbs – BZ167 was the only isolate inhibited by all polyclonal sera and plasma tested, and was also neutralized by 8/17 MAbs, in particular anti-V3 loop (419-D, 447-52D, 782-D, and 838-D), anti-CD4bd (559/64-D, 654-D and 830-D and a cluster II of gp41 directed MAb (98-6) – isolates 92HT593 and 91US056 were neutralized by V3 loop (419-D, and 447-52D)and cluster II gp41 (98-6) MAbs at higher concentrations – US4 was neutralized by some of the polyclonal sera/plasma tested and not at all by MAbs individually or by a cocktail of ten MAbs consisting of 419-D, 447-52D, 782-D, 838-D, 559/64-D, 654-D, 450-D, 670-D, 1281-D and 98-6. [Hioe1997a]				
1221	polyclonal	HIV-1			no	HIV-1 infection	human (IgA, IgG)
		References Oelemann2002					
		• A urine based commercial EIA kit from Calypte Biomedical Corporation, Berkeley, CA was found to work well as a primary screening for HIV in Brazilian samples – 76 HIV+ samples were correctly identified (100% sensitivity), and 278/284 negative samples 97.9% specificity. [Oelemann2002]					
1222	polyclonal	HIV-1	HIV-1		no	HIV-1 infection	human (IgE)
		References Pellegrino2002, Secord1996					
		• Pediatric long term survivors (LTS) have been found to carry HIV-1 specific IgE – serum from these children inhibit HIV-1 production in culture, but this inhibition did not seem to be due to neutralization, rather due to a cytoxic event – serum lost the HIV-1 inhibitory effect when depleted of IgE. [Pellegrino2002]					
		• HIV-specific IgE found in clinically healthy HIV-1 infected children. [Secord1996]					
1223	polyclonal	HIV-1	gp120 and p55		no	Vaccine	macaque
		Vaccine *Vector/Type:* vaccinia *Strain:* B clade 89.6 *HIV component:* Env, Gag-Pol *Adjuvant:* E. coli mutant heat labile enterotoxin (LT-R72)					
		References Ambrose2003					
		Keywords genital and mucosal immunity.					
		• Systemic priming with rVVs expressing HIV-1 Env and SHIV Gag-Pol followed by intragastric and intranasal mucosal boosting of LT(R192G) and aldrithiol-2 (AT-2)-inactiviated SHIV induced SHIV-specific IgA and IgG plasma and mucosal Abs. Viral loads in vaccinated animals were reduced after vaginal challenge with SHIV 89.6. [Ambrose2003] (**genital and mucosal immunity**)					

IV-D

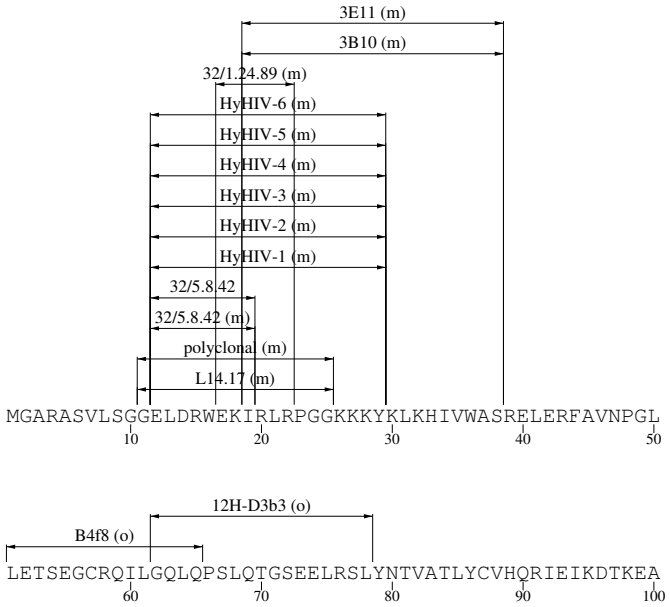
Maps of MAb Locations Plotted by Protein

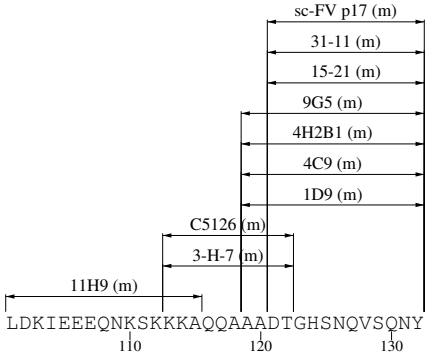
Linear epitopes less than twenty-two amino acids long are shown with their antibody ID and the experimental species.

Key	Species
h	human
p	non-human primate
m	murine
o	other

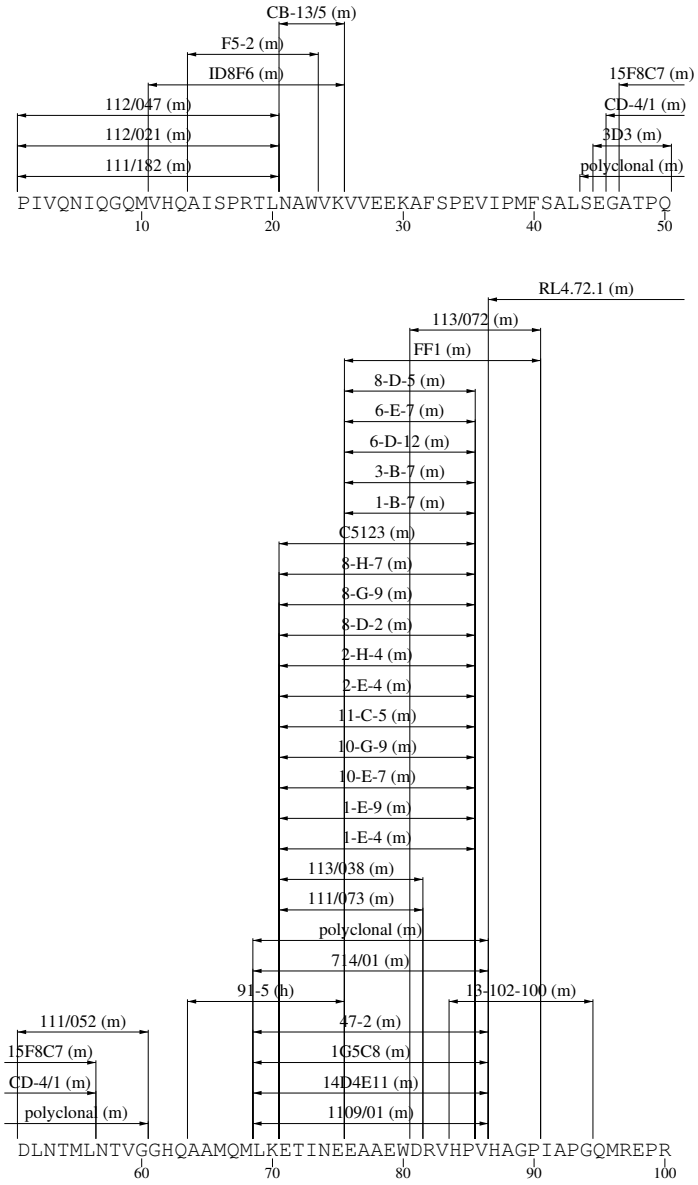
Table IV-D.1: The species for which the epitopes react

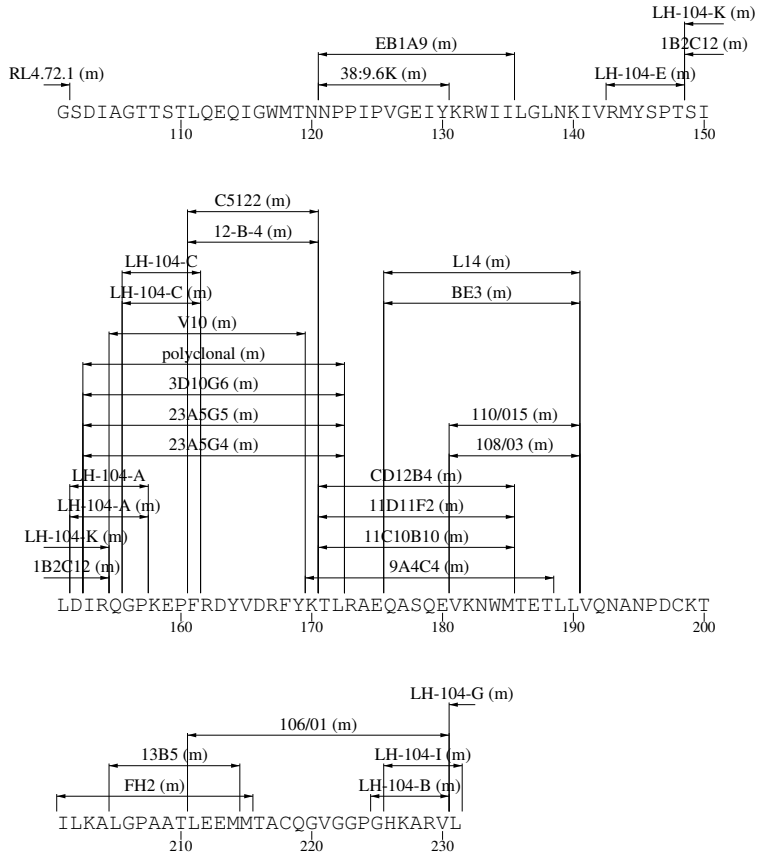
IV-D-1 p17 Ab epitope map



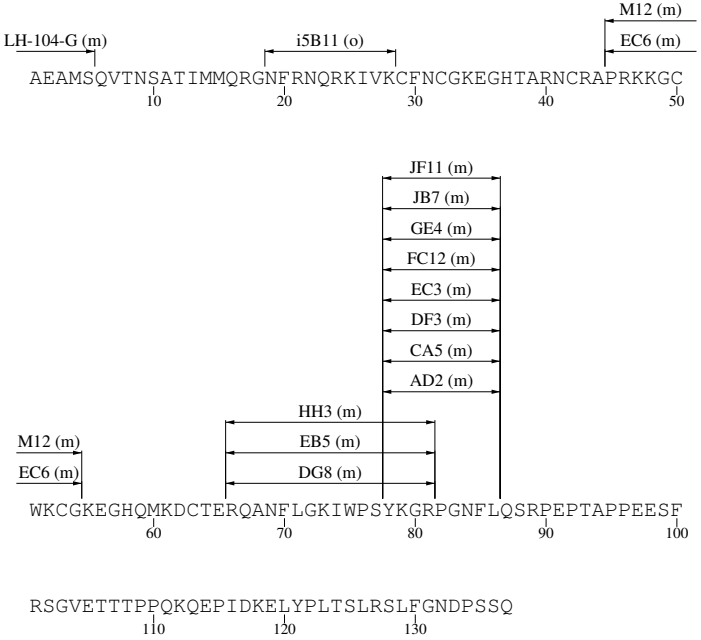


IV-D-2 p24 Ab epitope map



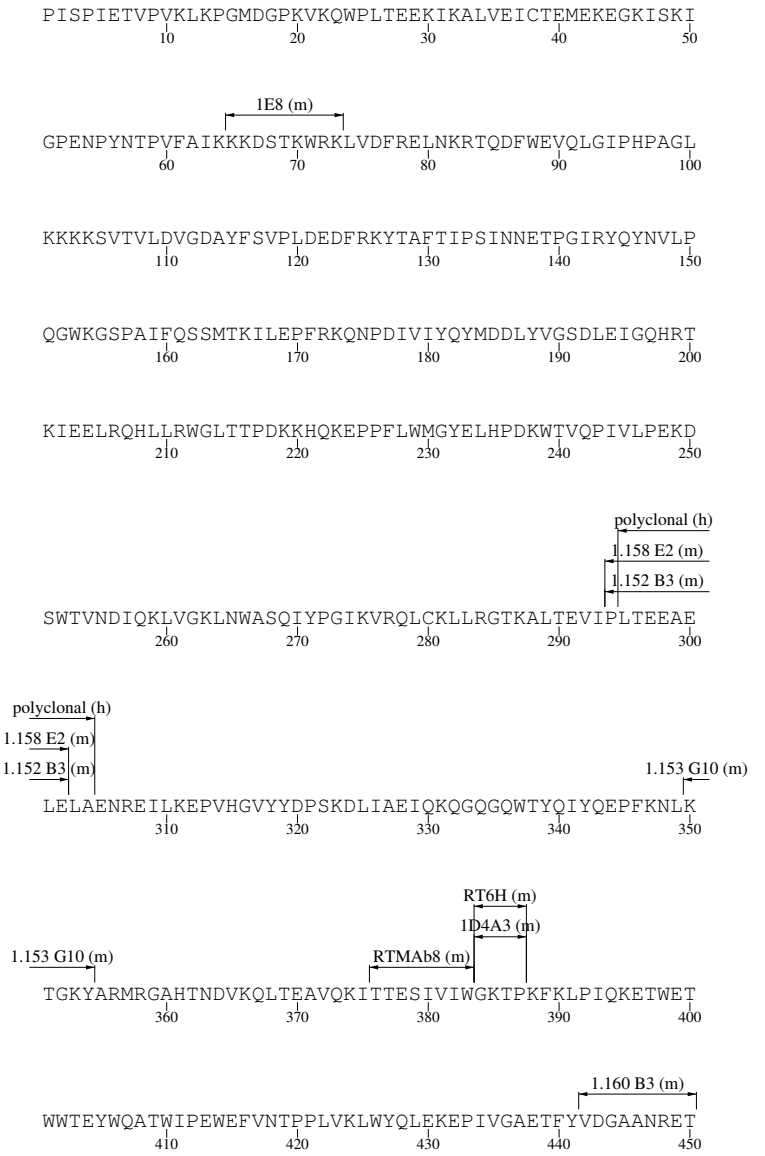


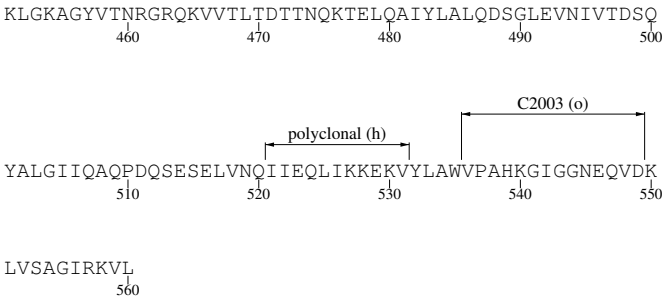
IV-D-3 p2p7p1p6 Ab epitope map



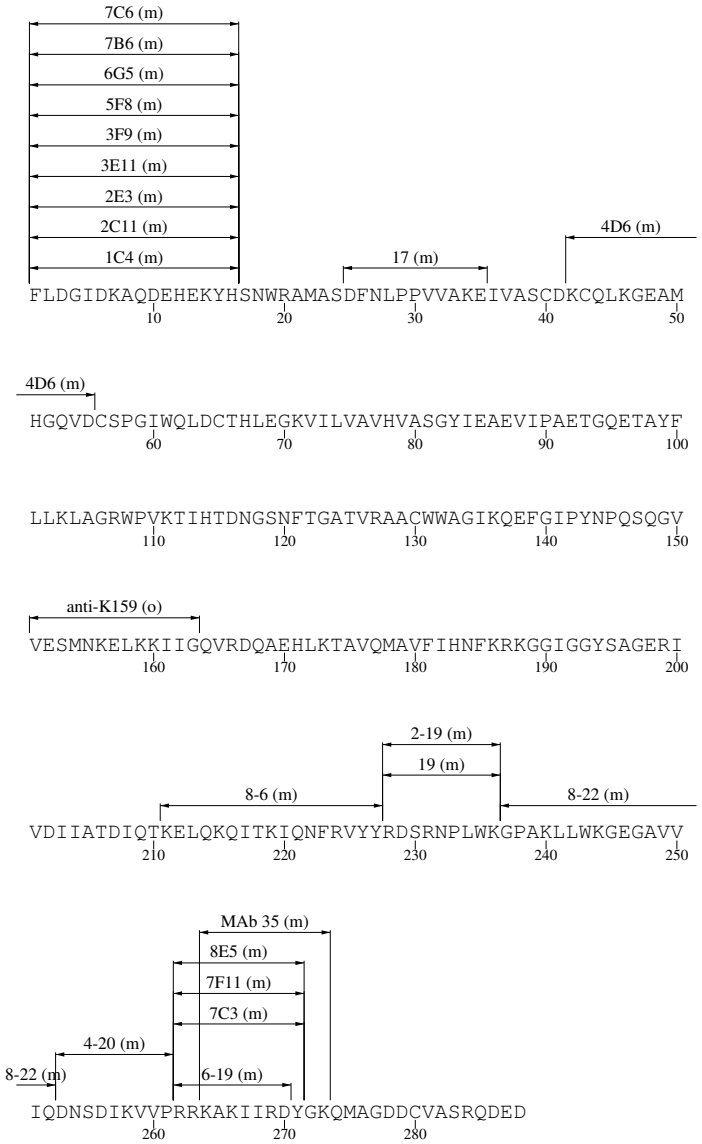
IV-D-4 Protease Ab epitope map

IV-D-5 RT Ab epitope map

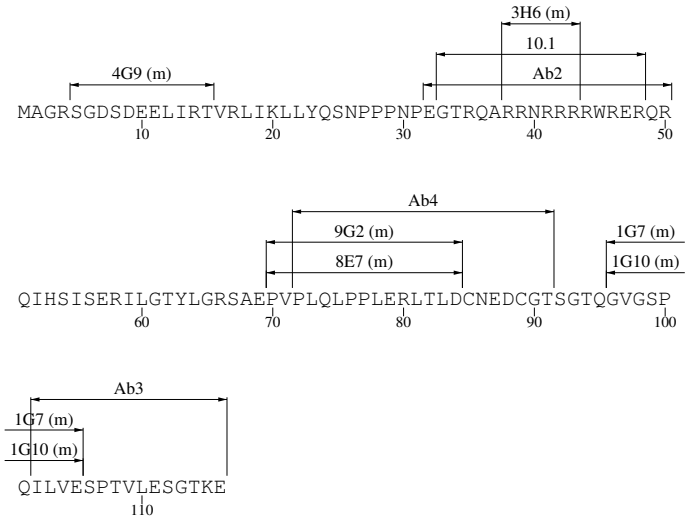




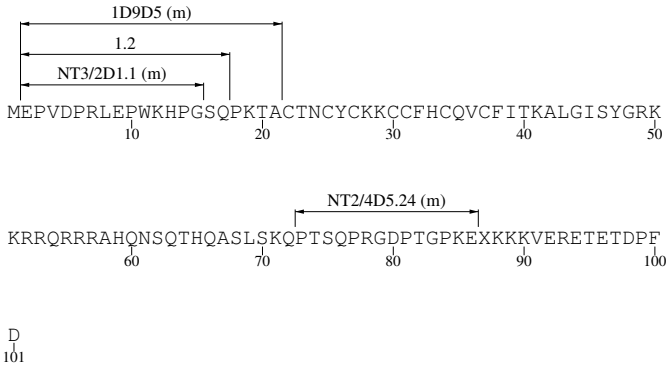
IV-D-6 Integrase Ab epitope map



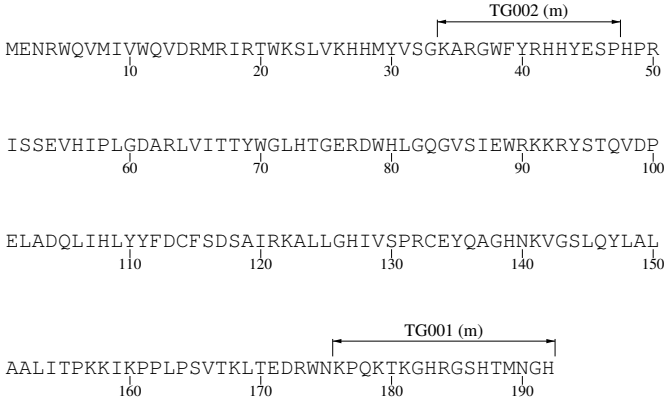
IV-D-7 Rev Ab epitope map



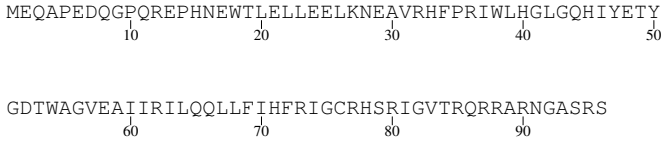
IV-D-8 Tat Ab epitope map



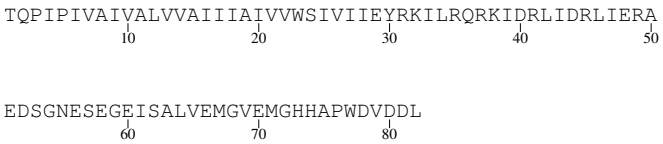
IV-D-9 Vif Ab epitope map



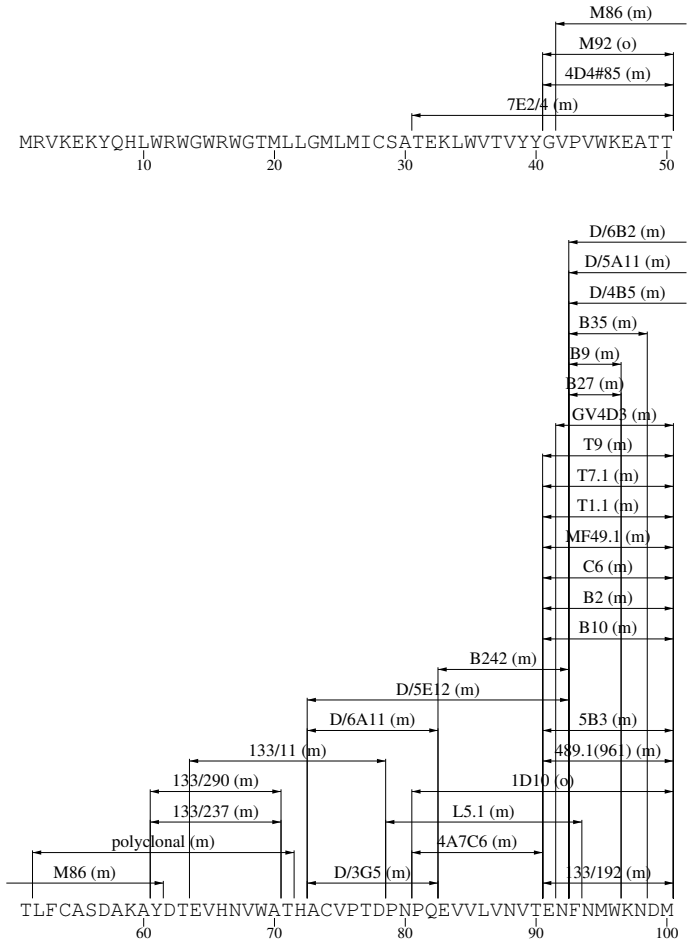
IV-D-10 Vpr Ab epitope map

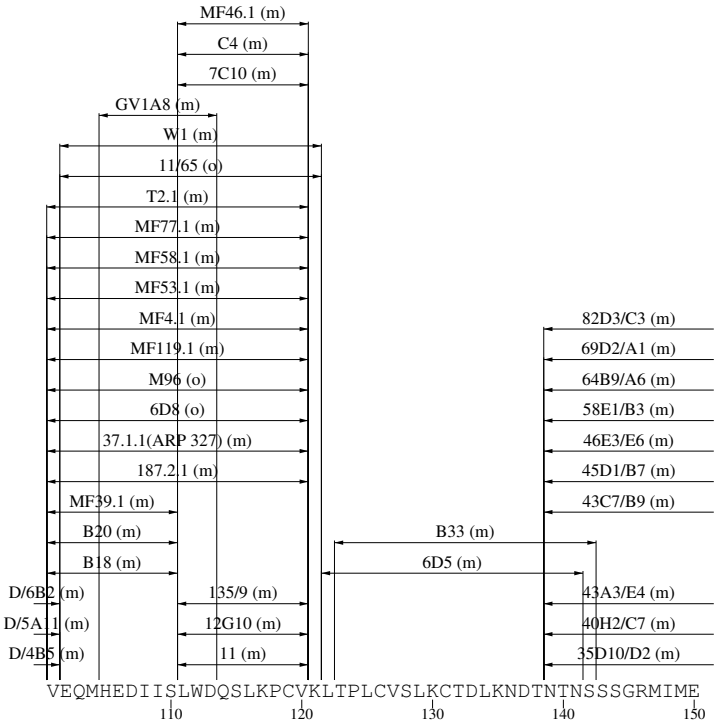


IV-D-11 Vpu Ab epitope map



IV-D-12 gp160 Ab epitope map




MF46.1 (m)
C4 (m)
7C10 (m)
GV1A8 (m)
W1 (m)
11/65 (o)
T2.1 (m)
MF77.1 (m)
MF58.1 (m)
MF53.1 (m)
MF4.1 (m)
MF119.1 (m)
M96 (o)
6D8 (o)
37.1.1(ARP 327) (m)
187.2.1 (m)
MF39.1 (m)
B20 (m)
B18 (m)
D/6B2 (m)
D/5A1 (m)
D/4B5 (m)
135/9 (m)
12G10 (m)
11 (m)
B33 (m)
6D5 (m)
82D3/C3 (m)
69D2/A1 (m)
64B9/A6 (m)
58E1/B3 (m)
46E3/E6 (m)
45D1/B7 (m)
43C7/B9 (m)
43A3/E4 (m)
40H2/C7 (m)
35D10/D2 (m)
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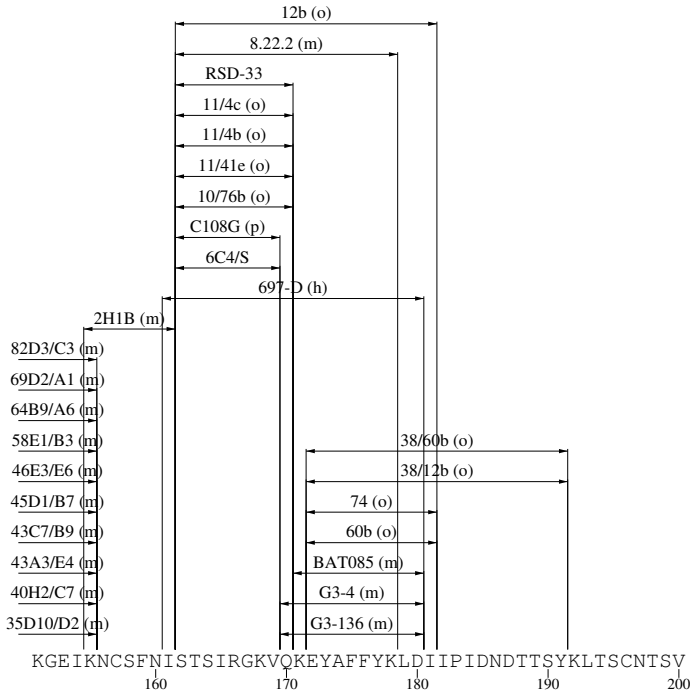
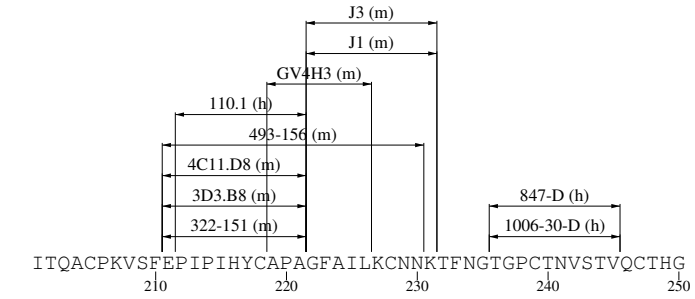
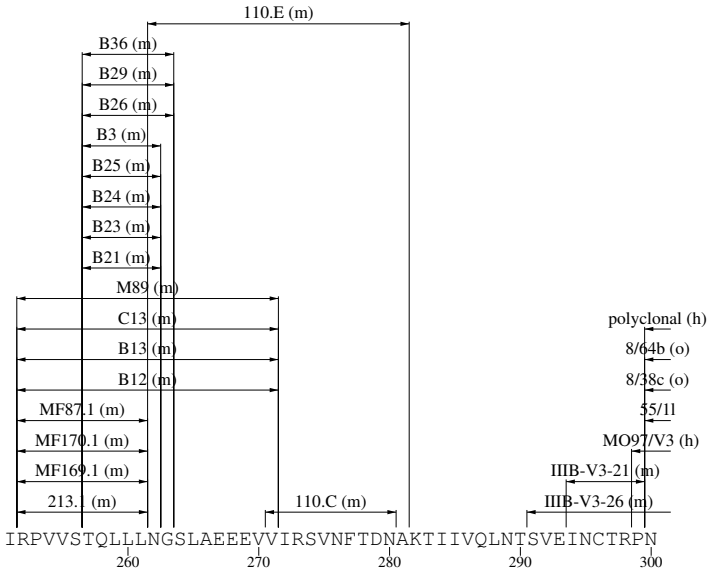
110
120
130
140
150


12b (o)
8.22.2 (m)
RSD-33
11/4c (o)
11/4b (o)
11/41e (o)
10/76b (o)
C108G (p)
6C4/S
697-D (h)
2H1B (m)
82D3/C3 (m)
69D2/A1 (m)
64B9/A6 (m)
58E1/B3 (m)
46E3/E6 (m)
45D1/B7 (m)
43C7/B9 (m)
43A3/E4 (m)
40H2/C7 (m)
35D10/D2 (m)
38/60b (o)
38/12b (o)
74 (o)
60b (o)
BAT085 (m)
G3-4 (m)
G3-136 (m)
KGEIKNCSFNISTSIRGKVQKEYAFFYKLDIIPIDNDTTSYKLTSCNTSV
160
170
180
190
200


J3 (m)
J1 (m)
GV4H3 (m)
110.1 (h)
493-156 (m)
4C11.D8 (m)
3D3.B8 (m)
322-151 (m)
847-D (h)
1006-30-D (h)
ITQACPKVSFEPIPIHYCAPAGFAILKCNNKTFNGTGPCTNVSTVQCTHG
210
220
230
240
250


110.E (m)
B36 (m)
B29 (m)
B26 (m)
B3 (m)
B25 (m)
B24 (m)
B23 (m)
B21 (m)
M89 (m)
C13 (m)
B13 (m)
B12 (m)
MF87.1 (m)
MF170.1 (m)
MF169.1 (m)
213.1 (m)
110.C (m)
polyclonal (h)
8/64b (o)
8/38c (o)
55/11
MO97/V3 (h)
IIIB-V3-21 (m)
IIIB-V3-26 (m)
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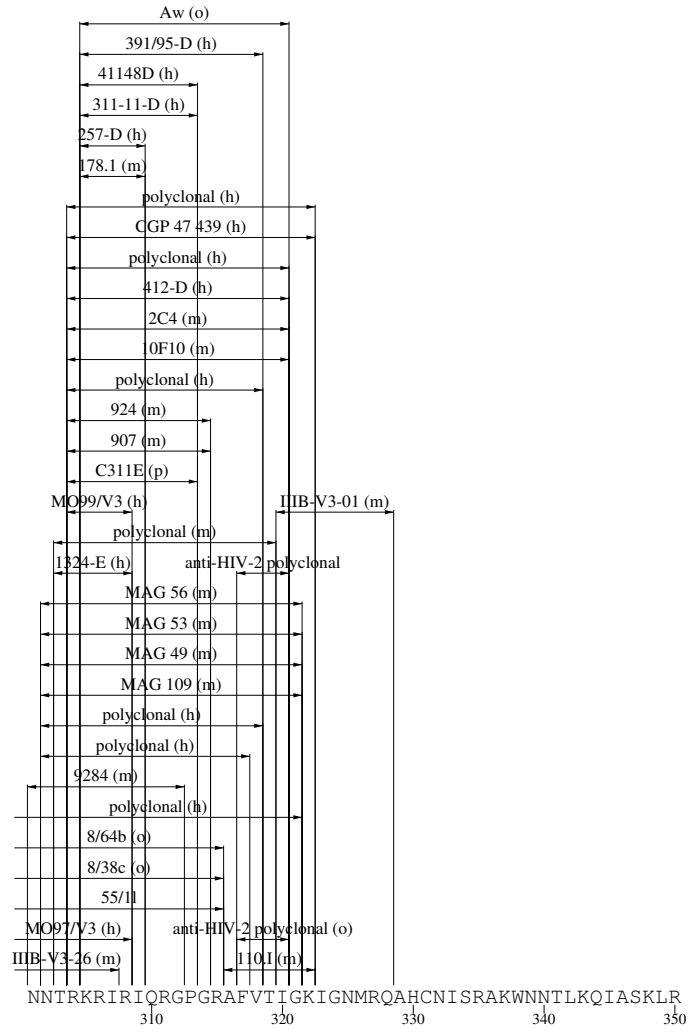
260
270
280
290
300


Aw (o)
391/95-D (h)
41148D (h)
311-11-D (h)
257-D (h)
178.1 (m)
polyclonal (h)
CGP 47 439 (h)
polyclonal (h)
412-D (h)
2C4 (m)
10F10 (m)
polyclonal (h)
924 (m)
907 (m)
C311E (p)
MO99/V3 (h)
IIIB-V3-01 (m)
polyclonal (m)
1324-E (h)
anti-HIV-2 polyclonal
MAG 56 (m)
MAG 53 (m)
MAG 49 (m)
MAG 109 (m)
polyclonal (h)
polyclonal (h)
9284 (m)
polyclonal (h)
8/64b (o)
8/38c (o)
55/11
MO97/V3 (h)
anti-HIV-2 polyclonal (o)
IIIB-V3-26 (m)
110.I (m)
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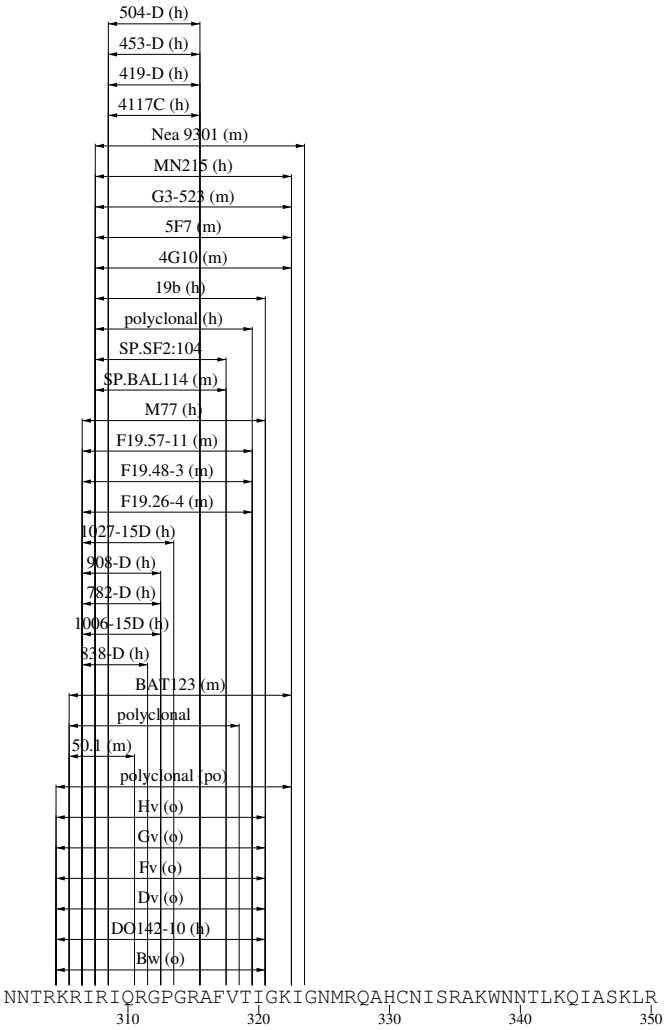
310
320
330
340
350

B Cell


504-D (h)
453-D (h)
419-D (h)
4117C (h)
Nea 9301 (m)
MN215 (h)
G3-523 (m)
5F7 (m)
4G10 (m)
19b (h)
polyclonal (h)
SP.SF2:104
SP.BAL114 (m)
M77 (h)
F19.57-11 (m)
F19.48-3 (m)
F19.26-4 (m)
1027-15D (h)
908-D (h)
782-D (h)
1006-15D (h)
838-D (h)
BAT123 (m)
polyclonal
50.1 (m)
polyclonal (po)
Hv (o)
Gv (o)
Fv (o)
Dv (o)
DO142-10 (h)
Bw (o)
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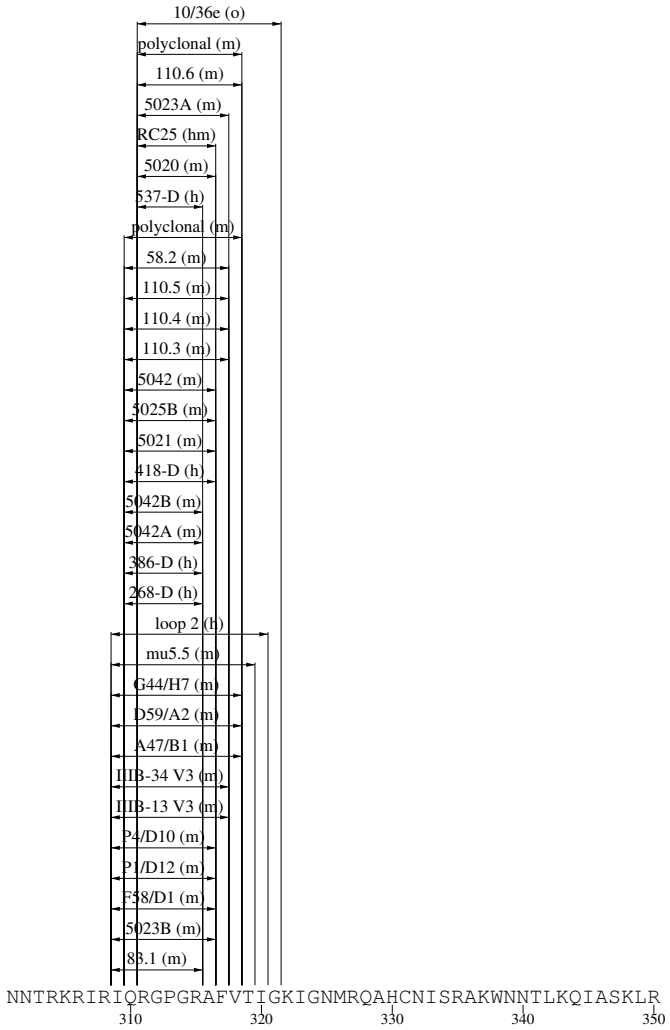
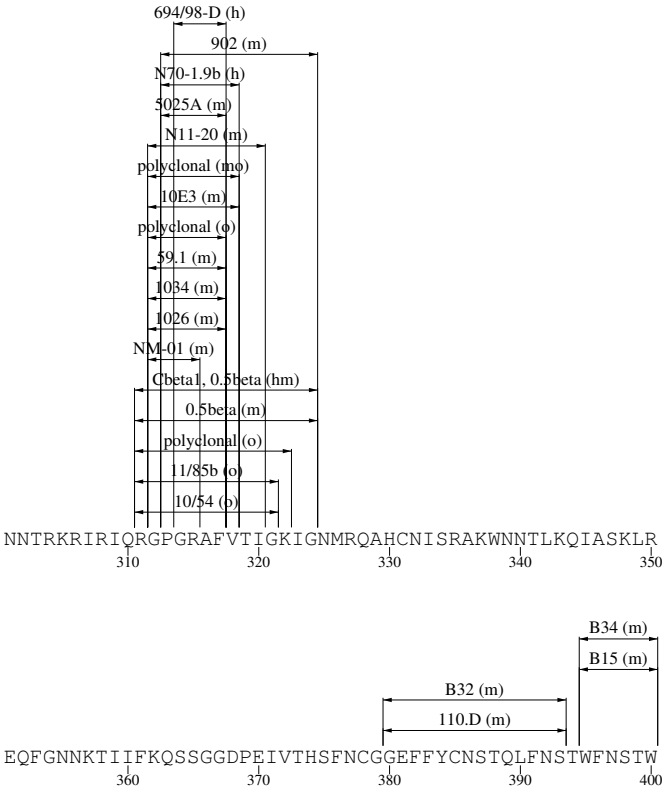
310
320
330
340
350


10/36e (o)
polyclonal (m)
110.6 (m)
5023A (m)
RC25 (hm)
5020 (m)
537-D (h)
polyclonal (m)
58.2 (m)
110.5 (m)
110.4 (m)
110.3 (m)
5042 (m)
5025B (m)
5021 (m)
418-D (h)
5042B (m)
5042A (m)
386-D (h)
268-D (h)
loop 2 (h)
mu5.5 (m)
G44/H7 (m)
D59/A2 (m)
A47/B1 (m)
IIIB-34 V3 (m)
IIIB-13 V3 (m)
P4/D10 (m)
P1/D12 (m)
F58/D1 (m)
5023B (m)
83.1 (m)
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
310
320
330
340
350

B Cell


694/98-D (h)
902 (m)
N70-1.9b (h)
5025A (m)
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310
320
330
340
350
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B15 (m)
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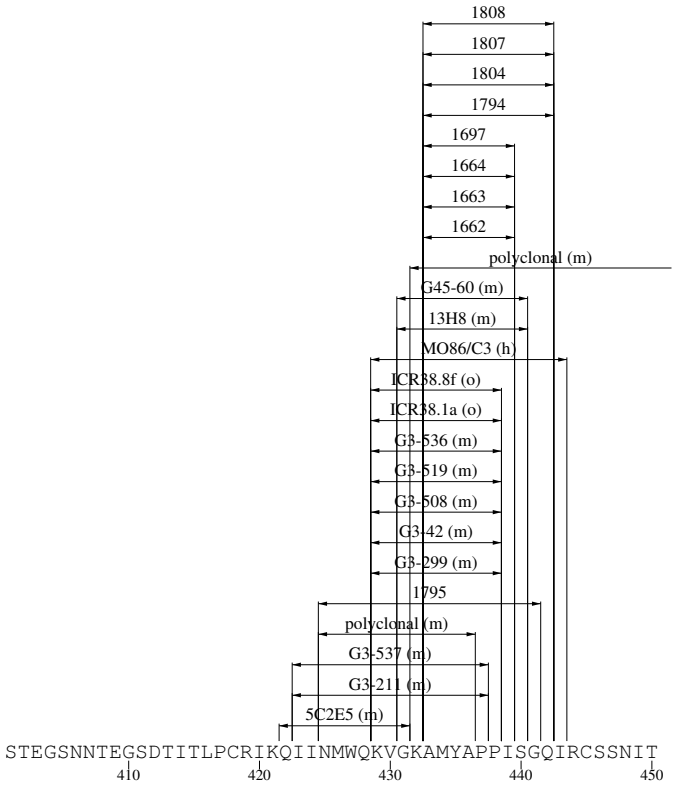
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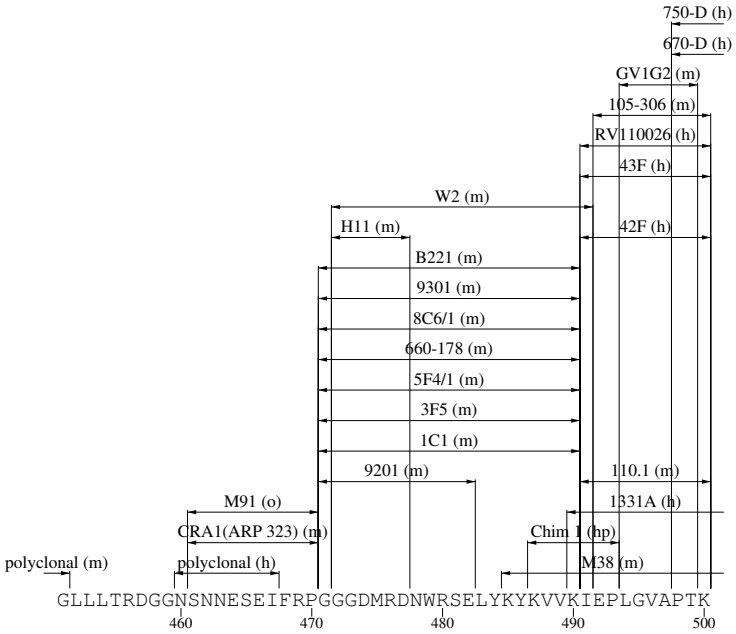
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8C6/1 (m)
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5F4/1 (m)
3F5 (m)
1C1 (m)
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Chim 1 (hp)
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490
500
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858-D (h)
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M38 (m)
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25C2 (h)
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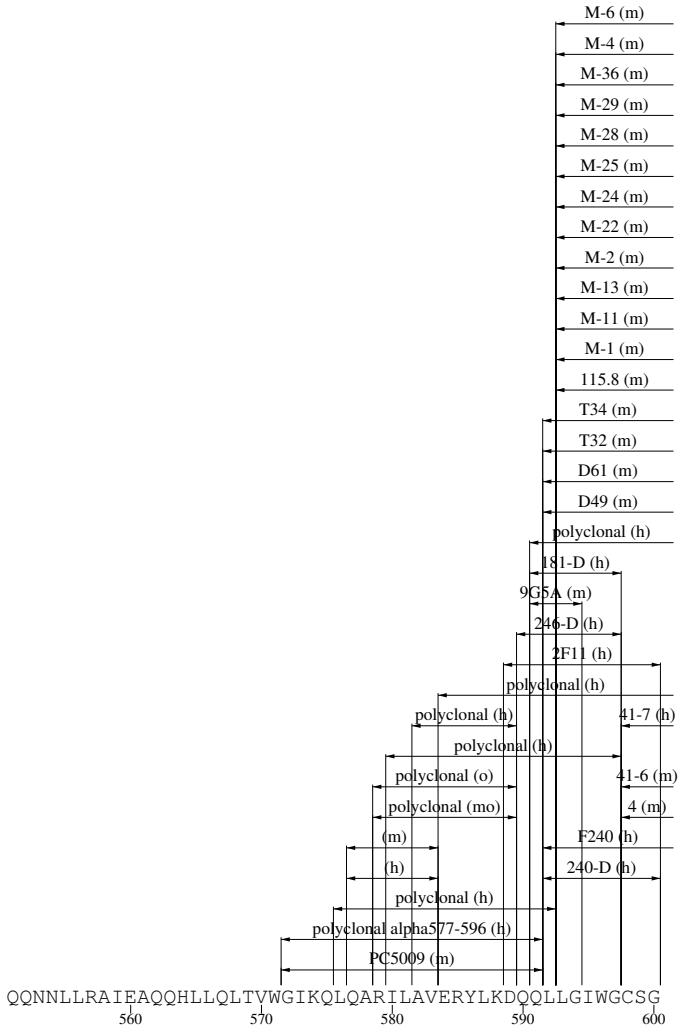
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(m)
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(h)
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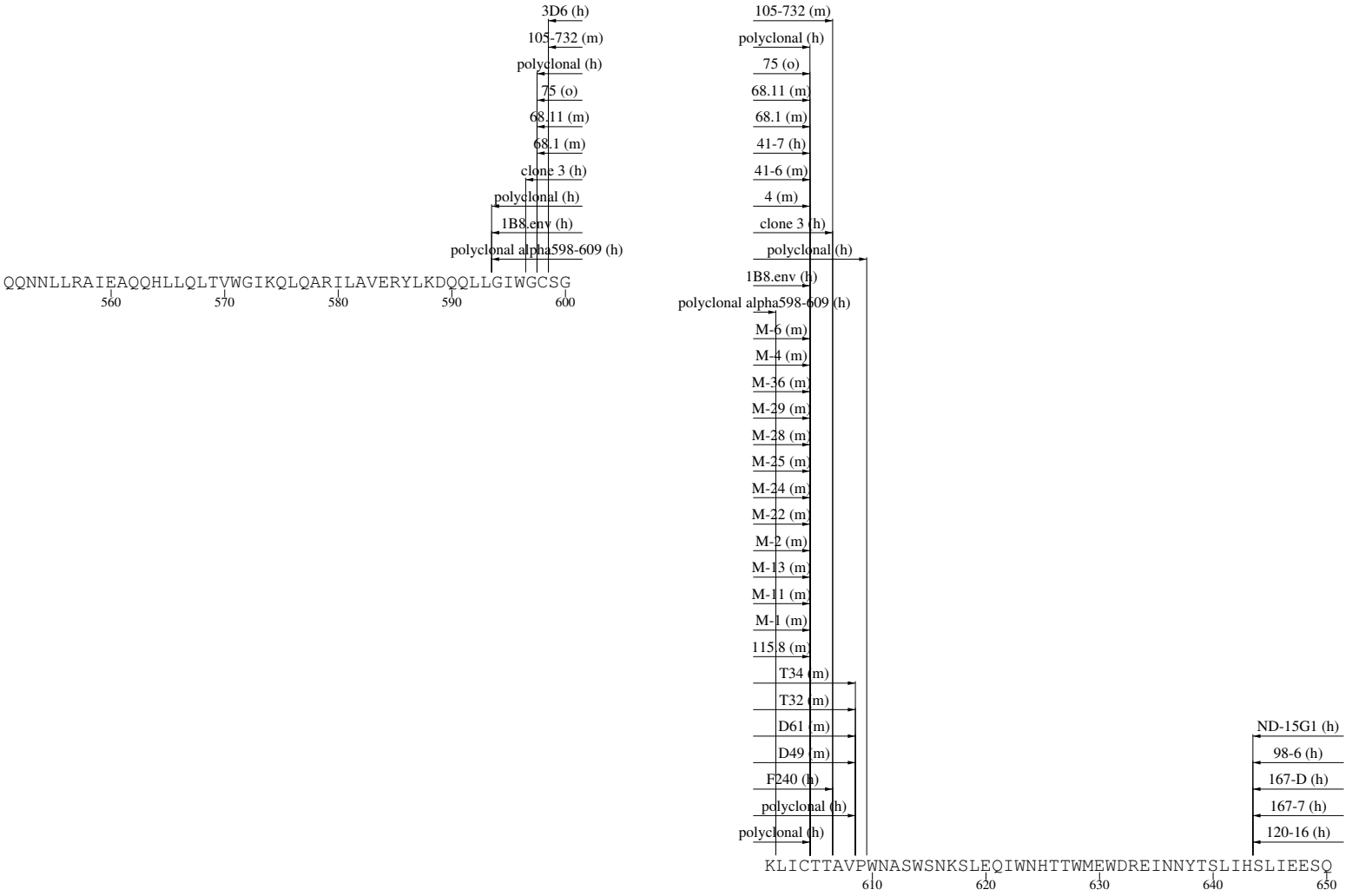
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ND-15G1 (h)
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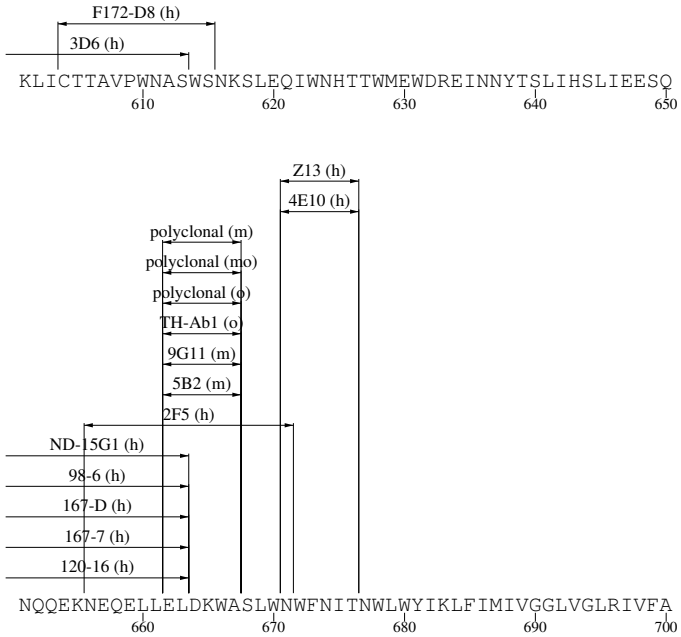
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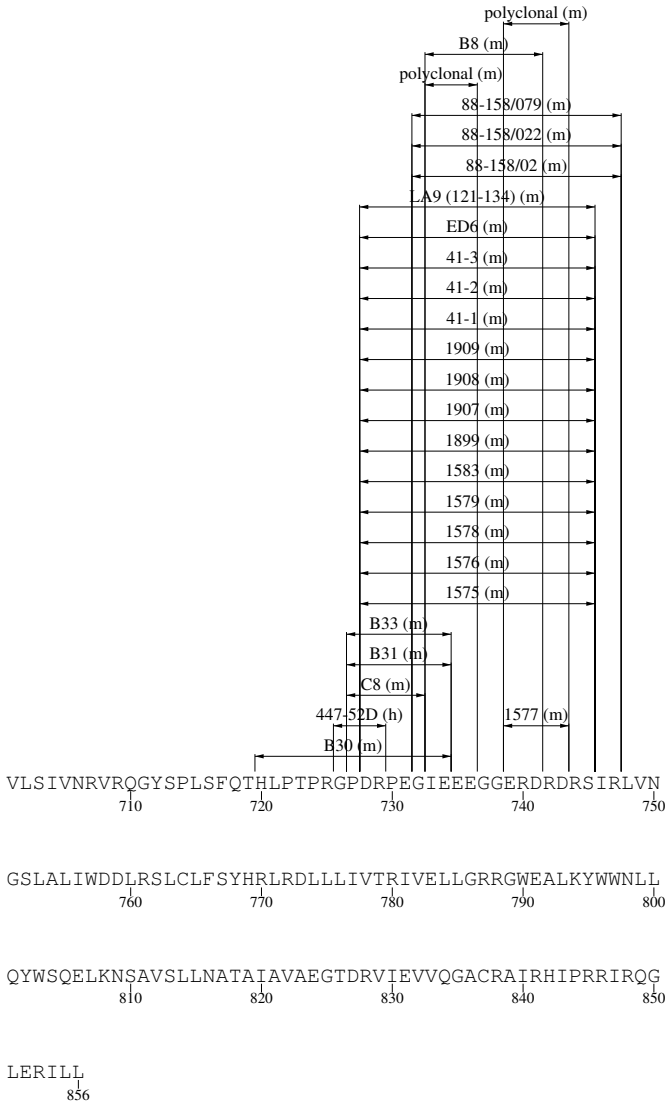
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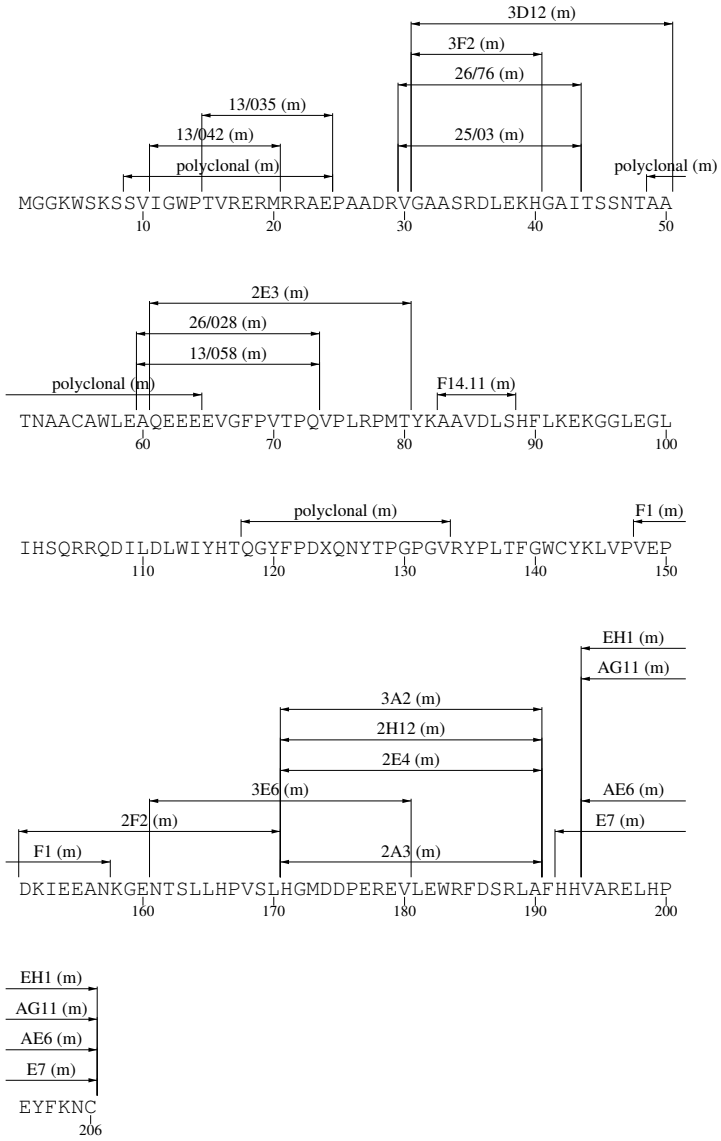
IV-D-13 Nef Ab epitope map



Part V

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Part VI

Nonhuman Primates HIV/SIV Vaccine Trials Database

Nonhuman Primates HIV/SIV Vaccine Trials Database 2003

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VI-A

Introduction and Historical Overview of the Nonhuman Primates HIV/SIV Vaccine Trials Database

The development of an effective vaccine against HIV is urgently needed given the continual increase in the number of people infected with HIV, estimated to be about 40 million, in addition to 20 million people who have already died due to HIV since the beginning of the epidemic two decades ago. A general consensus is that the development of an effective vaccine is the best way to tackle this epidemic. Unfortunately, the effort to develop a good and reliable vaccine against HIV has proven to be difficult. HIV is the most studied infectious agent in medical history. The vaccine research is increasingly becoming an important focus as a large number of data continue to emerge from different laboratories. As of October 2004, a quick search using a string argument containing "HIV or SIV and vaccine" yielded 6439 references. Using the search string "((HIV OR SIV) AND vaccine) AND macaque", 820 references were retrieved from PUBMED.

Since traditional approaches for vaccine development have proven ineffective for HIV, it is important to encourage new methodologies and to increase the numbers of studies in order to speed up the process required to develop an effective vaccine against HIV. Consequently, a large number of studies on HIV and SIV-related vaccine are being generated. In addition, studies vary considerably in the way the vaccine trials are being conducted, including the design and formulation of vaccines, the doses, the animals used, the challenge viruses, etc. This makes it difficult to adequately compare the studies. It is important to continue to monitor the ever growing number of data generated by researchers working to understand the complexity of HIV pathogenicity and to follow up the ongoing preclinical research in animal models and phase I-III human trials.

To begin to address this problem, we have constructed a relational database named *Nonhuman Primate HIV/SIV Vaccine Trials Database* to serve the scientific community, particularly those engaged in vaccine development as well as policy makers.

The published data pertaining to HIV vaccine development in nonhuman primate models have been curated and compiled in such a way that users can interactively search and retrieve them online through the internet. In order to qualify for entry in the database, the trial must meet the following criteria: 1) SIV or HIV-based vaccine or passive immunization have been used in nonhuman primates; 2) an assessment for immunogenicity or immunotherapeutic property of the immunogen has been performed. A challenge virus may also have been injected to the immunized and control animals to assess the efficacy of the vaccine.

Historically, prior to the development of this database, Dr. Jon Warren at the EMMES Corporation had maintained a similar database, though organized differently, and with different data fields and somewhat different nomenclature. The studies in that database include those published through 1999. We have made that database accessible through the internet, and integrated it into the search interface of the Los Alamos National Laboratory vaccine database. This will be available to the public until we have integrated all of those studies into the Los Alamos database.

The Los Alamos Nonhuman Primate HIV/SIV Vaccine Trials Database home page can be accessible at `http://www.hiv.lanl.gov/cgi-bin/vaccine/public/index.cgi`, and is depicted in Figure VI-A.1.

The data in the database can be accessed in two ways, using the Search Form or the Cross-Table Form which are displayed on the home page. The Search Form allows users to retrieve technical information pertaining to vaccine studies using multiple choice menus to construct logical arguments for searching the database. The search argument is a combination of items chosen from the menus which include the study Objectives, the Species or experimental animal model, the Reference, the Vaccine and Challenge virus (Figure VI-A.2).

The search argument formulated by the user sends an electronic query to both the Los Alamos (also known as the *Current Database*) and the data collected by

In *HIV Immunology and HIV/SIV Vaccine Databases 2003*. Publisher: Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico. LA-UR 04-8162. pp. 1127–1332.

Figure VI-A.1: Home page of the vaccine trials database

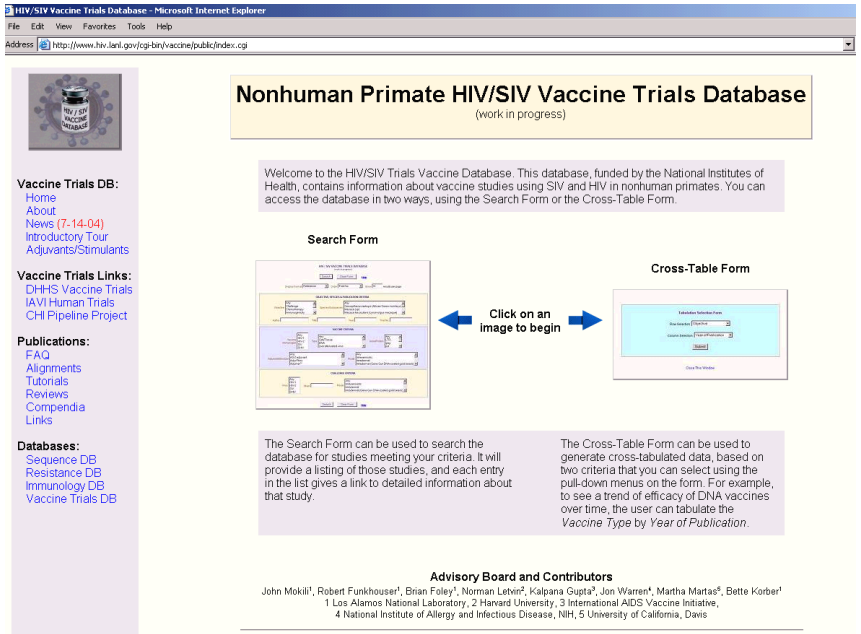
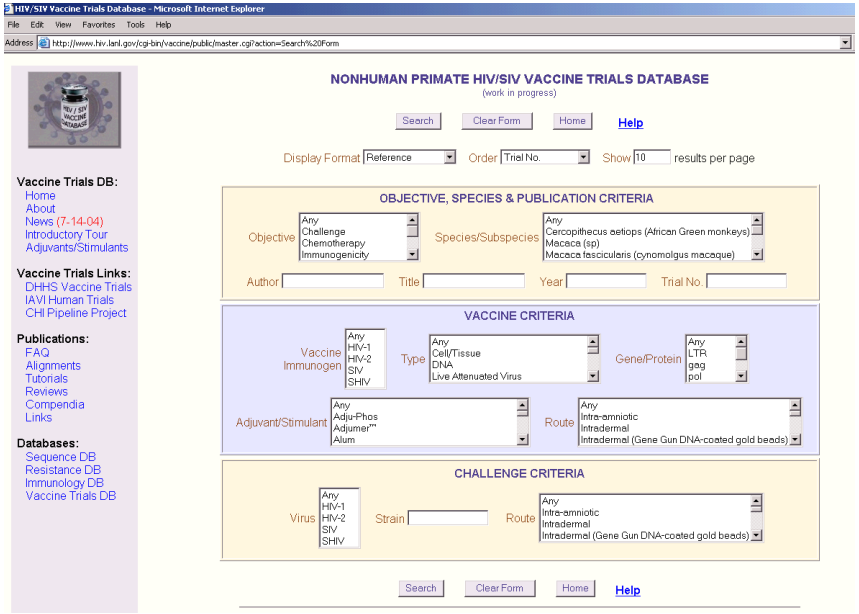


Figure VI-A.2: Search Form



Jon Warren (also known as the *Previous Database*). Where the search argument cannot be applied to the Previous Database, a message to this effect is displayed. Of note, the Previous Database has fewer display choices, and the data were organized by Stage. A *Stage* is generally defined as a point in a trial where results for a group of test subjects was assessed. In some cases, stages span multiple published studies. The Los Alamos Database or Current Database does not organize data along the concept of stages, rather each published paper is treated as a distinct trial. However, in some few cases a published study may encompass multiple but directly related experiments. In such cases a suffix *experiment number* is added so that the first experiment of, say, NHP92 will be shown as NHP92.1, the second as NHP92.2, etc. In this compendium, we have selected only the information contained in the Current Database; a hard copy summary of Jon Warren's final database was published in the Journal of Clinical Primatology under the title "Preclinical AIDS vaccine research: survey of SIV, SHIV, and HIV challenge studies in vaccinated nonhuman primates" (please see *J Med Primatol* 2002 Aug; 31(4-5):237-256).

Table VI-A.1: Example of an output using the Cross-Table Form. In this specific case, the HIV subtype (across) and the Virus (down) from which the immunogen was based.

	HIV-1 subtype										
Immunogen Origin	**A**	**B**	**C**	**CRF02_AE**	**D**	**F**	**G**	**H**	**J**	**K**	**L**
HIV-1	1	66 [65/321]	1	1	1	0	0	0	0	0	0
HIV-2	0	0	0	0	0	0	0	0	0	0	0
SHIV	0	10 [2/42]	0	0	0	0	0	0	0	0	0
SIV	0	21 [22/142]	0	0	0	0	0	0	0	0	0

The data entered in the database can also be retrieved using the Cross-Table Search Form. This tool was designed to allow users to retrieve data in a cross-tabulated format. For example, Table VI-A.1 shows a tabulation of the origin of vaccine immunogens (HIV-1, HIV-2, SIV or SHIV) by the subtype shows that the great majority of vaccines trials used so far are based on subtype B. The number in each bifurcation box refers to the number of studies in the database and the ratio of animals protected from infection with the challenge virus over the total number of animals immunized and challenged.

VI-A-1 Organization and contents of the compendium

This vaccine trials compendium is divided in 5 chapters.

- Vaccines
- Challenges
- Adjuvants and Stimulants
- Trial Summaries
- References

An introduction is provided at the beginning of each section.

VI-B

Vaccines

This section contains a list of vaccines used in the studies compiled in the database. We devised a simple nomenclature to group the vaccines by type of vaccine. This includes the following:

- DNA
- Live Attenuated Virus
- Recombinant Live Attenuated Virus
- Live Virus
- Cell/Tissue
- Whole (killed) Inactivated Virus
- Virus-like Particle
- Purified Viral Products
- Synthetic Protein/Peptide
- Recombinant Subunit Protein
- Recombinant Vector (virus/bacteria)
- Passive Antibody
- Other

In most cases the name and description of the vaccine, as provided by the authors of the paper, was retained. The virus (HIV, SIV or SHIV), the viral component (gene or protein) and the subtype (for HIV or HIV fragment in SHIV) were also recorded. The database trial numbers (NHP number) where the vaccine was used are listed for reference.

VI-B-1 DNA vaccines

Vaccine Name **bSIVgp120**
Description Recombinant baculovirus expressing SIV gp120

Trial(s) NHP.33

Vaccine Name **CHO-SIVgp120**
Description Recombinant Chinese hampster cells expressing SIV gp120

Trial(s) NHP.33, NHP.156

Vaccine Name **CMV SHIV dEN**
Description CMV-SHIVdEN) was constructed from an env and nef deletion SHIV DNA (SIVGP1 DNA) by replacing the 5' long terminal repeat region with a cytomegalovirus promoter with an immediate-early enhancer and the 3' long terminal repeat region with simian virus 40 poly(A).

Virus SHIV *Strain:* SIVGP1 DNA *Subtype:* B *Gene/Protein:* gag, pol, Accessory (vif,vpx, vpr (partial))
Notes lacking env and nef

Trial(s) NHP.326

Vaccine Name **CMVKm2-gp140TM**
Description The sequence for the native subtype B HIV-1US4 envelope was modified to reflect the optimal codon usage in highly expressed human genes. Contained the oligomeric secreted membrane-bound gp140TM, which include the membrane-spanning domain of gp41 (residues1-691). The gene cassettes constructedsynthetically using EcoR1 and Xba1 by the Midland Certified Reagent Company, and were cloned into plasmid vectors for DNA vaccination (pCMVKm2).

Virus HIV-1 *Strain:* HIV-1.US4 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.354

Vaccine Name **d81**
Description In this vaccine the SIVmac239 env-nef expression cassette was inserted into the TK gene of the HSV-1 genome. It has a deletion in the essential ICP27 gene in addition to the deletion in TK, rendering it replication defective in Vero cells. CMV, promoter/enhancer sequences of the CMV IE gene; PA, signal sequences for poly(A) addition. The SIV sequences are from the SphI site (nucleotide 6450) rightward in SIVmac239. These include rev exon 1, the entire env ORF, rev exon 2, and the nef open reading frame
Notes Herpes simplex vector

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env

Trial(s) NHP.54

Vaccine Name **DNA (pCMVKm2) gp140**
Description Unmodified gp140. pCMVKm2 vector expressing the gp140 ectodomain form of the HIV envelope immunogen, with an intact gp120-gp41 cleavage site

Virus HIV-1 *Strain:* SF162 *Subtype:* B

Trial(s) NHP.22

Vaccine Name **DNA Vaccine pNL432-ZF1***

Description DNA vaccine derived from pNL432, an infectious molecular clone of HIV-1 in which the first two cysteine residues of the N-terminal zinc finger motif (Cys-X2-Cys-X4-His-X4-Cys) were replaced by serine residues

Virus HIV-1 *Strain:* NL432 *Subtype:* B *Gene/Protein:* All (Full genome (modified))
Notes first two amino cysteine residues of the N-terminal zinc finger motif (Cys-X2-Cys-X4-His-X4-Cys) were replaced by serine residues

Trial(s) NHP.31, NHP.149.2

Vaccine Name **DNA-gag,env**
Description DNA vaccines encoding SIVmac239 Gag and HIV-1-89.6P Env
Notes 2 constructs

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.23

Vaccine Name **DNA-pCI-rev**
Description Eukaryotic expression vector pCI (Promega, Charbonnieres, France) with HIV-1 primary isolate ACH320 2.1 rev cDNA. Expression checked in 293T cells.

Virus HIV-1 *Strain:* ACH320 2.1 *Subtype:* B *Gene/Protein:* rev
HXB2 5970-6045 (exon 1) and 8379-8653 (exon 2)

Trial(s) NHP.276

Vaccine Name **DNA-pCI-tat**
Description Eukaryotic expression vector pCI (Promega, Charbonniers, France) with tat cDNA cloned from primary isolate ACH320 2.1. Expression checked in 293T cells.

Virus HIV-1 *Strain:* ACH320 2.1 *Subtype:* B *Gene/Protein:* tat
HXB2 5831-6045 (exon 1) and 8379-8479 (exon 2)

Trial(s) NHP.276

Vaccine Name **DNA-SIV**
Description This vaccine consists of five plasmids expressing different combinations of SIV mac proteins. The 5 plasmids enconded for non-infectious SIVmac239 virus particle, envelope of SIVmac239 and SIVmac251, and a monocyte/macrophage tropic isolate of SIVmac316

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All
Virus SIV *Strain:* SIVmac251 *Gene/Protein:* env
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env
Virus SIV *Strain:* SIVmac316

Trial(s) NHP.275

Vaccine Name **DNA.pND14-G1.SIVmac251.env**
Description DNA vaccine; DNA vector using hCMV IE promoter and expressing SIVmac251 structural env gene

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* env

Trial(s) NHP.58

Vaccine Name **DNA.PTH.SIVmac.J5.gptnr**
Description DNA vaccine; DNA vector using hCMV IE promoter expressing SIVmac251J5 structural (gag,pol) and regulatory (tat, nef and rev) genes

Virus SIV *Strain:* SIVmac251.J5 *Gene/Protein:* gag, pol

Trial(s) NHP.58

Vaccine Name **DNA.SF162ΔV2 gp140**

Description This is a DNA vector expressing the SF162ΔV2 gp140 envelope with an intact gp120-gp41 cleavage site. The DNA construct was codon optimized for high expression in mammalian cells

Virus HIV-1 *Strain:* HIV-1.SF162 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.62

Vaccine Name **FMSIV**

Description This is a chimeric simian-human immunodeficiency virus (SHIV) with ecotropic Friend murine leukemia virus (FMLV) env in place of SHIV env in combination with FMLV receptor , mCAT1, which is not normally expressed in primate cells. FMSIV DNA has SIV-derived LTR, gag, pol, vif, vpx and partial vpr sequences, HIV-1-derived partial vpr, tat, rev and partial env (containing the second exon of tat, the second exon of rev, and RRE) sequences and FMLV-derived env sequences.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* LTR, gag, pol, Accessory (vif,vpx)

Virus HIV-1 *Strain:* HIV-1DH12 *Subtype:* B *Gene/Protein:* env, Accessory (vpr,tat,partial env (containing the second exon of tat, the second exon of rev, and RRE))

Trial(s) NHP.67, NHP.70, NHP.350

Vaccine Name **HIV env_{MN}/rev(pCEnv)**

Description Plasmid DNA containing HIV-1 env/rev

Virus HIV-1 *Strain:* HIV-1.MN *Subtype:* B *Gene/Protein:* env, Accessory (rev)

Trial(s) NHP.16.1, NHP.16.2, NHP.363

Vaccine Name **HIV-1 89.6P Env gp140 (KB9) DNA**

Description KB9 plasmid expressing HIV-1 89.6P

Virus HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B *Gene/Protein:* env (gp140)

Trial(s) NHP.400

Vaccine Name **HIV-1.89.6P env DNA**

Description

Virus HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.126

Vaccine Name **HIV-1.89.6P env DNA**

Description

Virus SHIV *Strain:* SHIV89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.60.1, NHP.60.3, NHP.98

Vaccine Name **HIV-2UC2.tat.nef.gag**

Description A mixture of 3 plamids constructs based on the gene sequences of the gp140 envelope, p55 Gag, Nef, and Tat proteins from the HIV-2UC2 isolate. The plasmid DNA was then resuspended to 2 mg/ml in 2x phosphate buffer saline for intramuscular and intradermalimmunizations
or in water for intranasal immunizations and stored at −20^{0}C.

Virus HIV-2 *Strain:* HIV-2UC2 *Gene/Protein:* gag, Accessory (tat,nef,p55)

Trial(s) NHP.378

Vaccine Name **K81**

Description This is a replication-competent HSV recombinant K81. The SIVmac239 env-nef expression cassette was inserted into the TK gene of the HSV-1 genome. CMV, promoter/enhancer sequences of the CMV IE gene; PA, signal sequences for poly(A) addition. The SIV sequences are from the SphI site (nucleotide 6450) rightward in SIVmac239. These include rev exon 1, the entire env ORF, rev exon 2, and the nef open reading frame

Notes Herpes simplex vector

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env

Trial(s) NHP.54

Vaccine Name **MVA.HIVA**

Description Same vaccine used in human trial in Oxford, UK and Nairoby, Kenya

Trial(s) NHP.118

Vaccine Name **p55gagSF2**

Description

Virus HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B *Gene/Protein:* gag

Trial(s) NHP.354

Vaccine Name **pC-SIV17E-Fred (gagpolenv)**

Description This is a plasmid DNA vaccine encoding the SIVmac17E-Fr (which is closely related to SIVmac239) gag-pol-env, including vif, vpx, vpr, tat, and rev, except that the 5' LTR is deleted and the 3' LTR is truncated by 360 bp. SIV nef was truncated atthe sequencefor amino acid 93 by insertion of a stop codon

Virus SIV *Strain:* SIVmac17E-Fr *Gene/Protein:* env, gag

Trial(s) NHP.52

Vaccine Name **pC-SIVrev**

Description DNA vaccine; Contains pC-SIVnef-TPA and pC-SIVnef (both constructed based on pC-SIVmac17E-Fred)

Trial(s) NHP.52

Vaccine Name **pc-synGag (SIVmac239)**

Description Contains a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.374

Vaccine Name **pc-syngp120 (SHIV-189.6p)**

Description Contains a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct

Virus SHIV *Strain:* SHIV-1.89.6P *Subtype:* B *Gene/Protein:* env (gp120)

Trial(s) NHP.374

Vaccine Name **pc-synTat (HIV-1IIIB)**

Description contain a codon-optimized gene, cloned under transcriptional control of the cytomegalovirus immediate-early promoter-enhancer unit in pcDNA 3.1 (Invitrogen). Protein expression is about four- to fivefold greater than that of the corresponding wild-type construct

Virus HIV-1 *Strain:* HIV-1IIIB *Subtype:* B *Gene/Protein:* Accessory (tat)

Trial(s) NHP.374

Vaccine Name **pcDNA3–tet.CCR5**

Description This DNA vaccine encodes for CCR5 and tetanus genes.

Trial(s) NHP.68

Vaccine Name **pcDNA3-CCR5**

Description

Trial(s) NHP.68

Vaccine Name **pCGag/Pol**

Description DNA constructs expressing HIV-1-IIIB gag/pol protein

Virus HIV-1 *Strain:* HIV-1.IIIB *Gene/Protein:* gag, pol

Trial(s) NHP.71

Vaccine Name **pCI-Nef plasmid**

Description A mixture of six pCI-Nef plasmids expressing the nef epitopes from SIVmac251 primary isolate (BK28, SO4, SO5, SO8, SO9 and SO12)

Virus SIV *Strain:* SIVmac251 (BK28)
Virus SIV *Strain:* SIVmac251 (SO4)
Virus SIV *Strain:* SIVmac251 (SO5)
Virus SIV *Strain:* SIVmac251 (SO8)
Virus SIV *Strain:* SIVmac251 (SO9)
Virus SIV *Strain:* SIVmac251 (SO12)

Trial(s) NHP.12

Vaccine Name **pCMN160 (HIV-1 MN env)**

Description DNA constructs expressing HIV-1-MN env and rev proteins (pCMN160)

Virus HIV-1 *Strain:* HIV-1.MN *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.71

Vaccine Name **pCMN160 HIV-1.MN env-rev**

Description A DNA vaccine (plasmid) expressing HIV-1 MN env and rev

Virus HIV-1 *Strain:* HIV-1.MN *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.202

Vaccine Name **pCMV-gag-mod**

Description HIV-1SF2 p55 Gag modified to highly expressed human codons; regions with INS were inactivated. Produces a p55 Gag protein with three amino acid changes (Asn377Thr, Ile403Thr, and Lys405Arg). An optimal initiation of translation (GCCACCAUGG) was employed. This 1,527 bp SF2-gag-mod sequence was cloned into the SalI and EcoRI sites of pCMVKm2(Chiron Corporation, Emeryville, Calif.).

Notes zur Megede et al J Virol 74(6): 2628 (2000) PubMed ID 10684277

Virus HIV-1 *Strain:* SF2 *Subtype:* B *Gene/Protein:* gag

Trial(s) NHP.321, NHP.354

Vaccine Name **pCMV-V3.S (HBV-HIV vaccine)**

Description HIV-1 LAI V3 inserted within the frame of HBV envelope in pCV-S2.S

Virus HIV-1 *Strain:* *Subtype:* B

Virus HIV-1 *Strain:* HIV-1.LAI *Subtype:* B

Trial(s) NHP.10

Vaccine Name **pCMV/nef**

Description pCMV/nef plasmid vaccine comprises the PstI-StuI Nef-encoding fragment of clone BK28 inserted into pCMV5

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.56

Vaccine Name **pCMV/SIVsmH4/rev-gp160**

Description

Virus SIV *Strain:* SIVsmH4 *Gene/Protein:* env, Accessory (rev)

Trial(s) NHP.371

Vaccine Name **pCMVKm2-Delta-V2 gp140**

Description Modified V2-deleted gp140. pCMVKm2 vector expressing the unmodified gp140 ectodomain form of the HIV envelope immunogen, with an intact gp120-gp41 cleavage site

Virus HIV-1 *Strain:* SF162 *Subtype:* B

Trial(s) NHP.22

Vaccine Name **pCMVKm2-gp140mut**

Description The sequence for the native subtype B HIV-1US4 envelope was modified to reflect the optimal codon usage in highly expressed human genes. Contained the oligomeric secreted gp140mut (uncleaved, containing a single R522S cleavage site mutation; includes residues 1-668). The gene cassettes constructedsynthetically using EcoR1 and Xba1 by the Midland Certified Reagent Company, and were cloned into plasmid vectors for DNA vaccination (pCMVKm2).

Virus HIV-1 *Strain:* HIV-1US4 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.354

Vaccine Name **pCMVmCAT1**
Description constructed from pCMV (Clontech) by replacing the B-gal gene with a PCR fragment encoding mCAT1B (See Matano, 2000 for details)

Virus HIV-1 *Strain:*

Trial(s) NHP.350

Vaccine Name **pCSGag/Pol.SIV**
Description SIV gag/pol

Virus SIV *Strain:* ND *Gene/Protein:* gag, pol

Trial(s) NHP.16.1, NHP.16.2

Vaccine Name **pCV-tat**
Description DNA vaccine: the plasmid pCV-tat contains the cDNA of the HIV-1 tat gene (BH-10) under the transcriptional control of the adenovirus major late promoter and the vector pCV-0. Plasmids were purified on CsCl gradient and dialyzed for 48 h against 300 volumes of sterile PBS without calcium and magnesium.

Virus HIV-1 *Strain:* BH10 *Subtype:* B *Gene/Protein:* Accessory (tat)

Trial(s) NHP.2, NHP.162

Vaccine Name **pGA1-gag-pol DNA vaccine**
Description The Gag-Pol (SIVmac239) insert was cloned into the pGA1 expression vector (GenBank accession no. AF425297)

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.89

Vaccine Name **pGA2/JS2-HIV-1.gag.pol.env**
Description A vaccine derived from pGA1/JS1 after a series of safety measures (mutation and deletion) in the HIV-1 inserts. The vaccine uses pGA expression vectors that use the CMV immediate early promoter and the bovine growth hormone polyadenylation sequence to express RNAs.

Virus HIV-1 *Strain:* HIV-1.BH10 *Subtype:* B *Gene/Protein:* gag, pol, env, Accessory

Trial(s) NHP.384

Vaccine Name **pGagpol/EnvRev SIV239 DNA**
Description This is a DNA vaccine containing a plasmaid backbone which takes advantages of a CMV promoter and a SV40 poly A signal to express SIV239 gagpol and EnvRev (in two recombinant plasmid constructs). The effect of the rev gene is thought to increase the expression of gagpolconstruct (in vitro assays)

Virus SIV *Strain:* SIVmac239
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env

Trial(s) NHP.300

Vaccine Name **pJW4303/HXB-2.dpol**
Description A DNA immunogen expressing the pol gene of SHIV-IIIB

Virus SHIV *Strain:* SHIV-IIIB *Subtype:* B *Gene/Protein:* pol

Trial(s) NHP.56

Vaccine Name **pJW4303/HXB-2.gp120**

Description Same as pHXB2gp120; This is a eukaryotic expression vector that uses enhancer and promoter elements, including intron A from the cytomegalovirus immediate-early promoter, and polyadenylation sequences from the bovine growth hormone pJW4303 supports Env expression in the absence of Rev. A stop codon introduced at the boundary of the surface (SU) and transmembrane (TM) subunits of Env followed by a BamHI site for cloning into the BamHI site in pJW4303

Virus HIV-1 *Strain:* HIV1.HXB2 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.56

Vaccine Name **pJW4303/HXB-2.gp140**

Description A recombinant plasmid onstructed by cloning env fragments in frame with a synthetic tissue plasminogen activator-(tPA)- leader sequence in pJW4303. This is an eukaryotic expression vector that uses enhancer and promoter elements, including intron A from the cytomegalovirus immediate-early promoter, and polyadenylation sequences from the bovine growth hormone pJW4303 supports Env expression in the absence of Rev. Contain a stop codon immediately prior to the transmembrane domain of TM

Virus HIV-1 *Strain:* HIV-1.HXB2 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.56

Vaccine Name **pMA SHIV89.6**

Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* Accessory, gag, LTR, pol (LTR, gag,pol,vpx,vpr,nef)

Virus HIV-1 *Strain:* HIV89.6 *Subtype:* B *Gene/Protein:* Accessory, env (tat,rev,vpu,env)

Trial(s) NHP.140

Vaccine Name **Pooled SIVgag/HIVtat.rev DNA vaccine**

Description Mixture of 3 plasmids encoding SIVmac239gag (pSIVoptgag), HIV-1.NL4.3 tat and rev. Plasmid pCMVNLtat, encoding the HIV-1NL4- tat, was constructed from plasmid vector pEGFP-N1 by replacing the EGFP coding sequence with the SalI-BamHI restricted tat fragment from the cDNA clone pCR2-tat1. The expression of tat is under the control of the human cytomegalovirus (CMV) immediate-
early promoter. HIV-1NL4.3 rev expression is under the control of the rous sarcoma virus promoter

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Virus HIV-1 *Strain:* HIV-1.NL4.3 *Subtype:* B *Gene/Protein:* Accessory (tat)

Virus HIV-1 *Strain:* HIV-1.NL4.3 *Subtype:* B *Gene/Protein:* Accessory (rev)

Trial(s) NHP.339

Vaccine Name **pRS102 -SIVmac239 gag-pol proteins**

Description The plasmid pRS102 expresses SIVmac239 Gag and Pol proteins. The vaccine insert for pRS102 comprised a Kozak sequence, the SIV239 gag-pol region (nucleotides 1309-5753) and the Mason-Pfizer Monkey virus cytoplasmic transport element. This insert wasclonedinto the HindIII and NheI sites of the eukaryotic expression vector pJW4303, and expression in transiently transfected COS cells was verified.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.56

Vaccine Name **pSabRV1-SIV**

Description Polio virus vector expressing SIV gag, pol, env, nef, and tat in overlapping fragments

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env, gag, pol

Trial(s) NHP.13

Vaccine Name **pSabRV2-SIV**
Description Polio virus vector expressing SIV gag, pol, env, nef, and tat in overlapping fragments

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env, gag, pol

Trial(s) NHP.13

Vaccine Name **pSHIV-NM-3rn ZF1***
Description the construct was based on the infectious molecular clone of SHIV-NM-3rn (Kuwata et al., 1995) from which the BamHI-PvuII fragment was subcloned between the BamHI/HincII sites of pUC119 and, using this plasmid as a template, site-directed mutagenesis ofthe zinc-finger motifs was performed by PCR. The plasmid pSHIV-NM-3rn ZF1* has mutations (Cys... Cys... His... CysSer... Ser... His... Cys) in an N-terminal zinc-finger motif of the NC protein in the gag region of SHIV-NM-3rn see paper for details)

Virus HIV-1 *Strain:* HIV-1.NL432 *Subtype:* B *Gene/Protein:* env, Accessory (vpr,tat,vpu,env,nef)
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* LTR, gag, pol, Accessory (vif,vpx)

Trial(s) NHP.322

Vaccine Name **pSIVNef-TPA**
Description DNA vaccine; Constructed based on SIVmac17E-fred +nef

Trial(s) NHP.323

Vaccine Name **pTH.HW DNA**
Description A DNA vaccine contained an SIV gag-derived epitope, TPYDINQML, recognized by CTLs in rhesus macaques (Macaca mulatta) in the context of the Mamu-A*01 MHC class I molecule

Trial(s) NHP.57

Vaccine Name **pTHr.HIVA DNA**
Description Same vaccine used in human trial in Oxford, UK and Nairoby, Kenya

Trial(s) NHP.118

Vaccine Name **pUCgp120SF2-gold particle**
Description Vaccine based on a modification of pCMV6agp120SF2 which has been previously described. pUCgp120 expresses gp120 of HIV-1 SF2 by using the cytomegalovirus promoter-intron A, tissue plasminogen activator signal sequences, and bovine growth hormone termination sequences; Plasmid DNA was isolated by using plasmid purification columns and endotoxin-free buffers (Qiagen, Chatsworth, Calif.). DNA was bound to 2.6-μm-diameter gold particles to a concentration of 2 μg of DNA/mg of gold

Virus HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.75

Vaccine Name **pV1P-HIV-1.89.6P env**
Description Plasmid DNA expressing HIV-1 89.6P env

Virus HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.24.1

Vaccine Name **pV1P-SIVmac239 gag**
Description Plasmid DNA expressing SIVmac239

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.24.1

Vaccine Name **pV1R-SIVmac239-gag**
Description A plasmid DNA constructed by annealing a series of overlaping oligonucleotides.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.306.1, NHP.306.2

Vaccine Name **pVacc1 DNA**
Description pVacc1 includes a full SIVmac239 genome with multiple mutations in the NC basic domain and the functional domains of RT and INT, under the control of the CMV promoter. A 3.1-kb SphI-NcoI fragment that includes the env gene from pSHIV-KB9-3' replaced the corresponding SphI-SnaBI fragment of pVacc1 that includes the SIV env of SIVmac239. In addition, a stop codon replaced the initiation codon of the vpr gene.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All

Trial(s) NHP.61

Vaccine Name **pVacc4 DNA**
Description The DNA plasmid pVacc4 used in the vaccination is a derivative of pVacc1; It includes a full SIVmac239 genome with multiple mutations in the NC basic domain and the functional domains of RT and INT, under the control of the CMV promoter. A 3.1-kb SphI-NcoI fragment that includes the env gene from pSHIV-KB9-3' replacedthe corresponding SphI-SnaBI fragment of pVacc1 that includes the SIV env of SIVmac239. In addition, a stop codon replaced the initiation codon of the vpr gene.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All

Trial(s) NHP.366

Vaccine Name **rFPV**
Description Designed to express the gag, pol, env and nef genes of SHIV-IIIb

Virus SHIV *Strain:* SHIV.IIIB *Subtype:* B *Gene/Protein:* gag

Trial(s) NHP.56

Vaccine Name **SeV-gag**
Description This is a Gag-expressing Sendai virus (SeV is a nonsegmented negative-strand RNA virus considered nonpathogenic for humans and nonhuman primates)

Virus SIV *Strain:* ND *Gene/Protein:* gag

Trial(s) NHP.69, NHP.70, NHP.326

Vaccine Name **SIV Diected GLV**
Description SIV GLV of PC-derived, directed inserts in the UB vector

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.120

Vaccine Name **SIV mac239 Gag DNA**
Description pV1R plasmid expressing SIVmac239 gag.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag (gag)

Trial(s) NHP.400

Vaccine Name **SIV Random-GLV**
Description SIV GLV comprised of random genomic-DNA inserts expressed in the UB and tPA vectors (Random-GLV)

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.120

Vaccine Name **SIV-HIV89.6 DNA vaccine**
Description SHIV-89.6 sequences cloned into the vector pGA2; This cloning deleted both LTRs and nef; SHIV sequence is internally mutated for a 12bp region encoding the first four amino acids of the 2nd zinc finger in nucleocapsid which renders it noninfectious

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env, Accessory (tat,rev)
Virus SIV *Strain:* *Gene/Protein:* gag, pol, Accessory (vpr, vpx)
Notes No LTR

Trial(s) NHP.19, NHP.132, NHP.325, NHP.349

Vaccine Name **SIV-pcDNA3gag/pol**
Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.9.2

Vaccine Name **SIV-Run-Cyt. GLV**
Description An SIV random library from sheared proviral DNA plus plasmids encoding IL-2 and GMCSF

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.120

Vaccine Name **SIV/17E-Fr gag-pol-env**
Description SIV strain 17E-Fr (SIV/17E-Fr) gag sequences isolated using StuI and BamHI sites and cloned into pCMV-BGHpA/AMP. pol-env sequences isolated from SIV/17E-Fr and were ligated into WRG7132 by using BsiEI and DraIII sites to generate vaccine plasmid WRG7135 carrying SIV/17E-Fr gag-pol-env. Cloning fully deleted the 5' LTR and truncated the 3' LTR by 360 bp. SIV nef truncated at amino acid 93 by the insertion of a stop codon

Virus SIV *Strain:* SIV17E-Fr *Gene/Protein:* env, gag, pol

Trial(s) NHP.63

Vaccine Name **SIVmac17E-Fr Nef**
Description DNA vaccine

Virus SIV *Strain:* SIVmac17E-Fr

Trial(s) NHP.52

Vaccine Name **SIVmac239 gag DNA**
Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.126

Vaccine Name **SIVmac239 gag DNA**
Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.60.1, NHP.60.3, NHP.98

Vaccine Name **SIVmac239 sbbvΔ3 DNA**
Description Contains the full genome of mac239 with a 105-bp (35-amino-acid) deletion in the 3' nef/LTR, analogous to the common deletion observed in HIV-1 strains isolated from the Sydney Blood Bank Cohort (SBBC)

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.66

Vaccine Name **SIVmac239 sbbvΔ3Delta5 DNA**
Description Contains the full genome of mac239 with a 105-bp (35-amino-acid) deletion in the 3' nef/LTR, analogous to the common deletion observed in HIV-1 strains isolated from the Sydney Blood Bank Cohort (SBBC) and additional deletion at the 5'LTR

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.66

Vaccine Name **V1R-SIV gag**
Description pUC-based vector that utilizes the human cytomegalovirus immediate-early promoter with intron A and bovine growth hormone transcription terminator/polyadenylation signal as expression regulatory elements and expresses full-length SIV gag. The SIV gag openreading frame is homologous to that of SIVmac239 and was synthesized using optimal codons for human gene expression.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.59

Vaccine Name **VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP)**
Description VEE replicon plasmid pVR2 with SIVgag (Gly to Ala change in codon 2 ablate myristylation signal; entire env ORF (gp160; base 6587 to 9244); env lacking 3' region encoding membrane-spanning domain and cytoplasmic tail (gp140; base 6587 to 8626)
Notes gag encoding matrix-capsid (MA/CA; nucleotides 1049 to 2143, numbering from the 5' end of the SIVsm H-4i genome)

Virus SIV *Strain:* SIVsm H-4i *Gene/Protein:* gag
MAC239 1049 -2143
Virus SIV *Strain:* SIVsm H-4i *Gene/Protein:* env
MAC239 6587 to 9244
Virus SIV *Strain:* SIVsm H-4i
MAC239 6587 to 8626

Trial(s) NHP.27

Vaccine Name **vSIVgp160**
Description Recombinant vaccinia virus expressing SIV gp160

Trial(s) NHP.33

Vaccine Name **vvrgp140**
Description Vaccinia expressing SIVmac251 env gp140

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* env

Trial(s) NHP.73

VI-B-2 Live attenuated virus vaccines

Vaccine Name **AT-2 rx HIV-1.DH12**
Description Aldrithiol-2 (AT-2)-inactivated HIV-1.DH12

Trial(s) NHP.303

Vaccine Name **AT-2 rx SIVmac239**
Description Aldrithiol-2 (AT-2)-inactivated SIVmac239

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.303

Vaccine Name **DeltavpuDeltaNefSHIV-4**
Description

Trial(s) NHP.107, NHP.112

Vaccine Name **DeltavpuSHIV-ppc**
Description

Trial(s) NHP.107, NHP.112

Vaccine Name **S8-NCΔZF2**
Description This onstruct is based on the pCEP4 mammalian expression vector from Invitrogen Corp. (Carlsbad, Calif.); contains the complete coding region of SIV(Mne), including the nef gene. The 5' portion of the U3 region in the 5' long terminal repeat (LTR) and host genomic sequences upstream from the StyI site were removed. In addition, the R and U5 regions of the 3' LTR were also deleted and replaced with the simian virus 40 (SV40) poly(A)

Virus SIV *Strain:* SIV.Mne

Trial(s) NHP.64, NHP.65.2, NHP.265

Vaccine Name **SHIV-4 (Deltavpu-Deltanef)-I**
Description
Notes T-cell tropic

Virus SHIV *Strain:* SHIV-4 *Subtype:* B

Trial(s) NHP.17

Vaccine Name **SHIV-dn**
Description Live attenuated SHIV lacking the nef gene. The deletion is at the 5'-portion including the initial codon of the nef gene.

Virus SIV *Strain:* mac239 *Gene/Protein:* gag, LTR (LTR, gag, pol, vif and/or vpx)
Virus HIV-1 *Strain:* NL432 *Subtype:* B *Gene/Protein:* pol (env, tat, rev and vpu)

Trial(s) NHP.35, NHP.131

Vaccine Name **SHIV-drn**

Description Live attenuated SHIV lacking the nef gene. The deletion is at the 5'-portion including the initial codon of the nef anf vpr genes. The splicing of vpr was modified so that it does not function..

Virus SIV *Strain:* mac239 *Gene/Protein:* gag, LTR (LTR, gag, pol, vif and/or vpx)
Virus HIV-1 *Strain:* NL432 *Subtype:* B *Gene/Protein:* pol (env, tat, rev and vpu)

Trial(s) NHP.28, NHP.35

Vaccine Name **SHIV-dxrn**
Description Live attenuated SHIV lacking the nef gene. The deletion is at the 5'-portion including the initial codon of the nef, vpr gene and the 3' portion of vpx. The initial codon of vpx was modified to a non-sense codon.

Virus SIV *Strain:* mac239 *Gene/Protein:* gag, LTR (LTR, gag, pol, vif and/or vpx)
Virus HIV-1 *Strain:* NL432 *Subtype:* B *Gene/Protein:* pol (env, tat, rev and vpu)

Trial(s) NHP.28, NHP.35

Vaccine Name **SHIV-NM3n**
Description

Trial(s) NHP.114

Vaccine Name **SHIV-PPC (Deltavpu)**
Description
Notes This vaccine is dual tropic and was administered orally

Virus SHIV *Strain:* SHIV-PPC

Trial(s) NHP.17

Vaccine Name **SIMmac239Δ2**
Description Contains 182bp deletion in nef and a 172bp deletion upstream of U3 of LTR.

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.207

Vaccine Name **SIV(Mne)NCΔZF2 DNA**
Description A live attenuated SIVMne. It consists of a 12-nucleotide deletion in the gene coding for the NC protein [nucleotide positions 1772 to 1783 of the SIV(Mne) sequence (GenBank accession no. M32741) were deleted]. Also known as ΔCys 33-Cys 36 or pRB130.

Virus SIV *Strain:* SIVMne

Trial(s) NHP.64, NHP.65.1, NHP.65.2, NHP.265

Vaccine Name **SIV-IFN**
Description This is a clone of SIVmac239 (SIVΔNU) for which a total of 513bp in the nef and U3 region has been replaced with the coding region of IFN

Trial(s) NHP.309

Vaccine Name **SIV-IL4**
Description This is a clone of SIVmac239 (SIVΔNU) for which a total of 513bp in the nef and U3 region has been replaced with the coding region of IL-4.

Trial(s) NHP.309

Vaccine Name **SIV-PBJ6.6Δnef**
Description

Trial(s) NHP.34

Vaccine Name **SIV.GX2**
Description SIVgx2 is a nef-disrupted molecular clone. EcoRI-NdeI fragment of an SIVmacJ5 proviral clone was replaced with a PCR product that was amplified from proviral DNA isolated from an SIVmacJ5-infected macaque. This resulted in a 66 bp deletion in nef, removing the coding sequence for aa 62-83.

Virus SIV *Strain:* SIV.GX2 *Gene/Protein:* All (nef disrupted)
Notes Nef gene disrupted

Trial(s) NHP.397

Vaccine Name **SIVDeltaNU**
Description SIVDeltaNef is a nef deleted mac239

Trial(s) NHP.327.1, NHP.327.2

Vaccine Name **SIVhu**
Description A pathogenic virus isolated from a lab. worker infected accidentally with biological materials from rhesus macaque infected with SIVsmB670; it has 97.9% genetic homology with parental SIVsmB670; 4 base deletion in nef gene causing a frame shift in nef

Virus SIV *Strain:* SIV.hu/SIVsmB670

Trial(s) NHP.36, NHP.72

Vaccine Name **SIVmac1A11**
Description The SIVmac1A11 is a live attenuated virus. The virus stock was grown on stimulated CD4-enriched rhesus macaque peripheral blood mononuclear cells (PBMC) and had a titer of 10^5 50% tissue culture infectious doses (TCID50)/ml.

Virus SIV *Strain:* SIVmac1A11

Trial(s) NHP.240, NHP.294

Vaccine Name **SIVmac239Δ3**
Description Contains 182bp deletion in nef and a 172bp deletion upstream of U3 of LTR. It has an additional 101-bp deletion in vpr. This is is a derivatives of SIVmac239. It lacks the nef, vpr and U5 sequences.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* LTR, gag, pol, env (Lacks nef, vrp and US)

Trial(s) NHP.37, NHP.150.2, NHP.207, NHP.305

Vaccine Name **SIVmac239Δ3**
Description Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ3 is missing unique nef, vpr, and nef sequences that overlap U3. Described by Gibbs et al ARHR 10(5): 607-616 (1994).

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All (All but nef, vpr and the U3 region overlapping with nef)

Trial(s) NHP.32, NHP.323

Vaccine Name **SIVmac239Δ3+**
Description Produced by infection of rhesus macaquest with cloned SIVmac239Δ3 DNA. SIVmac239Δ3 is missing unique nef, vpr, and nef sequences that overlap U3. A pathogenic variant named SIVmac239Δ3+ was selected and cloned. Described byGibbs et al ARHR 10(5): 607-616 (1994).

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All (all but vpr, nef and LTR/U3 regions.)

Trial(s) NHP.323

Vaccine Name **SIVmac239Δ3x**
Description Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ3X is missing nef, vpx,and US sequences.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All but nef, vpx and U

Trial(s) NHP.32

Vaccine Name **SIVmac239Δ4**
Description Produced by transfection of cloned DNA into CEMx174 cells; SIVmac239Δ4 is missing nef, vpr, vpx, and US.

Virus SIV *Strain:* Mac239 *Gene/Protein:* All but nef, vpr, vpx, and US

Trial(s) NHP.32

Vaccine Name **SIVmac239ΔNef**
Description

Virus SIV *Strain:* *Gene/Protein:* All
Notes Lacking nef

Trial(s) NHP.148

Vaccine Name **SIVmac239-Δnef**
Description Constructed by deleting a 186-base pair fragment of the nef coding sequences of SIV mac239
Notes dkdkd

Trial(s) NHP.33, NHP.34, NHP.109

Vaccine Name **SIVmac239Delta5G**
Description created by mutagenesis of the parental infectious DNA clone so that the asparagine residues for N-glycosylation at positions 79, 146, 171, 460, and 479 were converted to glutamine residues

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All

Trial(s) NHP.39

Vaccine Name **SIVmac251ΔNef**
Description derived from the SIVmac251 BK28 clone by three modifications: (i) the premature stop codon at position 8785 in the env gene was mutated to restore a complete env ORF, (ii) the nef initiator codon ATG was mutated to ACG (cont'd, see notes)
Notes at position 9059, and (iii) nucleotides 9225 to 9401 in the nef region, which do not overlap either the 3' end of env or the U3 part of the LTR, were deleted

Trial(s) NHP.38, NHP.101

Vaccine Name **SIVmac251Δnef**

Description

Trial(s) NHP.108

Vaccine Name **SIVmac251, 32H, (C8)**

Description grown in the human C8166 cell line. The nef coding region contains an in-frame deletion of four amino acids in pC8 and two conservative amino acid changes

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* All

Trial(s) NHP.40, NHP.194.1, NHP.194.2

VI-B-3 Recombinant live attenuated virus vaccines

Vaccine Name **SIV 17E-CL**

Description SIV/17E-CL is a recombinant molecular clone that contains gp120 and part of gp41 from SIV/17E-Br (a macrophage-tropic strain obtained by passage of SIVmac239 in rhesus macaques, Sharma et al., J. Infect. Dis. 66:3550, 1992) into the SIVmac239 molecular clone.

Virus SIV	*Strain:* SIVmac239	*Gene/Protein:* Accessory, gag, pol
Virus SIV	*Strain:* SIV/17E-Br	*Gene/Protein:* env (gp120, gp41)

Trial(s) NHP.100

VI-B-4 Live virus vaccines

Vaccine Name **HIV-2 SBL6669**
Description Isolated from the PBMCs of a patient from Gambia by cocultivation with the T cells of the neoplastic cell line HUT-78.
Notes under Franchini 30-JAN-1989 in sequence database.

Virus HIV-2 *Strain:* HIV-2 SBL6669 *Gene/Protein:* All

Trial(s) NHP.4

Vaccine Name **RT-SHIV**
Description The chimeric simian/human immunodeficiency virus (SHIV) containing the HIV-1 HXBc2 gene for reverse transcriptase (RT) in the genomic background of SIVmac239 (RT-SHIV)

Virus HIV-1 *Strain:* HXB2 *Subtype:* B *Gene/Protein:* pol
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* All

Trial(s) NHP.111

Vaccine Name **SFV- Pr56gag VLP-type II**
Description Components: Pr56-wt; gp120-TM

Trial(s) NHP.77

Vaccine Name **SHIV-4**
Description The chimeric SHIV-4 contains the gag, pol, vif, vpx, vpr and nef genes of SIVmac239 and the env, tat and rev genes of HIV-1IIIB

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol, Accessory (vif,vpx,vpr)
Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* env, Accessory (tat,rev)

Trial(s) NHP.93

Vaccine Name **SHIV89.6**
Description This is a chimeric virus containing HIV-1.89.6 env in the the SIV backbone

Virus HIV-1 *Strain:* HIV-189.6 *Subtype:* B *Gene/Protein:* env (Env,tat,rev,vpu)
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* Accessory, gag, LTR, pol (gag,pol,LTR,vpx,vpr,nef)

Trial(s) NHP.24.1, NHP.29.1, NHP.140

Vaccine Name **SHIV89.6P**
Description

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env
Virus SIV *Strain:* SIVmac *Gene/Protein:* LTR

Trial(s) NHP.24.1

Vaccine Name **SHIVIIIBc2**
Description

Virus HIV-1 *Strain:* HIVIIIBc2 *Subtype:* B

Virus SIV *Strain:* ???

Trial(s) NHP.24.1

Vaccine Name **SIV-Mac-32H**
Description Live SIV-Mac-32H virus propagated on MT-2 cells

Virus SIV *Strain:* MAC-32H *Gene/Protein:* All (All, complete genome)

Trial(s) NHP.320

Vaccine Name **SIV-Mac-MPBMC**
Description Not described by authors.

Virus SIV *Strain:* MAC-MPBMC *Gene/Protein:* All (all, complete genome)

Trial(s) NHP.320

Vaccine Name **SIVmac251**
Description

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* All

Trial(s) NHP.41, NHP.194.2, NHP.345

Vaccine Name **SIVsmE660**
Description

Virus SIV *Strain:* SIVsmE660 *Gene/Protein:* All

Trial(s) NHP.18, NHP.41, NHP.198

VI-B-5 Cell/tissue vaccines

Vaccine Name	**AT-2 inactivated SIV-loaded DC**
Description	AT-2 SIV (mac251) loaded dendritic cells suspended in RPMI 1640 medium
Virus	SIV *Strain:* SIVmac251
Trial(s)	NHP.299
Vaccine Name	**SIVmac239Δ3 (cell-infected)**
Description	SIVmac239Δ3-infected perpheral blood mononuclear cells
Trial(s)	NHP.305

VI-B-6 Whole (killed) inactivated virus vaccines

Vaccine Name **AT-2-Inactivated SHIV89.6**
Description Aldritiol-2 (AT-2) inactivated $SHIV_{89.6}$

Trial(s) NHP.319

Vaccine Name **Fixed inactivated SIVmac251 infected cells**
Description The vaccine was prepared from SIVmac251 recovered from infected a rhesus monkey, and was mixed with withC8166 cells and fixed in 0.2% of β-propiolactone

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* All

Trial(s) NHP.157.1, NHP.157.2, NHP.157.3

Vaccine Name **HIV-1 GB8**
Description Whole/killed inactivated HIV-1. A subtype B virus, GB8 was the first (October 1986) of a series of five sequential viral isolates isolated from a single British AIDS patient during his last 18 months of life.

Trial(s) NHP.203

Vaccine Name **$SIV/Delta_{B670}$**
Description Whole killed inactivated virus harvested from H9 cells . HPLC analysis revealed that complete virus particle was represented with 2-3% of the total protein consisting of the external glycoprotein gp110 and both full length and truncated glycoprotein gp41 and gp 35, respectively, along with the predicted stoichiometric amounts of the remaining viral core proteins (p61/61, p26, p17,p14 and p9). The harvested virion was formalin inactivated.

Virus SIV *Strain:* SIVB670 *Gene/Protein:* All

Trial(s) NHP.248

Vaccine Name **SIVmac HUT-78 ((Psoralem-UV)**
Description SIVmacgrown in HUT-78 T-cell cullture, inactivated with Psoralem and UV light

Virus SIV *Strain:* SIVmac *Gene/Protein:* All

Trial(s) NHP.239

Vaccine Name **SIVmac251 (encapsulated)**
Description Gradient-purified SIVmac251 treated with formalin, encapsulated with emulsion-based process to produce 1-10ul microphere

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* All

Trial(s) NHP.200

Vaccine Name **SIVmac251, 32H, (C8)**
Description Inactivated, partially purified SIVmac251 32H grown in C8166 cell line.

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.203

Vaccine Name **SIVmac251.whole inactivated**

Description Gradient-purifie d SIVmac251 grown in HuT-78 cells was treated with formalin before encapsulation by an emulsion-based process to produce 1- to 10-mm microspheres

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.73

Vaccine Name **SIVmac251/32H (Tween/Ether)**

Description The virus was obtained from in-vitro passage of SIVmac251 and the product was designated SIVmac251/32H. SIVmac251/32H was then grown in C81-66 cells, then purified by column chromatography. After TE extraction, , about 6 mg of the virus were dissolved in 4 ml PBS and 0.25% Tween. 4 ml of diethyl ether was added... (for details see Stahl-Hennig et al, 1992; Virology 186: 588-596)

Virus SIV *Strain:* SIVmac251/32H *Gene/Protein:* All

Trial(s) NHP.97, NHP.99.2, NHP.151

Vaccine Name **Whole inactivated HIV-1 IIIB**

Description A sucrose-gradient purified HIV-1 IIIB, inactivated by various methods including formaldehyde.

Virus HIV-1 *Strain:* HIV-1 IIIB *Subtype:* B

Trial(s) NHP.204

Vaccine Name **Whole inactivated SIVmac239 (encapsulated)**

Description This is a HuT-78 grown in sucrose gradient purified, formalin-inactivated and encapsulated in poly(DL-lactide-co-glycolide) microspheres. The median size of the resulting particle was 3 um

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.74

Vaccine Name **Whole inactivated SIVmac251**

Description

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.201.1, NHP.201.2, NHP.245.1, NHP.245.2, NHP.245.3

VI-B-7 Virus-like particle vaccines

Vaccine Name **HIV-IIIB-p55gag-VLP**
Description HIV-1 isolate LAI/IIIB p55 gag protein in virus-like particle

Virus	HIV-1	*Strain:* HXB2	*Subtype:* B	*Gene/Protein:* gag

Trial(s) NHP.321

Vaccine Name **HPV/SHIV-VLP**
Description This is a recombinant human papillona virus -like particle encoding HIV-1 tat and rev and SIV p27.

Virus	HIV-1	*Strain:* HIV-1.AD8	*Subtype:* B	*Gene/Protein:* Accessory (tat)
Virus	HIV-1	*Strain:* HIV-1.NL4.3	*Subtype:* B	*Gene/Protein:* Accessory (rev)
Virus	SIV	*Strain:* SIVmac239		*Gene/Protein:* gag (gag p27)

Trial(s) NHP.339

Vaccine Name **SFV-SIV Pr56gag VLP-type I**
Description Components: Pr56-V3, CD4BR,gp41

Trial(s) NHP.77

Vaccine Name **SIV Pr56gag VLP-type II**
Description This is a pseudovirion. The gp41 transmembrane domain of the Gp160 wild-type HIV-1 glycoprotein was replaced by a heterologous Epstein-Barr virus derived type I transmembrane region, consisting of a 22 amino acid spanning transmembrane domain and a shortcytoplasmic domain, which was covalently linked to the C-terminus of gp120 by a flexible -S-G-S-G-A-G- hinge region (gp120-TM). Components: Pr56-wt; gp120-TM

Trial(s) NHP.77

VI-B-8 Purified viral products vaccines

Vaccine Name **biologically active Tat protein**
Description

Trial(s) NHP.78

Vaccine Name **gp160/BSC-40**
Description This is a gp160 protein produced in BSC-40 cells infected with recombinant vaccinia virus

Trial(s) NHP.269

Vaccine Name **HIV-1 gp160**
Description subunit consisting of oligomeric gp160 purified from tissue culture fluid of cells productively infected with HIV-1 IIIB

Virus HIV-1 *Strain:* HIV-1.IIIB

Trial(s) NHP.47

Vaccine Name **HIV-1 HXBc2 Tat**
Description Contact authors

Virus HIV-1 *Strain:* HIVHXBc2 *Subtype:* B *Gene/Protein:* Accessory (tat)

Trial(s) NHP.121

Vaccine Name **HIV-1 IIIB gp120**
Description HTLV-III(451) gp120 purified by sequential affinity chromatographic steps. Amino acid sequence analysis of gp120 showed the loss of the signal peptide.

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.53, NHP.247, NHP.371

Vaccine Name **HIV-1 IIIB gp140**
Description gp140 protein was purified by lentil lectin chromatography from the serum-free medium of cells infected with the recombinant viruses, then further purified by chromatography on Superdex-200; Virtually all of the gp140 was oligomeric; Contained gp41

Virus HIV-1 *Strain:* IIIB *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.14, NHP.53

Vaccine Name **HIV-2 gp160**
Description subunit consisting of oligomeric gp160 purified from tissue culture fluid of cells productively infected with HIV-2.NIHZ

Virus HIV-2 *Strain:* HIV-2.NIHZ

Trial(s) NHP.47

Vaccine Name **HIV-2 native gp125**
Description purified native HIV-2 gp125 protein

Virus HIV-2 *Strain:* HIV-2 SBL6669 *Gene/Protein:* env (gp125)

Trial(s) NHP.4

Vaccine Name **MVA(SIVsmH-4)gag-pol-env**
Description Viral components from SIVsmH-4 env. Selected after transfection of transfer plasmid pMC03gag-pol into CEF infected with MVA-env recombinant

Virus SIV *Strain:* SIVsmH4 *Gene/Protein:* gag, pol

Trial(s) NHP.45

Vaccine Name **Native SIV gp120**
Description Purified by sequential affinity chromatographic steps using a monoclonal antibody to HIV-1 gp41 and an anti-HIV-1-positive human serum; heavily glycosylated and contain complex carbohydrates

Virus SIV *Strain:* SIVsmH4 *Gene/Protein:* env (gp120)

Trial(s) NHP.5, NHP.205.1, NHP.205.3

Vaccine Name **Native SIV gp148 env**
Description The glycoproteins were purified by a one-step procedure to a high level of purity by using Galanthus nivalis agglutinin (GNA).

Virus SIV *Strain:* SIVsm *Gene/Protein:* env

Trial(s) NHP.125

Vaccine Name **p55Gag**
Description p55Gag (source virus not specified, but presumed to be HIV-1 subtypeB) produced in yeast.

Trial(s) NHP.321

Vaccine Name **Prt-env gp160**
Description full- length, unmutated Env of HIV-1-IIIb. The IIIb Env had an apparent molecular weight of 160 kDa with gp120 and gp41 covalently attached

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.56

Vaccine Name **SHIV89.6P tat**
Description Contact authors

Virus SHIV *Strain:* SHIV89.6P *Gene/Protein:* Accessory (tat)

Trial(s) NHP.121

Vaccine Name **SIVmac251 p27**
Description

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.125

Vaccine Name **SIVmac251-gp120**
Description The SIV gp120 was purified from the serum-free culture supernatant of SIVmac251 chronically infected Hut 78 cells by immunoaffinity column chromatography using anti-gp120 Ab

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.30, NHP.328, NHP.363

Vaccine Name **soluble gp160**
Description HIV-1 MN strain from Pasteur Merieux Connaught, Paris)

Trial(s) NHP.78

VI-B-9 Synthetic protein/peptide vaccines

Vaccine Name **C4/89.6-V3**
Description Peptides were synthesized by SynPep Corporation (Dublin, Calif.) and purified by reverse-phase high-pressure liquid chromatography (HPLC). Peptides were >95% purified as determined by HPLC and mass spectrometry. SHIV-89.6 and SHIV-KB9 V3 loop peptideswere synthesized C-terminal to a T-helper determinant located in the C4 region of gp120 for enhanced immunogenicity
Notes Two additional peptides are available (89.6-V3 and 89.6P-V3) consisted of the V3 loop portions of the C4/89.6-V3 and C4/89.6P-V3 peptides lacking C4.

Virus SHIV *Strain:* 89.6 *Subtype:* B *Gene/Protein:* env (C4)
Notes Subtype is for the HIV-1 component
Virus SHIV *Strain:* 89.6 *Subtype:* B *Gene/Protein:* env (V3)
Notes Subtype is for the HIV-1 component

Trial(s) NHP.7

Vaccine Name **C4/89.6P-V3**
Description Peptides were synthesized by SynPep Corporation (Dublin, Calif.) and purified by reverse-phase high-pressure liquid chromatography (HPLC). Peptides were >95% purified as determined by HPLC and mass spectrometry. SHIV-89.6 and SHIV-KB9 V3 loop peptideswere synthesized C-terminal to a T-helper determinant located in the C4 region of gp120 for enhanced immunogenicity

Virus SHIV *Strain:* 89.6P *Subtype:* B *Gene/Protein:* env (C4)
Notes Subtype is for the HIV-1 component
Virus SHIV *Strain:* 89.6P *Subtype:* B *Gene/Protein:* env (V3)
Notes Subtype is for the HIV-1 component

Trial(s) NHP.7

Vaccine Name **CCR5 peptides**
Description N-terminus human CCR5 N1 MDYQVSSPIYDINYYTSEPC; N-terminus human CCR5 N1/N2 MDYQVSSPIYDINYYTSEPCQKINVKQIAA; 1st extracellular loop human CCR5 X1 HYLAAQWDFGNTMC;2nd extracellular loop human CCR5 X2.2 YTCSSHFPYSQYQFWKNFQT

Trial(s) NHP.68

Vaccine Name **gp120/gp41 mimotopes**
Description This is a coctail of 5 synthetic peptides (p195: KSSGKLISL, p217: CNGRLYCGP, p197: GTKLVCFAA, p287: CAGGLTCSV, p335: SGRLYDKP). p195, p217 and p197 display similarity with some discret regions of HIV-1 in V1, C2 and gp41, respectively. Peptides p287 andp335 have no obvious sequence homology with HIV protein domains.

Trial(s) NHP.81

Vaccine Name **o-gp140-US4**
Description Oligomeric gp140US4 (o-gp140US4) was purified and characterized by immunoblot, antigen capture enzyme-linked immunosorbent assay (ELISA), CD4 binding and glycosylation profile. After the purification, o-gp140US4 was stored in citrate buffer (10 mmol/l sodium citrate, 500 mmol/l sodium chloride) at a concentration of 0.2 mg/ml for immunizations.

Virus HIV-1 *Strain:* HIV-1 *Subtype:* B *Gene/Protein:* env (gp140)

Trial(s) NHP.354

Vaccine Name **oligomeric gp130**
Description gp130 oligomer s of Mac-32H

Virus SIV *Strain:* MAC-32H *Gene/Protein:* env gp130

Trial(s) NHP.320

Vaccine Name **P3CSS CTL**
Description The "P3CSS CTL epitopes" were a mixture of 4 lipopeptides. The sequences are taken from the SIVmac32H consensus sequences published or provided by Neil Almond et al (AIDS Research and Human Retroviruses, 8, 77 (1992)) and used for the basis of the overlapping peptides provided by the AIDS Reagent Repository at the NIBSC, UK

Virus SIV *Strain:* SIVmac251-32H *Gene/Protein:* gag
MAC239 35-59
Notes sequence: VWAANELDRFGLAESLLENKEGCQK
Virus SIV *Strain:* SIVmac251-32H *Gene/Protein:* gag
MAC239 171-195
Notes Sequence VPGFQALSEGCTPYDINQMLNCVGD
Virus SIV *Strain:* SIVmac251-32H
MAC239 108-123
Notes Sequence: LRTMSYKLAIDMSHFI
Virus SIV *Strain:* SIVmac251-32H
MAC239 155-178
Notes Sequence: DWQDYTSGPGIRYPKTFGWLWKLV

Trial(s) NHP.119

Vaccine Name **PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372**
Description Cocktail of 4 peptides each containing 1 CTL and 1 helper epitope
Notes This vaccine is a cocktail of 4 synthetic chimeric peptides containing T helper and CTL epitopes in HIV (env) and SIV(gag or pol), repectively.

Virus SIV *Strain:* MM239 *Gene/Protein:* gag
MAC239 181-190: (CTPYDINQML)
Notes LOCATION-SIVmac239: (amino acids) Gag 181 - 190 = Capsid(p27) 46 - 55
Virus HIV-1 *Strain:* IIIB *Subtype:* B *Gene/Protein:* env
HXB2 421-444: KQIINMWQEVGKAMYAPPISGQIR
Notes LOCATION: (amino acids) Env 421 - 444
Virus HIV-1 *Strain:* IIIB *Subtype:* B *Gene/Protein:* env
HXB2 827-853: DRVIEVVQGAYRAIRHIPRRIRQGLER
Virus SIV *Strain:* MM239 *Gene/Protein:* pol
MAC239 106-114: GPHYTPKIV
Virus SIV *Strain:* MM239 *Gene/Protein:* gag
MAC239 372-380: LAPVPIPFA

Trial(s) NHP.1

Vaccine Name **Peptomer SIVmac251 (gp120: 435-452)**

Description The SIV peptomer was constructed with an 18 amino acid peptide polymer, is representative of part of the putative CD4 binding region in SIVmac251 gp120 (amino acids435-452: HIRQIINTWHKVGKNVYL)),

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* env (gp120)
MAC239 435-452

Trial(s) NHP.5

Vaccine Name **Synthetic tat**
Description CVDPNLEPWKHPGS (tat HXB2: 3-16), CRQRRRAPDSSQNHQ(TatHXB2: 52-66) conjugated to diphtheria toxoid

Trial(s) NHP.268.1

Vaccine Name **Tat 1-61**
Description

Virus HIV-1 *Strain:* BRU *Subtype:* B *Gene/Protein:* Tat
HXB2 5831-6013 (amino acids 1-61 in protein)

Trial(s) NHP.330

Vaccine Name **Tat 19-53**
Description
Notes two amino acids different from HXB2 peptide

Virus HIV-1 *Strain:* BRU *Subtype:* B *Gene/Protein:* Tat
HXB2 5885-5986 (19 to 53 in Protein)

Trial(s) NHP.330

Vaccine Name **Tat 19-53m**
Description

Virus HIV-1 *Strain:* BRU *Subtype:* B *Gene/Protein:* Tat
HXB2 5885-5986 (amino acids 19 to 53 in protein)

Trial(s) NHP.330

Vaccine Name **Tat 44-61**
Description

Virus HIV-1 *Strain:* *Gene/Protein:* Tat
HXB2 5960-6013 (44 to 61 in protein)

Trial(s) NHP.330

Vaccine Name **Tat1-20**
Description HXB2 Tat peptide amino acids 1-20 synthesized on ABI433A

Virus HIV-1 *Strain:* HXB2 *Subtype:* B *Gene/Protein:* Tat
HXB2 5831-5890 (1-20 in Tat protein)

Trial(s) NHP.330

Vaccine Name **Tat8-53**
Description
Notes 2 amino acids different from same region of HXB2 peptide

Virus HIV-1 *Strain:* BRU *Subtype:* B *Gene/Protein:* Tat
HXB2 5851-5986 (8-53 in Tat protein)

Trial(s) NHP.330

Vaccine Name **V2-MAP**
Description The V2 fragment is a gp130 at positions 168-190: KFNMTGLKRDKTKEYNET; MAP: multiple antigen peptides (branched peptide)

Virus SIV *Strain:* SIVmac
MAC239 168-190

Trial(s) NHP.119

Vaccine Name **V2-P3CSS**
Description The V2 fragment is a gp130 at positions 168-190: KFNMTGLKRDKTKEYNET

Virus SIV *Strain:* SIVmac
MAC239 168-190

Trial(s) NHP.119

Vaccine Name **V2.V3.HIV-1.SF2 Synth.peptides**
Description

Virus HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B *Gene/Protein:* env (V2)
Virus HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B *Gene/Protein:* env (V3)

Trial(s) NHP.164

Vaccine Name **V4.32-MAP**
Description The V4 fragment is a gp130; MAP: multiple antigen peptides (branched peptide); gp130410-430 (V4.32), VEDRDVTNQRPKERHRRNYVP; gp130410-430 (V4.32H), VEDRNTTNQKPKEQHKRNYVP (Torres et al., 1993

Virus SIV *Strain:* SIVmac
MAC239 410-430

Trial(s) NHP.119

VI-B-10 Recombinant subunit protein vaccines

Vaccine Name	**CHO cell-expressed HIV-1SF2 gp120**			
Description				
Virus	HIV-1	*Strain:* HIV-1.SF2	*Subtype:* B	*Gene/Protein:* env (gp120)
Trial(s)	NHP.141, NHP.193			
Vaccine Name	**Delta-V2 gp140 oligomeric**			
Description	Purified oligomeric lacking the V2 region of gp140			
Virus	HIV-1	*Strain:* HIV-1.SF162	*Subtype:* B	
Trial(s)	NHP.22			
Vaccine Name	**Gag-Pol particles**			
Description				
Trial(s)	NHP.65.1			
Vaccine Name	**gp140 oligomeric**			
Description	Purified gp140 oligomeric			
Virus	HIV-1	*Strain:* HIVSF162		
Trial(s)	NHP.22			
Vaccine Name	**HIV BH10-tat protein**			
Description				
Virus	HIV-1	*Strain:* BH10	*Subtype:* B	*Gene/Protein:* Accessory (tat)
Trial(s)	NHP.2			
Vaccine Name	**HIV-1 W6.1D gp120**			
Description	recombinant gp120 of HIV-1W6.1D from an infectious molecular clone			
Virus	HIV-1	*Strain:* HIV-1 W6.1D	*Subtype:* B	
Trial(s)	NHP.21			
Vaccine Name	**HIV-1.MN.rgp120**			
Description				
Virus	HIV-1	*Strain:* HIV-1.MN	*Subtype:* B	*Gene/Protein:* env (gp120)
Trial(s)	NHP.198			
Vaccine Name	**HIV-1.SF2 gp120/p24 Recombinant**			
Description	Monomeric recombinant gp120 and p24 of HIV-1.SF2			
Virus	HIV-1	*Strain:* HIV-1.F2	*Subtype:* B	*Gene/Protein:* gag, env (gp120, p24)

Trial(s) NHP.164

Vaccine Name **HIV-189.6 Env gp140-ISCOM**
Description 200 µl of ISCOM matrix mixed overnight at 4°C with 25 µg of HIV-189.6 Env gp140 (produced in human 293T cells, containing gp120 and the gp41 ectodomain, and purified by lectin chromatography [University of Pennsylvania, Philadelphia]) in 250 µl of PBS.

Virus HIV-1 *Strain:* HIV-1.89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.374

Vaccine Name **HIV-1SF2 rgp120**
Description Recombinant protein produced in Chinese hamster ovary cells

Virus HIV-1 *Strain:* HIV-1.SF2 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.75

Vaccine Name **HIV-2 gp160**
Description

Virus HIV-2 *Strain:* ND *Gene/Protein:* env

Trial(s) NHP.174

Vaccine Name **HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27**
Description Recombinant SIVmac251 gp120 was expressed in Baculovirus-infected cells and recombinant SIV p27 was generated in pGEX-3X as a glutathione S-transferase fusion protein. With both preparations 100μg was covalently linked to HSP70 by 0.0025% glutaraldehyde (Sigma Fine Chemicals Ltd.) and 200 μg was mixed with equal concentration of HSP70; thus, a total of 400μg of HSP70 and 200μg
(3

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* gag, env (gp120, p27)

Trial(s) NHP.395

Vaccine Name **Mono-gp120H (89.6)**
Description Recombinant protein purified from plasmid expressing gp120 of HIV 89.6 strain; the proteines were tagged with histidine to facilitate their purification

Virus HIV-1 *Strain:* HIV-1 89.6

Trial(s) NHP.11, NHP.363

Vaccine Name **Mono-gp120H (DH12)**
Description Recombinant protein purified from plasmid expressing gp120 of HIV DH12 strain; the proteines were tagged with histidine to facilitate their purification

Virus HIV-1 *Strain:* HIV-1 DH12

Trial(s) NHP.11

Vaccine Name **Monomeric rgp120**
Description Monomeric rgp120 of the LAI isolate of HIV-1 was commercially produced by Intracel (Rockville, MD) by expressing HIV-1LAI gp120 DNA in CHO cells.The expression product was characterized by Western blot assay using sheep antibody to HIV-1 gp20 and sequencing. Purity of the recombinant product was >98%

Trial(s) NHP.79

Vaccine Name **Nef-Tat**
Description Nef-Tat is a full-length fusion protein of the two viral proteins. Antigens were expressed in the yeast <ital>Pichia pastoris</ital> as His-tagged proteins. The HIV-1 nef gene derived from the clone Bru/Lai, SIV nef was derived from the cloneSIVmac239 without a premature stop codon, and the HIV-1 tat gene derived from the clone BH10

Trial(s) NHP.296

Vaccine Name **Oligomeric HIV-1.89.6 gp140**
Description The 89.6 gp140 was produced from BS-C-1 cells infected with recombinant vaccinia virus vBD1 and purified by lentil lectin and Superdex 200 chromatography

Virus HIV-1 *Strain:* HIV-1.89.6 *Gene/Protein:* env

Trial(s) NHP.90.1, NHP.90.2

Vaccine Name **Poly-gp120H**
Description Recombinant protein purified from plasmid expressing gp120 of HIV AD8, Bal, Lai, RF, 89.6 and DH12 strains; the proteines were tagged with histidine to facilitate their purification

Virus HIV-1 *Strain:* HIV-1 DH12 *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 AD8 *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 BAL *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 LAI *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 RF *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 89.6 *Subtype:* B

Trial(s) NHP.11

Vaccine Name **Poly-gp120H (-DH12)**
Description Recombinant protein purified from plasmid expressing gp120 of HIV AD8, Bal, Lai, RF and 89.6 strains; ; the proteines were tagged with histidine to facilitate their purification

Virus HIV-1 *Strain:* HIV-1 AD8 *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 BAL *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 LAI *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 RF *Subtype:* B
Virus HIV-1 *Strain:* HIV-1 89.6 *Subtype:* B

Trial(s) NHP.11

Vaccine Name **Recombinant gagpol particles**
Description

Virus SIV *Strain:* SIVmne *Gene/Protein:* gag, pol

Trial(s) NHP.134

Vaccine Name **Recombinant gagpolenv particles**
Description

Virus SIV *Strain:* SIVmne

Trial(s) NHP.134

Vaccine Name **Recombinant gp120**
Description Antigen derived from the Dutch clinical HIV isolate ACH320, expressed in CHO cells

Virus HIV-1 *Strain:* HIV-1.ACH320

Trial(s) NHP.296

Vaccine Name **Recombinant gp130**
Description Recombinant subunit protein produced by African green monkey kidney (BSC-40) cells infected with recombinant vaccinia virus expressing the gp130 glycoprotein under the control of the late vaccinia virus 11K promoter

Virus SIV *Strain:* SIVmne

Trial(s) NHP.134

Vaccine Name **Recombinant HIV-1 env gp160 antigen**
Description This is a recombinant protein (HIV-1 gp160 antigen) expressed in pMB1790

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.204

Vaccine Name **Recombinant HIV-1 gag core (p24,p15) antigen**
Description This is a recombinant protein (HIV-1 p24 and p15 antigen) expressed in pCO1

Virus HIV-1 *Strain:* HIV-1.IIIB *Gene/Protein:* gag

Trial(s) NHP.204, NHP.328

Vaccine Name **Recombinant p27**
Description rSIVp27 was expressed in pGEX3X as a glutathione-S-transferase fusion protein

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.106, NHP.185.1, NHP.185.2, NHP.201.1, NHP.201.2

Vaccine Name **rgp120**
Description This protein was purified from cell culture medium containing 1%- -vo/vol- fetal calf serum) conditioned by the growth of the gD-env-trunc cell line

Trial(s) NHP.242, NHP.267

Vaccine Name **rgp120W6.1D**
Description recombinant gp120W6.1D antigen derived from HIV-1 clone 320.3 isolated from a Dutch AIDS patient

Trial(s) NHP.80

Vaccine Name **rgp140-env (HIV-1.89.6)**
Description

Virus HIV-1 *Strain:* 89.6 *Subtype:* B *Gene/Protein:* env (gp140)

Trial(s) NHP.348.1, NHP.348.2

Vaccine Name **rgp160**
Description Recombinant subunit protein produced by African green monkey kidney (BSC-40) cells infected with recombinant vaccinia virus expressing the gp160 glycoprotein under the control of the late vaccinia virus 11K promoter

Virus SIV *Strain:* SIVmne

Trial(s) NHP.134

Vaccine Name **rgp160**
Description See Mannhalter et al, 1991; ARHR, Vol. 7 (5) 485-493.

Virus HIV-1 *Strain:* HIV-1 IIIB *Subtype:* B *Gene/Protein:* env (gp160)

Trial(s) NHP.362

Vaccine Name **rsgp160**
Description Glycosylated This protein was produced in CHO under the transcriptional control of the SV40 early promoter. It differ from the wild type gp160 at the N terminus. The signal signal sequence and 12 amino acids of the wild type gp160 have been replaced with the signal sequence and 9 amino acids from the mature N-terminus of herpes simplex virus type 1 glycoprotein D

Trial(s) NHP.267

Vaccine Name **rSIV-gp120 protein**
Description Recombinant SIVmac251 gp120 was expressed in Baculovirusinfected cells

Virus SIV *Strain:* SIVmac251

Trial(s) NHP.106, NHP.185.1, NHP.185.2, NHP.201.1, NHP.201.2

Vaccine Name **SF162ΔV2 gp140 protein**
Description gp140 lacking the V2 region

Virus HIV-1 *Strain:* HIV-1.SF162 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.62

Vaccine Name **SIV Nef**
Description

Virus SIV *Strain:* SIVmac239

Trial(s) NHP.296

Vaccine Name **SIV(Mne) gp160Env protein**
Description

Trial(s) NHP.65.1

Vaccine Name **SIVenv-Bgal peptides**
Description This is a cocktail of 4 SIVenv epitopes (2 from gp120 and 2 from gp32). These epitopes appear to be homologous in sequence and location to thehighly concerved HIV-env epitopes as well as being hydrophilic in nature. The oligonucleotides coding for thesepeptides were prepared and inserted at the 5' end of thegene under the trp expresiionelement of E. coli. The four recombinant SIVenv-B-galactosidase polipetides were expresed in bacteria and purified by HPLC.

Virus SIV *Strain:* SIVmac *Gene/Protein:* env (gp32, gp120)

Trial(s) NHP.94, NHP.154

Vaccine Name **SIVmac239 Gag-Pol-ISCOM**

Description 25 µl SCOM matrix (Isconova, Uppsala, Sweden) mixed overnight at 4°C with either 25 µg SIVmac239 Gag-Pol in 250 µl of PBS

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.374

Vaccine Name **Soluble 89.6 gp120 protein**

Description Produced by infection of BS-C-1 cells with recombinant vaccinia virus, vBD2,13 at a multiplicity of infection of 5 plaque-forming units (pfu) per cell. Protein was purified from the media by lectin and Superdex-200 chromatography

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env (gp120)

Trial(s) NHP.349

Vaccine Name **tat protein**

Description HIV-1 Tat (IIIB) expressed in Eschericia coli, purified to homogeneity by heparin-affinity chromatography and high-performance liquid chromatography and stored lyophilized at -80 °C. Purified Tat had full biological activity in several assays. Tat wasresuspended in degassed buffer before use in vitro or in saline containing 20% of autologous serum for monkey injection.

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* Accessory (tat)

Trial(s) NHP.374

VI-B-11 Recombinant vector (virus/bacteria) vaccines

Vaccine Name **AD4-gp160(MN)**
Description

Virus HIV-1 *Strain:* HIV-1.MN *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.141

Vaccine Name **AD5-gp160(MN)**
Description

Virus HIV-1 *Strain:* HIV-1.MN *Gene/Protein:* env

Trial(s) NHP.141

Vaccine Name **Ad5-SIVgag**
Description This vaccine was constructed using the adenovirus as the vector. The adenovirus vector was based on the serotype 5 that has been rendered incompetent to replicate by the deletion of E1 and E3 viral genes. The adenoviral vector, pHCMVIBGHpA1 contains Ad5nucleotides 1-341 and 3,534-5,798 and an expression cassette containing the human cytomegalovirus promoter with intron and the bovine growth hormone poly adenylation signal (see paper for more information)

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.306.1, NHP.306.2

Vaccine Name **Ad5hr-SIVenv**
Description E3-deleted Ad5hr vector containing the SIVsmH4 (also known as F236, accession number X14307)envelope gene
Notes An E3-deleted Ad5hr vector containing the SIVsmH4 envelope gene

Virus SIV *Strain:* SIVsmH4 *Gene/Protein:* env
Notes The H4 (F236) isolate of SIV-SMM is not related to the MAC251/MAC239 lineage.

Trial(s) NHP.5, NHP.205.1, NHP.205.3, NHP.324.1, NHP.328

Vaccine Name **Ad5hr-SIVmac239gag**
Description Adenovirus Ad5hr with a codon-optimized Gag cDNA derived from Mac239, with silent mutations to optimize expression and eliminate the inhibitory sequences.

Virus SIV *Strain:* Mac239 *Gene/Protein:* gag (Gag)
MAC239 1053-2585

Trial(s) NHP.324.1, NHP.328, NHP.363

Vaccine Name **Ad5hr-SIVnefδ1-13**
Description

Virus SIV *Strain:* Mac239 *Gene/Protein:* Nef
MAC239 9115-9858 delta 1-13 amino acids 1-39 bases premature stop corrected to GAA

Trial(s) NHP.328, NHP.363

Vaccine Name **Ad5hr-SIVsmH4 env/rev**

Description Ad5hr-SIVsmH4 env/rev, a replication-competent Ad5hr-SIV recombinant carrying the SIVsmH4env and rev genes in the deleted E3 region and expressing the entire SIV envelope and Rev proteins

Virus SIV *Strain:* *Gene/Protein:* env, Accessory (rev)

Trial(s) NHP.363, NHP.371

Vaccine Name **AD7-gp160(MN)**
Description

Virus HIV-1 *Strain:* HIV-1.MN *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.141

Vaccine Name **ALVAC-HIV-2 (gag,pol,gp125)**
Description Recombinant canarypox virus expressing HIV-2 env, gag and pol genes

Virus HIV-2 *Strain:* HIV-2 SBL6669 *Gene/Protein:* gag, pol
Virus HIV-2 *Strain:* HIV-2 SBL6669 *Gene/Protein:* env (gp125)

Trial(s) NHP.4

Vaccine Name **ALVAC-SIV-gp**
Description Recombinant SIV vaccine composed of a live, weakened canarypox virus (ALVAC™) into which parts of SIV genes (gag and pol) were inserted. When ALVAC infects a human cell, the inserted SIV genes direct the cell to make SIV proteins. These proteinsare packaged into SIV-like particles that bud from the cell membrane. The particles are not infectious, fool the immune system and mount immune response to SIV. As a safety precaution, ALVAC can infect but not grow in human or macaques cells.

Virus SIV *Strain:* ? *Gene/Protein:* pol

Trial(s) NHP.345

Vaccine Name **ALVAC-SIV-gpe (vcp180)**
Description The ALVAC-SIV-gpe (vcp180) was engineered to express the gag, pol, and env genes of SIVmac251(K6W)

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* env, gag, pol

Trial(s) NHP.30, NHP.123, NHP.274

Vaccine Name **ALVAC/vCP153 HIV-2 gag,pol,env**
Description

Virus HIV-2 *Strain:* ND *Gene/Protein:* env, gag, pol

Trial(s) NHP.174

Vaccine Name **FP-SIV-gp (FP74)**
Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.9.2, NHP.345

Vaccine Name **FPV.HIV-1.gag/pol**

Description recombinant fowlpoxvirus (rFPV) vaccines expressing HIV-1 antigens gag and pol. The HIV-1gag/pol genes of ARV-2/SF2 strain were inserted into the FPV genome (FPV M3 strain) along with the E. coli Beta-gal and/orgpt selection and marker genes.

Virus HIV-1 *Strain:* HIV-1.ARV-2/SF2 *Subtype:* B *Gene/Protein:* gag, pol

Trial(s) NHP.48

Vaccine Name **FPV.HIV-1.gag/pol-IFNgamma**
Description recombinant fowlpoxvirus (rFPV) vaccines expressing both HIV-1 antigens and interferon-gamma. The HIV-1gag/pol genes of ARV-2/SF2 strain with the human IFNgamma gene were inserted into the FPV genome (FPV M3 strain) along with the E. coli Beta-gal and/orgpt selection and marker genes.

Virus HIV-1 *Strain:* ARV-2/SF2 *Subtype:* B *Gene/Protein:* gag, pol

Trial(s) NHP.48

Vaccine Name **MVA SIVsmH4 gag-pol**
Description

Virus SIV *Strain:* SIVsmH4 *Gene/Protein:* gag, pol

Trial(s) NHP.3, NHP.45, NHP.46

Vaccine Name **MVA-mac(J5)**
Description MVA constructs expressing env, gag-pol, nef, rev and tat genes of SIVmacJ5

Virus SIV *Strain:* SIVmacJ5 *Gene/Protein:* gag, pol, env

Trial(s) NHP.51

Vaccine Name **MVA-rev**
Description Modified Vaccinia Anlkara expressing HIV-1 subtype B isolate IIIB rev cDNA.

Virus HIV-1 *Strain:* IIIB *Subtype:* B *Gene/Protein:* rev
HXB2 5970-6045 (exon 1) and 8379-8653 (exon 2)

Trial(s) NHP.276

Vaccine Name **MVA-SIV gag-pol and HIV-1 89.6 env**
Description MVA vectors (pLW-9 and pLW-17) expressing SIV gag-pol and HIV-1 89.6 env

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol
Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.24.2

Vaccine Name **MVA-SIV239tat**
Description This vector encodes the full-length SIVmac239 Tat

Trial(s) NHP.88

Vaccine Name **MVA-SIV251 32H tat**
Description This vector encodes the full-length SIVmac251 32H Tat (clone J5)

Virus SIV *Strain:* SIVmac251.32H

Trial(s) NHP.88

Vaccine Name **MVA-SIVgag**
Description This MVA-SIV gag vaccine was constructed by cloning the SIV gag gene into the pSC59 shutle vector. This plasmid was designed to insert the transgene fragment into a viral thymidine kinase region and to drive the transgene from a synthetic early/late promoter. The recombinant plasmid was inserted into the MVA for immunization of monkeys.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.306.1, NHP.306.2

Vaccine Name **MVA-SIVmac239gag**
Description Recombinant MVA virus vT338 contains the gag gene from SIVmac239 inserted into the deletion III region of the MVA genome under the control of the vaccinia virus 40K (H5R) promoter. The virus also contains the Escherichia coli lacZ gene under the control of the fowlpox C1 promoter for use as a colorimetric screen for recombinant viruses

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.308

Vaccine Name **MVA-SIVmacJ5 (gag-pol)**
Description MVA constructs expressing gag-pol genes of SIVmac251 32H (pJ5) under the transcriptional control of the natural vaccinia virus early/late promoter P7.5
Notes poorly immunogenic

Virus SIV *Strain:* SIVmac251 32H (pJ5) *Gene/Protein:* gag, pol

Trial(s) NHP.3

Vaccine Name **MVA-SIVSL8-tat28-35**
Description This vector encodes a single Mamu-A*01-restricted CTL epitope Tat-SL8(positions 28-35)(STPESANL) inserted within the immunodominant region of hepatitis B core antigen

Virus SIV *Strain:* SIVSL8
MAC239 28-35

Trial(s) NHP.88

Vaccine Name **MVA-SIVsmH-4 -env**
Description MVA recombinants expressing the SIVsmH-4 env (MVA-env)

Virus SIV *Strain:* SIVsmH-4 *Gene/Protein:* env

Trial(s) NHP.45

Vaccine Name **MVA-tat**
Description Modified Vaccinia Ankara expressing HIV-1 IIIB strain tat cDNA

Virus HIV-1 *Strain:* IIIB *Subtype:* B *Gene/Protein:* tat
HXB2 5831-6045 (exon 1) and 8379-8479

Trial(s) NHP.276

Vaccine Name **MVA.HW**

Description This is a recombinant MVA.HW expressing an MVA and SIV gag-derived epitope, TPYDINQML, recognized by CTLs in rhesus macaques (Macaca mulatta) in the context of the Mamu-A*01 MHC class I molecule

Virus SIV *Strain:* ND *Gene/Protein:* gag

Trial(s) NHP.57

Vaccine Name **MVA.pUCII.SIVmac.J5**
Description MVA vaccine expressing SIV structural (gag,pol) and regulatory genes (tat,nef and rev)

Virus SIV *Strain:* SIVmac.J5 *Gene/Protein:* gag, pol

Trial(s) NHP.58

Vaccine Name **MVA/HIV 48**
Description MVA/HIV 48 is an rMVA expressing HIV-1 clade B Gag, protease, RT, and Env constructed by homologous recombination in chick embryo fibroblasts. Contains HXB2 gag and BH10 pol. The pol sequences contained three safety mutations in RT and a truncated integrase. The env from CCR5-tropic HIV-1.ADA contained silent mutations to eliminate two copies of a TTTTTNT sequence that acts as a poxvirus transcription termination signal (See LINDA S. WYATT, et al. 2004)

Virus HIV-1 *Strain:* HIV-1.BH10 *Subtype:* B *Gene/Protein:* pol
Virus HIV-1 *Strain:* HIV-1.HXB2 *Subtype:* B *Gene/Protein:* gag
Virus HIV-1 *Strain:* HIV-1.ADA *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.384

Vaccine Name **MVAgagpol**
Description The SIVsmH4 gag pol ORF (1049-5397) cloned into pMC03, then the product transfected into chicken embryo fibroblasts that had been infected with MVA. Plaques that stained blue upon addition of X-Gluc (CLONTECH) were purified

Virus SIV *Strain:* SIVsmH4 *Gene/Protein:* gag, pol
MAC239 1049-5397

Trial(s) NHP.44

Vaccine Name **MVAmacJ5-nef**
Description A highly immunogenic vector construct with high anti-CTL response; associated with protection

Virus SIV *Strain:* SIVmac251 32H (pJ5) *Gene/Protein:* Accessory (nef)

Trial(s) NHP.3

Vaccine Name **MVApIII-sp.SIVmac.J5.env**
Description Recombinant MVA vaccine expressing SIVmac.J5 env gene

Virus SIV *Strain:* SIVmac.J5 *Gene/Protein:* env

Trial(s) NHP.58

Vaccine Name **NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe)**
Description A highly attenuated poxvirus NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe); Induce both CD4+ and CD8+ t cell responses in rhesus macaques and demonstrate effectiveness as a preventive vaccine candidate.
Notes vaccinia

Virus	SIV	*Strain:* Mac251		
Notes	Described by Benson et al. J Virol. 1998 May;72(5):4170-82. PMID: 9557706			
Virus	SIV	*Strain:* Mac251		*Gene/Protein:* env expression cassette under control of vaccinia H6 promoter and gag-pol with I3L promoter.
Notes	Described by Benson et al. J Virol. 1998 May;72(5):4170-82. PMID: 9557706			
Trial(s)	NHP.9.1, NHP.274			

Vaccine Name	**Polio (Sabin 1) - HIV-1.gag/env (2)**			
Description				
Virus	HIV-1	*Strain:* IIIB?LAI (HXB2)		*Gene/Protein:* gag, env (gp120,gp140 (lacking signal sequece) gp120+gp140 ectodomain, p55 fused with VP4)
Virus	HIV-1	*Strain:* 92TH021	*Subtype:* D	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* 92TH022	*Subtype:* CRF02_AE	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* 92RW020	*Subtype:* A	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* 92BR025	*Subtype:* C	*Gene/Protein:* env (gp120)
Trial(s)	NHP.348.1			

Vaccine Name	**Polio (Sabin 1) -HIV-1.gag/env (1)**			
Description				
Virus	HIV-1	*Strain:* 92RW020	*Subtype:* A	*Gene/Protein:* env (GP120)
Virus	HIV-1	*Strain:* 92TH022	*Subtype:* CRF02_AE	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* 92UG021	*Subtype:* D	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* IIIB/LAI (HXB2)	*Subtype:* B	*Gene/Protein:* gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)
Trial(s)	NHP.348.1			

Vaccine Name	**Polio (Sabin 2) - HIV-1.gag/env (3)**			
Description				
Virus	HIV-1	*Strain:* IIIB/LAI (HXB2)	*Subtype:* B	*Gene/Protein:* gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)
Virus	HIV-1	*Strain:* 92UG021	*Subtype:* D	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* 92RW09	*Subtype:* A	*Gene/Protein:* env (gp120)
Virus	HIV-1	*Strain:* 92TH026	*Subtype:* CRF02_AE	*Gene/Protein:* env (gp120)
Trial(s)	NHP.348.1			

Vaccine Name	**Polio (Sabin 2) - HIV-1.gag/env (4)**			
Description				
Virus	HIV-1	*Strain:* IIIB/LAI(HXB2)	*Subtype:* B	*Gene/Protein:* gag, env (gp120,gp140 (lacking signal sequence), gp120+gp41 ectodomain, p55 fused with VP4)
Trial(s)	NHP.348.1			

Vaccine Name **Polio- SIVmac239gag**

Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.348.2

Vaccine Name **Polio-LAI/IIIB-Env**
Description

Virus HIV-1 *Strain:* IIIB/LAI *Subtype:* B *Gene/Protein:* env (gp120)

Trial(s) NHP.348.2

Vaccine Name **rBCG-SIV[3]**
Description A mixture of 3 transformed strains of <ital>Mycobacterium bovis</ital> BCG expressing the SIV-MAC-251 gag, nef and env genes.

Virus SIV *Strain:* MAC251 *Gene/Protein:* Accessory, env, gag (nef, gag, env)

Trial(s) NHP.353

Vaccine Name **Recombinant fowlpox (rFPV) SIVmac239 gag**
Description Recombinant fowlpox virus expressing SIVmac239 gag. The SIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.400

Vaccine Name **Recombinant fowlpox (rFPV).SHIV89.6P env**
Description Recombinant fowlpox virus expressing SHIV89.6P env. The SHIV gene was inserted in the BamJHI region of POXVAC-TC (Schering-Plough) strain of FPV.

Virus SHIV *Strain:* SHIV89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.400

Vaccine Name **Recombinant MVA-SHIV89.6P env**
Description Recombinant MVA expressing SHIV89.6P gp140 (env). The SHIV gene was inserting in the deletion III region of a plaque-purified isolate of the replication-defective strain of vaccinia virus designated MVA. The env gene was under the control of the vacciniavirus 40K(H5R) promoter.

Virus SHIV *Strain:* SHIV89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.400

Vaccine Name **Recombinant MVA-SIVmac239 gag**
Description Recombinant MVA expressing SIVmac239 gag. The SIVmac239 gene was inserting in the deletion III region of a plaque-purified isolate of the replication-defective strain of vaccinia virus designated MVA. The gag gene was under the control of the vacciniavirus 40K(H5R) promoter.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.400

Vaccine Name **Recombinant vaccinia gagpol (v-SG11)**
Description

Virus SIV *Strain:* SIVmne *Gene/Protein:* gag, pol

Trial(s) NHP.134

Vaccine Name **Recombinant vaccinia gagpolenv (v-SGE14)**
Description

Virus SIV *Strain:* SIVmne *Gene/Protein:* env, gag, pol

Trial(s) NHP.134

Vaccine Name **Recombinant vaccinia gp130 (v-SE6)**
Description

Virus SIV *Strain:* SIVmne

Trial(s) NHP.134

Vaccine Name **Recombinant vaccinia virus vac-gp160 (v-SE5)**
Description Recombinant vaccinia virus vac-gp160 (v-SE5) contains the coding sequence of the full-length gp160 of SIVmne molecular clone 8 (GenBank accession number M32741) in a New York City Board of Health strain (v-NY) of vaccinia virus (16, 17). v-SE5 was plaquepurified and propagated on African green monkey kidney cells (BSC-40)

Virus SIV *Strain:* SIVmne *Gene/Protein:* env

Trial(s) NHP.134, NHP.269

Vaccine Name **Recombinant vaccinia virus-HIVgp160 (cocktail)**
Description Recombinanat vaccinia virus expressing gp160 of HIV-1 isolates Bal, LAI, RF (vCB43, vCB41, and vCB36, respectively), 89.6 (vBD3), DH12, and AD8 (vvDHenv and vvADenv, respectively).

Virus HIV-1 *Strain:* HIV-1 BAL *Subtype:* B *Gene/Protein:* env
Virus HIV-1 *Strain:* HIV-1 LAI *Subtype:* B *Gene/Protein:* env
Virus HIV-1 *Strain:* HIV-1 RF *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.11

Vaccine Name **Recombinant vaccinia viruse (rVac).SHIV89.6P Env**
Description Recombinant vaccinia virus expressing SHIV89.6P env, constructed by inserting the SHIV env gene in the HindIII M region of TBC-Wy Therion strain of vaccinia (see Mazzara, G. P., Destree, A.&Mahr, A. (1993) Methods Enzymol. 217, 557-581).

Virus SHIV *Strain:* SHIV89.6P *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.400

Vaccine Name **Recombinant vaccinia viruse (rVac).SIVmac239 gag**
Description Recombinant vaccinia virus expressing SIVmac239 gag, constructed by inserting the SIV gag gene in the HindIII M region of TBC-Wy Therion strain of vaccinia (see Mazzara, G. P., Destree, A.&Mahr, A. (1993) Methods Enzymol. 217, 557-581).

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.400

Vaccine Name **rMVA (SIVsm) gagpolenv**

Description The rMVA-SIVsm co-expresses the gag-pol and env of SIVsmmH4. gag-pol was under the transcriptional control of the vaccinia early-late promoter P7·5. Env was expressed using a strong synthetic vaccinia virus early-late promoter. MVA-SIVsmwas amplified on primary chicken embryo fibroblasts and purified by ultracentrifugation. Purified viruses were reconstituted in PBS and titrated by end-point dilution in CEF to obtain the TCID50, aliquotted and stored at -70 °C.

Virus SIV *Strain:* SIVsmmH4 *Gene/Protein:* gag, pol, env

Trial(s) NHP.125

Vaccine Name **rMVA 89.6**

Description The MVA double recombinant virus expressed both the HIV 89.6 Env and the SIV 239 Gag-Pol, which were inserted into deletion II and deletion III of MVA, respectively . The 89.6 Env protein was truncated for the COOH-terminal 115 amino acids of gp41

Notes The modified H5 promoter controlled the expression of both foreign genes

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env
Virus SIV *Strain:* SIVmac329 *Gene/Protein:* gag, pol

Trial(s) NHP.19, NHP.132, NHP.325, NHP.349

Vaccine Name **rMVA SIV239 gag-pol**

Description this recombinant MVA expresses SIV239 Gag-Pol

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.89

Vaccine Name **rMVA SIVmac239 gagpolenv**

Description For construction of MVA-SIVgpe, chicken embryo fibroblast cells were incubated simultaneously with five infectious units each of MVA/SIV239gagpol and MVA/SH4wt. The latter virus expresses the SIVmac239 env gene, truncated after amino acid 733, under the control of the moderate-strength vaccinia virus promoter p7.5. A virus isolate expressing all three genes was clonally purified and amplified.

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* env, gag, pol

Trial(s) NHP.294

Vaccine Name **rMVA-SIVmac251 32H**

Description Recombinant MVA expressing SIVmac251 genes (gag,pol,tat,rev or nef, separetly) under the transcriptional control of vaccinia virus early and late promoters P7.5 and sP

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* gag, pol

Trial(s) NHP.52

Vaccine Name **rMVA.SIVmac239gagpolHIVenv**

Description

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol
Virus HIV-1 *Strain:* Unknown *Gene/Protein:* env

Trial(s) NHP.366

Vaccine Name **rMVA.SIVmac32H.tat.rev**

Description Recombinant MVA expressing SIVmac32H tat and rev genes

Virus SIV *Strain:* SIVmac32H *Gene/Protein:* Accessory (tat,rev)

Trial(s) NHP.49

Vaccine Name **rMVASIV239gagpol.HIV89.6env**

Description A recombinant virus expressing the SIVmac239gagpol gene was constructed by insertion of the entire open reading frame from plasmid p239SpSp5' into a plasmid transfer vector, pLW-9 (Wyatt et al., 1996). The rMVA, MVA/SIV239gagpol, was selected by immunostaining with serum from an SIV-infected macaque. For construction of the double recombinant virus, CEF were incubated simultaneously with 5 infectious units each of MVA/SIV239gagpol and MVA/89.6T

Virus HIV-1 *Strain:* HIV-1.89.6 *Gene/Protein:* env
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.24.1, NHP.90.1, NHP.90.2

Vaccine Name **rSalmonella typhi-SIVgag**

Description Salmonella typhi expressing SIV gag

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag
MAC239 146-213
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag
MAC239 4-284

Trial(s) NHP.308

Vaccine Name **rSalmonella typhimurium-SIVgag**

Description Salmonella typhimurium expressing SIV gag

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag
MAC239 146-213
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag
MAC239 4-507

Trial(s) NHP.308

Vaccine Name **rSFV-SIVmac32H.rev.tat**

Description Recombinant Semliki Forest Virus encoding SIVmac32H rev and tat genes.

Virus SIV *Strain:* *Gene/Protein:* Accessory (rev, tat)

Trial(s) NHP.49

Vaccine Name **rVaccinia-gp160**

Description Recombinant vaccinia virus expressing HIV-1 HXB2 gp160

Virus HIV-1 *Strain:* HIV-1 HXB2 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.78

Vaccine Name **rVaccinia-SIVmac-env.gagpol**

Description Recombinant vaccinia virus containing both SIVmac env and SIVmac gag-pol (vAbT386.6.1)

Virus SIV *Strain:* SIVmac *Gene/Protein:* env, pol

Trial(s) NHP.76

Vaccine Name **rVV-HIV-1.DH12env**
Description Recombinant vaccinia virus expressing HIV-1 DH12 gp160 (env) protein.

Virus HIV-1 *Strain:* HIV-1.DH12 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.303

Vaccine Name **rVV-SIVmacgag/pol**
Description This is a recombinant vaccinia virus expressing SIV gag and pol (for additional information on this vaccine please contact Dr M. Cho directly)

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag, pol

Trial(s) NHP.303

Vaccine Name **SFV-rev**
Description Semliki Forest Virus from pSFV (Invitrogen, Cergy-Pontoise, France) with rev cDNA from HIV-1 primary isolate ACH320 2.1 first subcloned in pCI (Promega, Charbonnieres, France) expression vector and then re-cloned into pSFV. Recombinant SFV-rev stocks prepared on BHK-21 cells.

Virus HIV-1 *Strain:* ACH320 2.1 *Subtype:* B *Gene/Protein:* rev
HXB2 5970-6045 (exon 1) and 8379-8653 (exon 2)

Trial(s) NHP.276

Vaccine Name **SFV-tat**
Description Semliki Forest Virus from pSFV (Invitrogen, Cergy-Pontoise, France) containing tat cDNA from HIV-1 subtype B primary isolate ACH320 2.1 first subcloned into pCI expression vector before re-cloning into pSFV.

Virus HIV-1 *Strain:* ACH320 2.1 *Subtype:* B *Gene/Protein:* tat
HXB2 5831-6045 (exon 1) and 8379-8479

Trial(s) NHP.276

Vaccine Name **SFVpSFVI.SIVmac.J5.gpetnr**
Description A recombinant semliki forest virus expressing SIVmac clone J5 structural (gag,pol) and regulatory (tat, nef and rev) genes

Virus SIV *Strain:* SIVmacJ5 *Gene/Protein:* env, gag

Trial(s) NHP.58

Vaccine Name **vAbT394**
Description Recombinant vaccinia (NYCBH) expressing SIV_{MAC251} Gag-Pol.

Virus SIV *Strain:* MAC251 *Gene/Protein:* Gag-Pol

Trial(s) NHP.319

Vaccine Name **Vaccinia-rDIsSIVgag**
Description A recombinant vaccinia virus DIs expressing SIV Gag. Contains a full-length gag gene of SIVmac239 in the vector construct. rDIs expressing SIVmac239 Gag (rDIsSIVGag)

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.365

Vaccine Name **vP1047, NYVAC HIV-2.SBL-ISY gp160.gag-pol**
Description To generate the NYVAC-recombinant viruses, plasmids encoding sequences for HIV-2.SBL-ISY gp160 plus gag-pol were used by invitro recombination, using the NYVAC vector vP866 as rescue virus

Virus HIV-2 *Strain:* HIV-2.SBL-ISY *Gene/Protein:* gag, pol

Trial(s) NHP.47

Vaccine Name **vP991, NYVAC HIV-1IIIB gp120.gag-pol**
Description To generate the NYVAC-recombinant viruses, plasmids encoding sequences for HIV-1 IIIB gp120 (aa residues 1-511) plus gag-pol were used by invitro recombination, using the NYVAC vector vP866 as rescue virus

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B
HXB2 1-511

Trial(s) NHP.47

Vaccine Name **vSIVgp120**
Description Recombinant vaccinia virus expressing SIV gp120

Trial(s) NHP.33

Vaccine Name **VSV(GCh)-Env+Gag**
Description Recombinant vesicular stomatitis virus (VSV) encoding HIV-1.89.6 env gene and SIV gag. The VSV G protein (Indiana serotype, GI) was subtitued with the VSV Chandipura glycoprotein (GCh)

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env
Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag

Trial(s) NHP.55

Vaccine Name **VSV(GNJ)-Env+Gag**
Description Recombinant vesicular stomatitis virus (VSV) expressing HIV-1.89.6 env and SIVmac239 gag. The VSV G protein (Indiana serotype, GI) was replaced with the G protein of the VSV New Jersey serotype (GNJ)

Virus SIV *Strain:* SIVmac239 *Gene/Protein:* gag
Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.55

Vaccine Name **VSV-(GI)-Env**
Description Recombinant vesicular stomatitis virus (VSV) vector encoding HIV-1 env gene

Virus HIV-1 *Strain:* HIV-1.89.6 *Subtype:* B *Gene/Protein:* env

Trial(s) NHP.55

Vaccine Name **vT107**
Description Recombinant vaccinia (NYCBH)expressing HIV-1 89.6 Env

Virus HIV-1 *Strain:* 89.6 *Subtype:* B *Gene/Protein:* env (Env)

Trial(s) NHP.319

VI-B-12 Passive antibody vaccines

Vaccine Name **Anti-HIV-1 ch1206**
Description Anti-HIV-1 antibodies obtaine from chimpanzees infected with HIV-1DH12. The chimpanzee was infected for 2.8 years prior to sample collection

Trial(s) NHP.86.1, NHP.86.2

Vaccine Name **Anti-HIV-1 ch4750**
Description Anti-HIV-1 antibodies obtaine from chimpanzees infected with HIV-1DH12, HIV-1DH20 and HIV-1DH20. The chimpanzee was infected for 3 years prior to sample collection

Trial(s) NHP.86.1

Vaccine Name **Anti-HIV-1 ch911**
Description Anti-HIV-1 antibodies obtaine from chimpanzees infected with HIV-1 IIIB. The chimpanzee was infected for 9.9 years prior to sample collection

Trial(s) NHP.86.1

Vaccine Name **Anti-HIV-2**
Description Antibody obtained from a Cynomolgous macaque inoculated with HIV-2 (SBL-6669) in a whole inactivated form. The monkey has subsequently shown to be protected from an autologous challenge.

Virus HIV-2 *Strain:* HIV-2 SBL6669) *Gene/Protein:* All

Trial(s) NHP.149.1, NHP.149.2

Vaccine Name **Anti-SHIV Plasma**
Description Pool of antiSHIV plasma from macaques infected with non-pathogenic SHIV-4. This pool consists mainly of polyclonal IgG

Trial(s) NHP.87

Vaccine Name **Anti-SIVmac251**
Description Antibodies generated by the immunization of pregnant macaques with whole-inactivated SIVmac251 plus montanide ISA 51 adjuvant.

Virus SIV *Strain:* SIVmac251 *Gene/Protein:* All

Trial(s) NHP.294

Vaccine Name **Anti-SIVmacC8**
Description Pool of antibodies collected from 4 cynomolgous macaques (L103, L106) inoculated with 10^4 TCID50 of 9/90 live attenuated virus SIVmacC8, prepared in C8166 cell. all macaques were shown to be infected and were subsequencently challenged with SIVmacJ5M and SHIV-4. The challenge did not induce superinfection. Serum collected from the 4 monkeys was stored at -70^{o}C and used as reagent.

Trial(s) NHP.215

Vaccine Name **Cβ1 anti-V3**
Description This is a mouse-human IgG1 chimeric monoclonal antibody. It contains the intact variable region of the murine 0.5 β monoclonal antibody which is directed to the V3 loop of HIV-1 IIIB variant gp120 and has potent in vitro IIIB-specific virus-neutralizing activity.

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* env (V3)

Trial(s) NHP.152.1, NHP.152.2

Vaccine Name **Chimp anti-HIV IgG**

Description Antibodies were obtained from chimpanzees that were infected with a variety of HIV-1 isolates and subsequently developed high-titer neutralizing antibodies

Trial(s) NHP.249

Vaccine Name **Chimp-anti-HIV-IgG**

Description The authors [Nishimura et al J Virol 76(5): 2123-30 (2002)] state that the IgG was harvested in 2000, from chimpanzee 4750 which had been infected in 1993 with 3 different HIV-1 strains including HIV-1 strain DH12.

Trial(s) NHP.354, NHP.394

Vaccine Name **F105/2G12/2F5 mab**

Description Coctail of 3 monoclonal antibodies (F105, 2G12 and 2F5)

Trial(s) NHP.85, NHP.117

Vaccine Name **HIVIG**

Description Anti-HIV-1 immunoglubulin obtained by plasmapheresis from HIV-1 infected individuals. The neutralising antibody titer was above or equal to 1:128. Virus-sterilized coagulation factors by application of solvents and detergents were used to inactivate thevirus in the plasma.

Notes derived from the pooled plasma of several HIV-1 positive donors

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B *Gene/Protein:* All

Trial(s) NHP.8, NHP.82.1, NHP.82.2, NHP.361

Vaccine Name **IgG1 b12**

Description Human antibody (IgG1,) recognizing an epitope overlapping the CD4 binding site of gp120 , contained <1 IU of endotoxin/ml

Trial(s) NHP.6, NHP.15, NHP.304

Vaccine Name **mAb B4**

Description This is a monoclonal antibody directed against HIV receptor complex;Broad neutralizing activity against HIV; Provides postexposure prophylaxis to hu-peripheral blood leukocyte (PBL)-severe combined immunodeficient mice and chimpanzees;Recognized a complexreceptor site for HIV on the T cell surfaceincludeing CD4;Preferentially neutralizes primary HIV-1 isolates compared with T cell line-adapted strains, including SI and NSI-inducing phenotypes, representatives from HIV-1 subtypes A-G, HIV-2, SIV, and SHIV

Trial(s) NHP.84

Vaccine Name **Monoclonal antibody 2F5**

Description

Notes 2F5 is an subclass IgG1. recognizes the gp41 sequence ELDKWA that is conserved among many HIV-1 strains

Trial(s) NHP.8, NHP.15, NHP.82.1, NHP.82.2, NHP.304

Vaccine Name **Monoclonal antibody 2G12**

Description 2G12 is a subclass IgG1. Binds to a conformationally sensitive epitope in the C3-V4 region of gp120

Trial(s) NHP.8, NHP.15, NHP.82.1, NHP.82.2, NHP.304

Vaccine Name **Monoclonal antibody 4E10**
Description This is a human monoclonal antibody that recognizesthe concerved HIV-1 gp41 epitope NWEDIT

Trial(s) NHP.304

Vaccine Name **Monoclonal antibody F105**
Description obtained by fusion of antibody- producing EBV-transformed cells with the HMMA2.11TG/O cell line; This is a IgG1 kappa antibody that binds to the surfaces of cells infected with all HIV-1 strains tested: MN, RF, IIIB, and SF2, but not uninfected cells

Trial(s) NHP.15

Vaccine Name **SIVIG**
Description Approximately 16 g of IgG purified from 1.5 liters of plasma obtained by plasmapheresis from a single long-term nonprogressing Macaca mulatta macaque, infected with the F236 isolate of SIVsm and remaining clinically healthy for more than 6 years

Virus SIV *Strain:* SIVsmF236 *Gene/Protein:* All

Trial(s) NHP.377

Vaccine Name **SIVIG-1**
Description Antibody preparation from pooled plasma from SIVmac251-infected macaques. The preparation contains 15 mg/ml of purified IgG, a titer of 68,000 gp120; 31,00 anti-p27 and 1.15 ug/ml 50% neutralization titer

Trial(s) NHP.83

Vaccine Name **SIVIG-2**
Description Antibody preparation from pooled plasma from SIVmac251-infected macaques. The preparation contains 16 mg/ml of purified IgG, a titer of 170,000 gp120; 30,00 anti-p27 and 0.6 ug/ml 50% neutralization titer

Trial(s) NHP.83, NHP.363

VI-B-13 Other vaccines

Vaccine Name **CD4 Immunoadhesin (CD4-IgG)**
Description A chimeric consisting of the N-terminal two immunoglobulin-like regions of CD4 joined to the Fc region of human IgG1. This is used as a CD4 analogue because it has a half life longer than CD4. In human, the complexe results in 25 folds increase of concentration of CD4-IgG in the blood compared with recombinant CD4.

Trial(s) NHP.156

Vaccine Name **Crosslinked gp120-CD4**
Description HIV-1 IIIB gp120 and CD4 chemically crosslinked with 0.5 mM bis(sulfosuccinimidyl)suberate (BS3, Sigma)

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B

Trial(s) NHP.53

Vaccine Name **Crosslinked gp140-CD4**
Description HIV-1 IIIB gp140 and CD4 chemically crosslinked with 0.5 mM bis(sulfosuccinimidyl)suberate (BS3, Sigma)

Virus HIV-1 *Strain:* HIV-1.IIIB *Subtype:* B

Trial(s) NHP.53

Vaccine Name **HIV-1 HXBc2 Tat Toxoid**
Description Contact authors

Virus HIV-1 *Strain:* HXBc2 *Gene/Protein:* Accessory (tat)

Trial(s) NHP.121

Vaccine Name **inactivated Tat toxoid**
Description

Trial(s) NHP.78

Vaccine Name **SHIV89.6P tat toxoid**
Description Contact authors

Virus SHIV *Strain:* SHIV89.6P *Subtype:* B *Gene/Protein:* Accessory (tat)

Trial(s) NHP.121

VI-C

Challenges

This chapter contains a list of challenge viruses used in the studies compiled in the database. Challenge viruses are grouped into the following categories:

- SHIV
- SIV
- HIV-1
- HIV-2

In most cases, the name and description of challenge viruses were retained as provided by the authors in the paper reporting the trial. For HIV-1, HIV-2 and simian/human synthetic recombinant viruses, the subtype of the HIV-1 or HIV-2 portion(s) of the genome has been recorded. In addition, the studies in which each challenge virus was used are also shown for each challenge virus.

Viruses used in primate models of AIDS and vaccine studies are tremendously variable in infectivity, sequence diversity, and pathogenicity. For example, the SHIV89.6P virus is much more rapidly lethal to Rhesus macaques than the SHIV-89.6 virus from which it was derived [1,2]. The SHIV89.6P acutely pathogenic virus has mutations which alter the carboxy terminus of the env gp41 protein and also alter the Nef protein. Similarly, some of the PBJ isolates are far more acutely lethal than the SMM9 stock from which they were derived [3,4].

The database contains links to genetic sequences of challenge viruses whenever such sequences are available. Caution should be used in interpreting such links because the sequence may not be 100% identical to the challenge virus. Even with an infectious molecular clone of a virus, the challenge dose is often created from culturing the clone though several amplification passages which could result in an accumulation of mutations.

References

[1] Karlsson GB, Halloran M, Li J, Park IW, Gomila R, Reimann KA, Axthelm MK,Iliff SA, Letvin NL, Sodroski J. Characterization of molecularly cloned simian-human immunodeficiency viruses causing rapid CD4+ lymphocyte depletion in rhesus monkeys. *J Virol* 1997 Jun; 71(6):4218-25. PMID: 9151808.

[2] Reimann KA, Li JT, Veazey R, Halloran M, Park IW, Karlsson GB, Sodroski J, Letvin NL. A chimeric simian/human immunodeficiency virus expressing a primary patient human immunodeficiency virus type 1 isolate env causes an AIDS-like disease after in vivo passage in rhesus monkeys. *J Virol* 1996 Oct; 70(10):6922-8. PMID: 8794335.

[3] Tao B, Fultz PN. Molecular and biological analyses of quasispecies during evolution of a virulent simian immunodeficiency virus, SIVsmmPBj14. *J Virol* 1995 Apr; 69(4):2031-7. PMID: 7884848.

[4] Fultz PN, McClure HM, Anderson DC, Switzer WM. Identification and biologic characterization of an acutely lethal variant of simian immunodeficiency virus from sooty mangabeys (SIV/SMM). *AIDS Res Hum Retroviruses* 1989 Aug; 5(4):397-409. PMID: 2765298.

VI-C-1 SHIV Challenges

Strain	**SHIV-4.vpu+**
Description	Contains gag, pol, vif and nef ORF of SIVmac239 (open nef) and tat, rev, vpu and env genes of HIVHXBc2, with defective start codon of vpu (ACG in HXB2) corrected. Obtained from Virus Research Institute, Cambridge MA, USA. Described in Li et al JAIDS 5:639-646 (1992) and J Virol 69(11):7061-7 (1995) PubMed ID 7474126
HIV Subtype	B
Notes	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1613662
Trials	NHP.77

Strain	**SHIV-BX08**
Description	The SHIV-BX08 construct is a chimeric virus derived from SIV-MAC239 (gag, pol, vif, vpx and nef genes), HIV-1 isolate BX08 (env gp120), and HIV-1 isolate LAI (env gp41, tat and rev). Although SHIV-BX08m has been used in numerous studies, no DNA sequencesare available for the BX08 virus.
HIV Subtype	B
Trials	NHP.276

Strain	**SHIV-C2/1**
Description	SHIV-C2/1 is an SHIV-89.6 variant isolated by passaging the peak of initial plasma viremia from an infected cynomologus macaque as described in J Gen Virol 80(5):1231-40 (1999) by Shinohara et al. The original pSHIV, containing the SHIV-89.6P (and not the 89.6 as implied by Shinohara in J Gen Virol) was kindly provided by Y. Lu at the Harvard AIDS Institute (Boston, Mass. yichenlu@hsph.harvard.edu).
HIV Subtype	B
Notes	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10355770
Trials	NHP.365

Strain	**SHIV-DH12clone7**
Description	Infectious molecular clone derived from SHIV-DH12R-PS1 which in turn was derived from HIV-MD14YE [Igarashi et al PNASU 96(24): 14049-14054 (1999)].
HIV Subtype	B
Trials	NHP.386

Strain	**SHIV-DH12clone8**
Description	Infectious molecular clone derived from SHIV-DH12R-PS1 which in turn was derived from HIV-MD14YE [Igarashi et al PNASU 96(24): 14049-14054 (1999)].
HIV Subtype	B
Trials	NHP.386

Strain	**SHIV-IIIB/HXB2**
Description	Also known as SHIV-4, Described in J AIDS 5: 639-646 (1992) by Li et al. SIV-Mac239 virus with HIV-1 HXB2 env inserted. Described in J Virol 70(5):3198-3206 (1996) only as the arent plasmid from which SHIV-89.6 was created by replacing part of HXB2 gp160 with the same region for another HIV-1 subtype B virus with different tropism.
HIV Subtype	B
Notes	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1613662
Trials	NHP.14, NHP.16.1, NHP.16.2, NHP.47, NHP.56

Strain	**SHIV-KU2**
Description	SHIV-Ku2 is a chimeric virus containing the HIV-1 IIIB strain (HXBc2) envelope gene and SIVmac239 gag and pol genes, and is pathogenic in rhesus macaque
HIV Subtype	B
Trials	NHP.1, NHP.79, NHP.107

Strain **SHIV-MD14YE (DH12)**
Description Derived from SHIV-1DH12, but with the HIV-1 nef gene replaced by SIV-Mac239 nef with two mutations R17Y and Q17E. The SIV nef R17Y mutation is known to create virus that depletes macaque T-cells self-activates T-cells such that the virus can replicate innon-stimulated PBMCs. R17Y creates SH2 binding ITAM motif YXXLXXXXXXXYXXL.
HIV Subtype B
Notes The tat, rev and env genes and the remainder of the vpr gene were derived mostly from HIV-1DH12, except for a small segment (145 bp) at the SIV/HIV-1 junction in vpr) that is of HIV-1NL4-3 origin.
Trials NHP.86.1, NHP.86.2, NHP.387, NHP.389

Strain **SHIV-NM-3rN**
HIV Subtype B
Notes The subtype relates to the HIV component only
Trials NHP.28, NHP.31, NHP.35, NHP.322

Strain **SHIV-vpu+**
Description Described in Li et al J Virol 69(11):7061-7 (1995) PubMed ID 7474126. SHIV-4 modified by site-directed mutagenesis to correct defective vpu. HIV-1 subtype B clone HXB2 has a defective vpu gene due to an ATG to ACG mutation in the vpu start codon. ThisSHIV has a corrected start codon, plus a P5Q mutation in vpu.
HIV Subtype B
Trials NHP.15, NHP.85, NHP.117

Strain **SHIV.229(mn)**
Description The SHIV229(mn) is based on $SHIV_{IIIB}$ encoding HIV-1_{HXBc2}tat, rev and env on a SIV_{mac239} backbone, passaged through M. nemestrina in vivo to become pathogenic. The challenge stock was generated by expanding the SHIV229(mn) on PHA-activated M. nemestrina PBMC.
HIV Subtype B
Trials NHP.339

Strain **SHIV.DH12 (MD1)**
Description This chimeric simian-human immunodeficiency virus (SHIVs) carries envelope glycoproteins from a T cell-macrophage dual-tropic primary isolate (human immunodeficiency virus type 1 [HIV-1] strain DH12) in the SIVmac239 backbone. DH12 is also known as MD1.MD14 is derived from MD1 by replacing the DH12 nef with Mac239 nef.
HIV Subtype B
Trials NHP.11

Strain **SHIV.DH12R-PS1**
Description This SHIV was obtained from the nonpathogenic SHIVDH12 (SHIVMD1) (Shibata, JID 176:362-73 1997). This highly pathogenic SHIVDH12R was isolated at week 68 from rhesus monkey 565Z (Igarashi et al PNASU 96(24):14049-14054 1999). Virus isolated at week 52 from animal 565Z also induced an irreversible and extremely rapiddepletion of CD4+ T lymphocytes following its inoculation into rhesus monkey PS1 and was designated SHIVDH12R-PS1.
HIV Subtype B
Notes http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10570196
Trials NHP.157.3, NHP.303, NHP.391

Strain **SHIV.KU1**
Description SHIV.KU1 was described in ARHR 13(8): 635-645 (1997) PMID: 9168232 and J Virol 73(2):976-84 (1999) PMID: 9882298. It is derived from SHIV-P3 by passage in donor PBMCs from a normal macaque.
HIV Subtype B

Notes This is an extremely virulent chimeric virus. Has an open vpu in addition to numerous mutations in the env and nef. Replicates efficiently in macrophage cultures and at extremely high titers in monkeys, with loss of CD4+ T cells and AIDS
Trials NHP.87, NHP.112

Strain **SHIV.MD1**
Description It carries a portion of the U3 LTR, the R-U5 LTR, gag, pol, vif, and vpx, and approximately 20% of vpr from SIVmac239. The remainder of vpr, tat, rev, env, and nef and a portion of the U3 LTR are derived from HIV-1; most of the HIV-1 sequences came from aT-cell/macrophage dual-tropic primary isolate HIV-1DH12 except for small segments at SIV-HIV-1 junctions (145 bp in vpr; 27 bp in nef) that were derived from HIV-1NL43. NRE, negative regulatory element.
Shibata et al. J Inf Dis 176:362 (1997)
HIV Subtype B
Notes http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9237701
Trials NHP.207, NHP.389, NHP.394

Strain **SHIV.SF13**
Description Described in AIDS 10(12): 1331-7 (1996) PubMed ID 8902061. This SHIV is a SIV-Mac239 LTR-Gag-Pol and Nef with HIV-1 subtype B clone SF13 Tat-Rev-Vpu-Env. The SF13 clone is from the same patient as the HIV-1 SF2 clone.
HIV Subtype B
Trials NHP.80, NHP.164

Strain **SHIV.W6.1D**
Description $SIV_{W6.1d}$ was constructred by replacing an NheI-to-AvrII fragment encompasing Env gp160, of SHIV-4 with the W6.1D cloned Env from HIV-1 subtype B isolate 320.3 which is a dual-tropic virus from a Dutch AIDS patient.
HIV Subtype B
Trials NHP.80

Strain **SHIV162P4**
HIV Subtype B
Trials NHP.6, NHP.62

Strain **SHIV33**
Description This SHIV contains the tat, rev, vpu, and env genes of HIV-1 subtype B isolate SF33. The SHIV-SF33 construct was then passaged in Rhesus macaque to generate SHIV-SF33A. See also the entry with accession number AF401229, from this same SHIV construct.
HIV Subtype B
Trials NHP.268.1

Strain **SHIV33A**
Description This SHIV contains the tat, rev, vpu, and env genes of HIV-1 subtype B isolate SF33. The SHIV-SF33 construct was then passaged in Rhesus macaque to generate SHIV-SF33A. See also the entry with accession number AF401229, from this same SHIV construct.
HIV Subtype B
Trials NHP.268.1

Strain **SHIV89.6**
HIV Subtype B
Trials NHP.7, NHP.15, NHP.90.1, NHP.114, NHP.126, NHP.319

Strain **SHIV89.6P**

Description Parental SHIV was SHIV-4 (also known as SHIV-IIIB/HXB2) from which env of HXB2 was replaced by env of 89.6 (also HIV-1 subtype B but different tropism). Described in J Virol 70(5): 3198-3206 (1996) by Reimann et al. Passaged to gain pathogenicity as described in J Virol 71(6): 4218-25 (1997) by Karlsson et al.
HIV Subtype B
Notes http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Retrieve&list_uids=9151808&dopt=Citation
Trials NHP.2, NHP.7, NHP.16.2, NHP.17, NHP.19, NHP.23, NHP.24.2, NHP.28, NHP.36, NHP.37, NHP.55, NHP.56, NHP.60.1, NHP.60.3, NHP.79, NHP.80, NHP.89, NHP.90.2, NHP.107, NHP.117, NHP.121, NHP.126, NHP.131, NHP.132, NHP.304, NHP.306.1, NHP.306.2, NHP.325, NHP.348.2, NHP.349, NHP.366, NHP.374, NHP.400

Strain **SHIV89.6PD**
HIV Subtype B
Trials NHP.8, NHP.34, NHP.70, NHP.72, NHP.78, NHP.81, NHP.82.1, NHP.82.2, NHP.326, NHP.398

Strain **SHIV89.6v**
Description This is a stock virus from the SHIV89.6 after passage in rhesus macaques through intra vaginal inoculation and brief culture in rhesus PBMC. The stock concentration was determined as 10^3 TCID50/ml by culture on CEMx174 cells and p27 production
HIV Subtype B
Trials NHP.20

Strain **$SHIV_{SF162-PC}$**
Description $SHIV_{SF162-PC}$ is derived from $SHIV_{SF162}$ by replacing env V1-V5 with env V1-V5 from a passaged $SHIV_{SF162}$ that was more infectious and pathogenic ($SHIV_{SF162-P3}$).
HIV Subtype B
Trials NHP.312

Strain **SHIVHan2**
Description Described in AIDS 10(12): 1331-7 (1996) PubMed ID 8902061. This SHIV is a SIV-Mac239 LTR-Gag-Pol and Nef with HIV-1 subtype B clone pNL43 Tat-Rev-Vpu-Env, from which the SacII-HindIII region (most of env) was replaced by HIV-1 subtype B isolate Han2.
HIV Subtype B
Trials NHP.80

Strain **SHIVsbg0.1**
Trials NHP.10

VI-C-2 SIV Challenges

Strain	**SIV mac251 (European) stock 5**
Description	prepared by passaging the European SIVmac251-32H 11/88 challenge virus once through rhesus PBMC
Trials	NHP.119
Strain	**SIV(Mne) Cell-free**
Trials	NHP.269
Strain	**SIV(Mne) clone E11S**
Trials	NHP.64, NHP.65.1, NHP.65.2, NHP.94, NHP.134, NHP.154, NHP.265, NHP.269
Strain	**SIVDeltaB670**
Description	The virus was described by Mickey Corb in a paper published by Gormus et. al. in the Journal of Infectious Diseases, Vol 160, No 3, Sept 1989. The virus came from mangabey A022 (naturally infected with SIV), was passed to rhesus macaque 8664, then passed to B670. Sooty mangabey A022 came from Yerkes to Tulane and appears to have been born at Yerkes.
Trials	NHP.63, NHP.248
Strain	**SIVmac (not detemined)**
Trials	NHP.239, NHP.240
Strain	**SIVmac220**
Notes	Viral challenge (SIVmac 220) which is a cell-free virus stock prepared from the spleen of a rhesus monkey infected with the J5 molecular clone of SIVmac 251 (32H)
Trials	NHP.106, NHP.397
Strain	**SIVmac239**
Trials	NHP.16.2, NHP.18, NHP.39, NHP.54, NHP.61, NHP.67, NHP.69, NHP.88, NHP.148, NHP.308
Strain	**SIVmac239/nef-open**
Trials	NHP.52, NHP.309
Strain	**SIVmac251**
Trials	NHP.9.1, NHP.13, NHP.32, NHP.33, NHP.38, NHP.51, NHP.57, NHP.66, NHP.73, NHP.74, NHP.108, NHP.109, NHP.120, NHP.123, NHP.148, NHP.157.1, NHP.157.2, NHP.200, NHP.201.2, NHP.205.1, NHP.205.2, NHP.205.3, NHP.245.1, NHP.245.2, NHP.245.3, NHP.294, NHP.300, NHP.324.1, NHP.327.1, NHP.327.2, NHP.353, NHP.363
Strain	**SIVmac251 (561)**
Description	This challenge stock was prepared by culturing PHA-activated peripheral blood mononuclear cells (PBMC) from a Mamu-A*01-positive infected macaque (561L) exposed to SIVmac251 by the vaginal route. The SIVmac251 (561) was titered in vivo in rhesus macaquesby inoculating 6 animals with different dilutions of virus stock via the rectal route. 6/6 animals inoculated with the virus (0.5 ml diluted to 1.5 ml with RPMI medium) became infected, evidenced by high plasma viremia and a drop in CD4 counts.
Trials	NHP.30, NHP.274
Strain	**SIVmac251 (J5)**
Trials	NHP.126, NHP.185.2
Strain	**SIVmac251(32H)**
Trials	NHP.5, NHP.41, NHP.49, NHP.97, NHP.99.2, NHP.116, NHP.151, NHP.152.1, NHP.152.2, NHP.185.1, NHP.194.1, NHP.203, NHP.205.2

Strain **SIVmac251,32H.spl**
Notes virus stock was prepared from a spleen homogenate of a rhesus monkey inoculated with SIVmac251, 32H and titrated in vitro in human T cells and in vivo in rhesus monkeys
Trials NHP.40

Strain **SIVmac251BK28**
Notes molecular clone grown in monkey PBMCs
Trials NHP.40

Strain **SIVmac32H.IXc**
Description Pathogenic cell-associated SIV from primary, uncultured rhesus monkey PBMC
Trials NHP.58

Strain **SIVmac8980**
Description SIVmac 8980 grown in rhesus monkey PBMC and analyzed for CCR5 coreceptor binding using the "Ghost system" (see Trkola A et al., J Virol 1998;72:1876-85).
Trials NHP.395

Strain **SIVmacJ5M**
Trials NHP.215

Strain **SIVmacR71**
Trials NHP.107

Strain **SIVmne clone A2-clone 5**
Trials NHP.41

Strain **SIVsm**
Description SIV-sm described by Fultz et al Proc Nat Acad Sci 83(14):5286-90 (1986) PubMed ID 3014542 from an infected macaque at Yerkes. This SIV-sm is from the same animal from which the SIV-SMM9 virus was obtained. J. Virol. 66(1); 414-9 (1992)
PubMed ID 1727495cites Fultz (1986) as the source of SMM9.
Trials NHP.4, NHP.68, NHP.93, NHP.125, NHP.194.2

Strain **SIVsmB670**
Trials NHP.36, NHP.203

Strain **SIVsmE660**
Trials NHP.18, NHP.27, NHP.37, NHP.44, NHP.45, NHP.59, NHP.377

VI-C-3 HIV-1 Challenges

Strain	**HIV-1 Han2**
Description	Isolate HAN was isolated from a 39 year old homosexual German patient with AIDS related complex, in 1986. This patient died from complications of AIDS in 1987. HAN was highly cytopathic in MT-2 T cell line, it was able to productively infect MT-4, H9 or Jurkatcell lines. Genomic DNA from infected MT-2 cells was used to prepare a lambda phage genomic library. Two full-length clones, HAN/2 and HAN/3 were purified. HAN/3 was used for DNA sequencing, and has a defective env gene
HIV Subtype	B
Trials	NHP.21
Strain	**HIV-1 IIIB**
HIV Subtype	B
Trials	NHP.71, NHP.202, NHP.242, NHP.247, NHP.267, NHP.361
Strain	**HIV-1.5016**
HIV Subtype	B
Trials	NHP.141
Strain	**HIV-1.DH12**
HIV Subtype	B
Trials	NHP.84, NHP.392
Strain	**HIV-1.LAI**
HIV Subtype	B
Trials	NHP.48, NHP.204
Strain	**HIV-1.SF2**
HIV Subtype	B
Trials	NHP.141, NHP.193
Strain	**LAV-1 or NY5**
HIV Subtype	B
Trials	NHP.249

VI-C-4 HIV-2 Challenges

Strain	**HIV-2 (UC2-10568)**
Description	HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboons 9429, 12281 and 10568.
HIV Subtype	A
Trials	NHP.310
Strain	**HIV-2 (UC2-11966)**
Description	HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons9429, 12281, 10568, 11999 and 11966.
HIV Subtype	A
Trials	NHP.310
Strain	**HIV-2 (UC2-11999)**
Description	HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons9429, 12281, 10568 and 11999.
HIV Subtype	A
Trials	NHP.310
Strain	**HIV-2 (UC2-12281)**
Description	HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboons 9429 and12281.
HIV Subtype	A
Trials	NHP.310
Strain	**HIV-2 (UC2-12741)**
Description	HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then serially passaged through a baboons9429, 12281, 10568, 11999, 11966 and 12741.
HIV Subtype	A
Trials	NHP.310
Strain	**HIV-2 (UC2-9429)**
Description	HIV-2 group A isolate UC2 was isolated from a woman originally from Burkina Faso but who was living in Cote d'Ivoire. She had developed AIDS and was co-infected with HIV-1. The isolate was cocultured in PBMC with then passaged through a baboon 9429.
HIV Subtype	A
Trials	NHP.310, NHP.378
Strain	**HIV-2.SBL6669**
HIV Subtype	A
Trials	NHP.47, NHP.149.1, NHP.174

VI-D

Adjuvants and Stimulants

As part of the vaccines database, we developed a separate and general database table and search interface for adjuvants and stimulants. The majority of the data on adjuvants was obtained from the National Institute of Allergy and Infectious Diseases. We are indebted to Dr. Carl Alving for making the adjuvant data available. In this vaccine compendium, we have listed only the adjuvants which were used in the Nonhuman Primate HIV/SIV Vaccine Trials Database. For information about other adjuvants and stimulants, the reader is advised to use the Adjuvant/Stimulant search form at `http://www.hiv.lanl.gov/cgi-bin/vaccine/public/adjuvant_search.cgi?process=start`.

Name	**Adju-Phos**
Other Names	Aluminum phosphate gel
Description	Amorphous aluminum hydroxyphosphate. A schematic of the unit layer of amorphous aluminum bydroxyphosphate showing the surface hydroxyl, water, and phosphate groups. Key: Al, small closed circle; OH, large closed circle; H_20, open circle; $P0_4$, hatched circle. Obtained by precipitation. The degree of substitution of phosphate for hydroxyl depends on the concentration of reactants and precipitation conditions. White gelatinous precipitate in aqueous suspension.
Trials	NHP.330
Name	**Adjumer™**
Other Names	PCPP salt; polyphosphazene; polyidi (carboxylatophenoxy) lphosphazene
Description	Synthetic Solid: beige to off white powder. Aqueous solution: clear, colorless liquid
Trials	NHP.72, NHP.78
Name	**Alum**
Other Names	Alhydrogel; Aluminum hydroxide gel;
Description	Crystalline aluminum oxyhydroxide AIOOH, known mineralogically as boehmite. The structure consists of corrugated sheets of aluminum octahedra. Obtained by precipitation of aluminum hydroxide under alkaline conditions. White gelatinous precipitate in aqueous suspension.
Trials	NHP.97, NHP.99.2, NHP.151, NHP.162, NHP.185.1, NHP.185.2, NHP.198, NHP.205.3, NHP.248, NHP.349, NHP.362
Name	**AS-2 adjuvant**
Trials	NHP.21
Name	**B7-2**
Description	The gene product encoded by B7-2 is a co-stimulatory molecule for GM-CSF. The genes had been cloned by PCR from baboon peripheral blood mononuclear cells (PBMC) and were sequenced, then sub-cloned into the mammalian expression vector, pND-14.
Trials	NHP.378
Name	**Bupivacaine**
Trials	NHP.2, NHP.16.1, NHP.202, NHP.322
Name	**Bupivacaine-HCl**

Trials NHP.300

Name **BWZL**
Trials NHP.204

Name **CCR5 peptides**
Description N-terminal (aa 1-20): Met-Asp-Tyr-Gln-Val-Ser-Ser-Pro-ILe-Tyr-Asp-ILe-Asp-Tyr-Tyr-Thr-Ser-Glu-Pro-Cys
First loop (aa 89-102): His-Tyr-Ala-Ala-Ala-Gln-Trp-Asp-Phe-Gly-Asn-Thr-Met-Cys-Gln Second loop (aa 178-197): Cys-Ser-Ser-His-Phe-Pro-Tyr-Ser-Gln-Tyr-Gln-Phe-Trp-Lys-Asn-Phe-Gln-Thr-Leu-Lys Neosystem Laboratories (Strasbourg, France)
Trials NHP.395

Name **CpG 2006**
Description Eurogentec, Seraing, Belgium
Trials NHP.330

Name **CRL1005**
Other Names Block Copolymer P1205
Description ABA block polymer with mean values of x = 8 and y = 205. SOURCE: Linear chain polymers are synthesized by condensation of propylene oxide and ethylene glycol initiator in the presence of a cesium salt catalyst to form polyoxypropylene chain, followed by condensation of ethylene oxide on either end of the chain. Individual polymeric species of triblock nonionic block copolymers result from controlled synthesis of chains with pre-determined length. Clear, colorless to slightly yellow, viscous liquid.
Trials NHP.306.1, NHP.306.2

Name **Diphtheria toxoid**
Trials NHP.268.1

Name **DL-PGL**
Other Names Polyester poly (DL-lactide-co-glycolide)
Trials NHP.200

Name **Freund's Complete Adjuvant**
Other Names Complete Freund's adjuvant; CIA; FCA
Description Mixture of mineral oil (Marco 52) and emulsifier (Arlacel A [mannide monooleate]) as an emulsion of 85% mineral oil and 15% emulsifier with 500 µg heat-killed and dried Mycobacterium tuberculosis per mL of emulsifier mixture. M. tuberculosis grown and adjuvant is manufactured at the Statens Seruminstitut, Copenhagen, Denmark. Thick viscous liquid without color.
Trials NHP.79, NHP.94, NHP.154, NHP.268.1

Name **Freund's Incomplete Adjuvant**
Other Names Incomplete Freund's Adjuvant; IFA;FIA
Description Mixture of mineral oil (Marcol 52) and emulsifier (Arlacel A [mannide monooleate]) as an 80% mineral oil, and 15% emulsifier emulsion. Manufactured by Statens Seruminstitut, Copenhagen, Denmark Thick viscous liquid without color.
Trials NHP.7, NHP.56, NHP.65.1, NHP.78, NHP.79, NHP.94, NHP.121, NHP.134, NHP.154, NHP.204, NHP.268.1, NHP.269, NHP.320, NHP.348.1

Name **GM-CSF**
Other Names Granulocyte-macrophage colony stimulating factor; Sargramostim (yeast-derived rh-GM-CSF)

Description STRUCTURE: GM-CSF is a glycoprotein of 127 amino acids. Recombinant human GM-CSF is produced in yeast and it differs from the natural human GM-CSF by substitution of Leu for Arg at position 23. Walter, M. R., et al., 1992, Three-dimensional structure of recombinant human granulocyte-macrophage colony stimulating factor, J. Mol. Biol. 224: 1075-1085. Sequence of recombinant human GM-CSF (Sargramostin): APARSPSPSTQPWEHVNAIQEALRLLNLSRDTAA-EMNETVEVISEMFDLQEPTC LQTRLELYKQGLRGSLTKLKGPLTMMASHYKQHCPPTPETSCATQIITFESFKE NLKDFLLVIPFDCWEPVQE Recombinant protein produced in yeast (S. cerevisiae). White, lyophilized powder (before reconstitution), or a clear colorless solution (after reconstitution).
Trials NHP.68, NHP.106

Name **IFN-gamma in pCDNA3**
Trials NHP.16.1

Name **IL-12 DNA**
Description The rhesus macaque IL-12 expression plasmid was derived from the plasmid pSFG.hIL12.p40.Lp35, which expresses human IL-12, by substituting the sequences encoding the human p40 and p35 subunits with the corresponding rhesus macaque sequences, positioned in the same configuration to produce plasmid pRM.IL-12.p40-p35. In this plasmid, the IL-12 p40 and -30 subunits are produced as a fusion protein in which the p35 subunit, deleted of its leader sequence, is fused to the p40 subunit by a Gly6Ser linker. IL-12 production by rmIL-12.p40.Lp35 was tested in 293T transfection supernatant by ELISA.
Trials NHP.366

Name **IL-12/GMCSF plasmid (Sykes)**
Description Plasmids expressing the human cytokine IL-12 and GMCSF. Constructed by amplifying the cDNA coding sequences from pED and pXM vectors. EcoRI and SalI sites were incorporated into the end of the cDNAs encoding GMCSF and IL-12 subunit p35 by PCR (for more information contact authors) Sykes et al
Trials NHP.120

Name **IL-2 in pCDNA3**
Trials NHP.16.1

Name **IL-2/lg plasmid**
Trials NHP.23, NHP.60.1, NHP.60.3, NHP.98, NHP.126, NHP.366, NHP.400

Name **IL-2/lg protein**
Trials NHP.24.1, NHP.60.1, NHP.98, NHP.126

Name **IL-4**
Trials NHP.106, NHP.309

Name **IL-4 in pCDNA3**
Trials NHP.16.1

Name **Interferon-γ**
Other Names Actimmune® (rhIFN-gamma, Genentech, Inc.); immune interferon; IFN-γ gamma-interferon
Description Noncovalent dimer. Low resolution crystal structure available. Monomer consists of 140 amino acids, no glycosylation or cysteines in human form. Murine form is a covalent dimer (one cysteine per monomer). Ealick, S. E. et al., 1991, Three-dimensional structure of recombinant human interferon-g , Science, 252: 698- 702. Sequence of human interferon-gamma: QDPYVKEAENLKKYFNAGHSDVADNGTLFLGILKNWKEESDRKIMQSQIVSFYFKLFKNFKDDQSI QKSVETIKEDMNVKF-FNSNKKKRDDFEKLTNYSVTDLNVQRKAIHELIQVMAELSPAAKTGKRKRS QMLFRGRRASQ Both human (rhIFN-gamma) and murine (rmuIFN-gamma) forms are expressed in Escherichia coli and distributed in a completely pure state. Clear aqueous solution.
Trials NHP.309

Name **Interleukin-2**
Other Names IL-2; T-cell growth factor; aldesleukin (des-alanyl-1, serine-125 human interleukin 2); Proleukin®; Teceleukin®

Description Native human IL-2 contains 133 amino acids (see below); aldesleukin contains 132 amino acids. IL-2 exists as six alpha helical domains, termed A to F. Glycosylation not essential for function. Rosenberg, S. A. et al., 1983, Biological activity of recombinant human interleukin-2 produced in Escherichia coli, Science, 223: 1412-14. Brandhuber, B. J. et al., 1987, Three dimensional structure of interleukin-2, Science, 238: 1707-09. Ju, G. et al., 1987, Structure function analysis of human interleukin-2: Identification of amino acid residues required for biological activity. J. Biol. Chem., 262: 5723-31. Sequence of human IL-2: APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLEEELKPLE EVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCE-YADETATIVEFLNRWITFCQSIISTLT Recombinant protein expressed in E. coli. Lyophilized, white to off-white colored solid, Reconstituted with water for injection to give a clear, colorless solution.

Trials NHP.106, NHP.126, NHP.245.3

Name **ISCOM(s)™**

Other Names Immune stimulating complexes

Description ISCOMs are a complex composed of typically 0.5% Quillaja saponins, 0.1% cholesterol, 0.1% phospholipid, and antigen in phosphate-buffered saline (PBS). Occasionally, surfactants are used t are ISCOMs (such as Mega 10) but are removed from the final formulation before use. The adjuvant-active components of ISCOMs are derived by aqueous extraction of the bark of Quillaja saponaria and are further purified by chromatography. Quil A is a purified form of this. Further chromatographic purification provides components with high adjuvant activity and ISCOM-forming properties (see Iscoprep 7.0.3 TM). ISCOMs form a clear product in solution.

Trials NHP.75, NHP.125, NHP.164, NHP.374

Name **Kehole Limpet Hemocyanin**

Description Unknown. Used in J Virol 71: 9475-9481 (1997) Jurkiewicz et al.

Trials NHP.320

Name **Lipid-based Adjuvant**

Other Names LBA

Description Data not available Mannhalter et al, 1991

Trials NHP.362

Name **Liposomes**

Other Names Liposomes (L) containing protein or Th-cell and/ or B-cell peptides, or microbes with or without co-entrapped interieukin-2, BisHOP or DOTMA (see below). A, [L (Antigen)]; B, [L (IL-2 or DOTMA or BisHOP + Antigen)]; C, [L (Antigen)-mannose]; D, [L (Th-cel

Description A: Multilamellar liposornes prepared by the dehydration-rehydration method (average diameter 600-800 nm) composed of egg phosphatidy1choline (PC) or distearoyl phosphatidylcholine (DSPQ and equimolar cholesterol and containing antigens such as tetanus toxoid and synthetic Th-cell peptides. 13: As in A with IL-2 (10^3 - 10^4 Cetus units) co-entrapped with the antigen in the aqueous phase or with 1,2-bis (hexadecylcycloxy)-3-trimethylaminopropane-HCL (BisHOP) or N-(2,3-dioleyloxy)-NNN-triethylammonium (DOTMA) incorporated into the lipid phase of liposomes (0.8: 1.0: 0.2 molar ratio for PC or DSPC, cholesterol and DOTMA or BisHOP). C, as in A with marmosylated albumin covalently coupled to the surface of antigen-containing liposomes. D: As in A with Th-cell and B-cell peptides co-entrapped in the aqueous phase. E: Giant liposornes (average diameter 5-9 μm) prepared as in A or by a solvent-spherule evaporation method, composed of PC or DSPC, cholesterol, triolein (TO), and phosphatidylglycerol (PG) (4: 4: 1: 2 molar ratio) and containing killed or live Bacillus subtilis or killed Bacille Calmette-Guérin (BCG) with or without co-entrapped tetanus toxoid. PC, DSPC, and PG in pure forin from Lipid Products, Nuthill, Surrey, U. K.; TO in pure form from Sigma Chemical Co., Poole, Dorset, U. K.; recombinant interieukin-2 (des-Ala1-Ser125 mutein; 3 x 10 6 Cetus units/ mg) obtained from Cetus Corporation, Emeryville, CA; BisHOP and DOTMA obtained from Syntex Research, Palo Alto, CA. White, opalescent colloidal suspensions (A-E).

Trials NHP.61, NHP.94

Name **LT(R192G)**

Other Names mutant heat-labile E. coli enterotoxin

Description heat-labile enterotoxin with R-192-G mutation, eliminating trypsin cleavage site required for enterotoxin activation. Dickinson and Clements Infect. Immunol. 63: 1617-1623 (1995)

Trials NHP.319

Name **LT-R192G**
Trials NHP.1

Name **LTK63**
Other Names mutated E. coli heat-labile enterotoxin
Description mutated E. coli heat-labile enterotoxin which eliminates toxicity while retaining adjuvant activity. Pizza et al. Int. J. Med. Microbiol. 290: 455-461 (2000)
Trials NHP.321

Name **MF59**
Other Names None
Description Squalene/ water emulsion. Composition: 43 mg/ mL squalene, 2.5 mg/ mL polyoxyethylene sorbitan monooleate (Polysorbate 80), 2.4 mg/ mL sorbitan trioleate (Span 85). Chiron Corporation, Emeryville, CA. White liquid.
Trials NHP.22, NHP.23, NHP.62, NHP.75, NHP.141, NHP.193, NHP.354

Name **MONTANIDE ISA 51**
Other Names Purified IFA; Incomplete Freund's adjuvant
Description Mannide oleate (mostly mannide monooleate, esters of mannitol and oleic acids -an example shown below) (MONTANIDE 80) in mineral oil solution (DRAKEOL 6VR). Manufactured by SEPPIC. Limpid clear yellow liquid.
Trials NHP.1, NHP.119

Name **MONTANIDE ISA 720**
Other Names metabolizable oil adjuvant
Description A highly refined emulsifier from the mannide monooleate family (an example of mannide monooleate shown below) in a natural metabolizable oil solution. The exact nature of the emulsifier and the metabolizable in MONTANIDE ISA 720 is proprietary, but can be disclosed under specific agreement with SEPPIC. manufactured by SEPPIC. Yellow, odorless liquid
Trials NHP.330

Name **MPL™**
Other Names 3-Q-desacyl-4
Description MPL™is composed of a series of 4'-monophosphoryl lipid A species that vary in the extent and position of fatty acid substitution. The hexaacyl structure shown below is the most highly acylated and most abundant component in MPLO. Species with five and four fatty acids are also present. All structures contribute to the adjuvant activity of MPLO. Derived from the lipopolysaccharide (LPS) of Salmonella minnesota R595. Obtained by treatment of LPS with mild acid and base hydrolytic conditions, and chromatographic purification of the resulting 3D-MLA. Colorless, odorless white powder.
Trials NHP.306.1

Name **MPL-SE**
Other Names MPL-SE (monophosphoryl A-stable emulsion)
Description Wyeth-Lederle Vaccines
Trials NHP.328, NHP.363

Name **MTP-PE**
Other Names N-acetyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1,2-dipalmitoyl-sn-glycero-3-(hydroxy-phosphoryloxy)) ethylamide, mono sodium salt.
Description Chemical synthesis by Ciba-Geigy Ltd., Basel, Switzerland. White powder.
Trials NHP.141

Name **p-Hydroxybenzoique acid methyl ester**

Trials NHP.2

Name **pCIL-10**
Trials NHP.71

Name **pCIL12**
Trials NHP.71, NHP.276

Name **pCMVmCAT1**
Trials NHP.67, NHP.70

Name **pCMVN**
Trials NHP.70

Name **Peptomer-NP**
Trials NHP.5

Name **PLG**
Other Names polyactide coglycolide
Trials NHP.321

Name **QS-21**
Other Names Stimulon™QS-21 Adjuvant.
Description Natural product of the bark of the Quillaja saponaria Molina tree (species native to Chile and Argentina). Extracted from the bark by aqueous extraction. Purified by normal phase and reverse phase chromatography. Kensil, C. R. et al., 1991, Separation and characterization of saponins with adjuvant activity from Quillaja saponaria Molina cortex. J. Immunol., 146: 431-437. Solid: white odorless powder. Aqueous solution: clear, colorless solution.
Trials NHP.11, NHP.14, NHP.53, NHP.81, NHP.303, NHP.371

Name **Quil-A**
Other Names Quil-A saponin, Quillaja saponin
Description A complex but purified mixture of Quillaja saponins which are glycosides of Quillaic acid and carbohydrates. The Higuchi formula of Quil A is shown below. Purified extract from the bark of the South American tree Quillaja saponaria Molina. Lyophilized powder. Color is light brownish, almost white.
Trials NHP.157.1, NHP.157.2

Name **Rehydragel HPA**
Other Names High Protein Adsorbency Aluminum Hydroxide Gel; alum
Description Crystalline aluminum oxyhydroxide AlOOH, known minerologically as boehmite. the structure consists of corrugated sheets of aluminum octahedra. Synthetic oxyhydroxide of aluminum (aluminum hydroxide) prepared by acid-base precipitation. Translucent, thixotropic, colloidal aqueous gel supplied sterile.
Trials NHP.47, NHP.174, NHP.201.1, NHP.201.2, NHP.203, NHP.204, NHP.242, NHP.306.1

Name **RIBI**
Trials NHP.94, NHP.119, NHP.162, NHP.320

Name **Ribilike adjuvant system (MPL, TMD,CWS)**
Trials NHP.68

Name **SAF-1**
Other Names SAF-m; Syntex Adjuvant Formulation
Description Composed of threonyl-MDP (0.05-1%) in an emulsion vehicle [5% squalane, 2.5% Pluronic® L121, 0.2% Polysorbate 80 and phosphate buffered saline (pH 7.4)]. See individual components. White, fluid, oil-in-water emulsion.

Trials NHP.203, NHP.205.1, NHP.245.2, NHP.245.3

Name **Squalene 2**
Other Names Spinacene; Supraene; 2,6,10,15,19, 23-hexamethyl-2,6,10,14,18,22 tetracosahexaene
Description Found in shark liver oil and some vegetable oils. Intermediate in the biosynthesis of cholesterol. Clear oil, colorless. Faint, agreeable odor.
Trials NHP.245.1

Name **Threonyl muramyl dipeptide (TMDP)**
Other Names Termurtide™; [thr^{1}]-MDP; N-acetyl muramyl-L-threonyl-D-isoglutamine
Description Synthetic. G. J. Jones, et al, Novel immunological adjuvant compounds and methods of preparation thereof. Syntex, U. S. A., U. S. Patent # 4,082,735. White to off-white, odorless powder.
Trials NHP.239, NHP.245.2, NHP.248

VI-E

Trial Summaries

This chapter contains a listing of studies compiled in the database. There are currently 388 trials in the relational database created at LANL and 218 trials carried over from Jon Warren's database. This listing is a printed version of the results of searching our database with the default settings (find any or all) and the Trial Summary display format. Each summary contains data from the following fields unless they are empty in the database:

- Trial number
- Title
- Authors
- Citation and PubMed ID number
- Objectives
- Species/subspecies
- Vaccine name, type, formulation and route of inoculation
- A short description of the vaccine
- Challenge virus name and route
- A summary of the main findings

The database itself contains much more detailed information for each trial, including information about each group of animals.

NHP.1 (11726972) **Mucosal AIDS vaccine reduces disease and viral load in gut reservoir and blood after mucosal infection of macaques**

Authors Belyakov IM, Hel Z, Kelsall B, Kuznetsov VA, Ahlers JD, Nacsa J, Watkins DI, Allen TM, Sette A, Altman J, Woodward R, Markham PD, Clements JD, Franchini G, Strober W, Berzofsky JA

Journal Nat Med 2001 Dec;7(12):1320-6

Objectives Challenge, Immunogenicity To compare whether a mucosal vaccine could induce mucosal CTLs and protect rhesus macaques against mucosal infection with SHIV more effectively than the same vaccine given subcutaneously.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name PCLUS3-CL10/PCLUS6.1-CL10/PCLUS3_POL_143/PCLUS3_GAG_372 *Type:* Synthetic Protein/Peptide *Routes:* Intrarectal, Subcutaneous

Challenge SHIV-KU2 *Route:* Intrarectal

Main Findings

- Mucosal SIV specific CTL can be induced by intrarectal immunization of macaques with synthetic-peptide vaccine coupled with LT(R192G) adjuvant.
- CTL response correlates with helper response.
- CD4+ T cells preserved better in animal mucosally immunized than in animals immunized by subcutaneous route and control.
- In contrast with subcutaneous immunization, intrarectal immunization reduced viral load to undetectable level.

NHP.2 (11282197) **Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P)**

Authors Cafaro A, Titti F, Fracasso C, Maggiorella MT, Baroncelli S, Caputo A, Goletti D, Borsetti A, Pace M, Fanales-Belasio E, Ridolfi B, Negri DR, Sernicola L, Belli R, Corrias F, Macchia I, Leone P, Michelini Z, ten Haaft P, Butto S, Verani P, Ensoli B
Journal Vaccine 2001 Apr 6;19(20-22):2862-77
Objectives Challenge, Immunogenicity To test the immunogenicity and protective value of a tat-expressing vector containing defined unmethylated CpG sequences (pCV-tat) in cynomolgus monkeys challenged with SHIV.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name HIV BH10-tat protein *Type:* Recombinant Subunit Protein *Routes:* Intradermal, Intramuscular
Vaccine Name pCV-tat *Type:* DNA *Routes:* Intradermal, Intramuscular
Challenge SHIV89.6P *Route:* Intravenous
Main Findings

- Intramuscular inoculation of the pCV-tat contained primary infection with HIV89.6P virus.
- Control of CD4 T cell decline in all the vaccinated monkeys.
- Correlation between undetectable virus replication and negative virus isolation in all caseswith anti-tat CTLs.
- CD8-mediated non-cytolytic antiviral activity not present in all protected animals.
- CpG-rich tat DNA vaccine, potential for cross-clade application in human as a therapeutic and preventive vaccine.

NHP.3 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity**

Authors Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M
Journal J Gen Virol 2001 Sep;82(Pt 9):2215-23
Objectives Immunogenicity To assess the immunogenicity of an MVA vaccine expressing structural and regulatory genes of SIV, and the influence of pre-existing immunity to vector in immunized Mamu A*01 MHC class 1 rhesus monkeys.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name MVA-SIVmacJ5 (gag-pol) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name MVAmacJ5-nef *Type:* Recombinant Vector (virus/bacteria) *Route:* Intraocular
Vaccine Name MVA SIVsmH4 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intraocular
Main Findings

- MVA SIVmacJ5 gag-pol construct was poorly immunogenic.
- Nab weak and transient.
- SIV-specific CTL detected in all animals immunized with MVA-SIV vaccines, 4-8 weeks post immunization (not in control animals). One immunization is enough and boosting does not increase the magnitude of immune response.
- MVA-SIVnef produced the strongest response compared to MVA-SIVtat and MVA-SIVrev.

NHP.4 (11413371) **Cross-protection against mucosal simian immunodeficiency virus (SIVsm) challenge in human immunodeficiency virus type 2-vaccinated cynomolgus monkeys**

Authors Walther-Jallow L, Nilsson C, Soderlund J, ten Haaft P, Makitalo B, Biberfeld P, Bottiger P, Heeney J, Biberfeld G, Thorstensson R
Journal J Gen Virol 2001 Jul;82(Pt 7):1601-12
Objectives Challenge, Immunogenicity To compare the efficacy of a live attenuated HIV-2 vaccine alone versus boosting with live non-pathogenic HIV-2 following priming with ALVAC HIV-2 (recombinant canarypox virus expressing HIV-2 env, gag and pol).
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name HIV-2 SBL6669 *Type:* Live Virus *Route:* Intravenous
Vaccine Name ALVAC-HIV-2 (gag,pol,gp125) *Type:* Recombinant Vector (virus/bacteria) *Route:* ND
Vaccine Name HIV-2 native gp125 *Type:* Purified Viral Products *Route:* ND
Challenge SIVsm *Route:* Intrarectal

Main Findings

- Vaccination with an ALVAC HIV-2 vaccine followed by exposure to live HIV-2 could induce cross-protection against mucosal infection with SIVsm and seemed to be more efficient than immunization with a live HIV-2 vaccine only

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NHP.5 (11429125) **A conformational C4 peptide polymer vaccine coupled with live recombinant vector priming is immunogenic but does not protect against rectal SIV challenge**

Authors Patterson LJ, Robey F, Muck A, Van Remoortere K, Aldrich K, Richardson E, Alvord WG, Markham PD, Cranage M, Robert-Guroff M

Journal AIDS Res Hum Retroviruses 2001 Jun 10;17(9):837-49

Objectives Challenge, Immunogenicity To compare SIV peptomer and native gp120 subunit boosts following two adenovirus type 5 host range (Ad5hr)-SIVenv recombinant priming immunizations.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Peptomer SIVmac251 (gp120: 435-452) *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular

Vaccine Name Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal

Vaccine Name Native SIV gp120 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge SIVmac251(32H) *Route:* Intrarectal

Main Findings

- Peptomer immunization elicited peptomer and SIV gp120-specific binding antibodies.
- Only native gp120 boosting elicited SIV neutralizing antibodies.
- Upon intrarectal challenge with SIVmac32H, all nine macaques became infected.
- The solely envelope-based vaccine conferred no protection.

NHP.6 (11483779) **Antibody protects macaques against vaginal challenge with a pathogenic R5 simian/human immunodeficiency virus at serum levels giving complete neutralization in vitro**

Authors Parren PW, Marx PA, Hessell AJ, Luckay A, Harouse J, Cheng-Mayer C, Moore JP, Burton DR

Journal J Virol 2001 Sep;75(17):8340-7

Objectives Challenge, Immunogenicity To evaluate the role of passive intravenous transfer of the human neutralizing monoclonal antibody b12 to provide dose-dependent protection to macaques vaginally challenged with the R5 virus SHIV162P4.

Species/Subspecies Macaca (sp)

Vaccine Name IgG1 b12 *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV162P4 *Route:* Vaginal or perivaginal

Main Findings

- Passive immunization with b12 antibody protects monkeys from challenge with SHIV.
- The immunization with b12 antibodies induced sterile protection in vaccinees

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NHP.7 (11287566) **Vaccine-elicited V3 loop-specific antibodies in rhesus monkeys and control of a simian-human immunodeficiency virus expressing a primary patient human immunodeficiency virus type 1 isolate envelope (a)**

Authors Letvin NL, Robinson S, Rohne D, Axthelm MK, Fanton JW, Bilska M, Palker TJ, Liao HX, Haynes BF, Montefiori DC

Journal J Virol 2001 May;75(9):4165-75

Objectives Challenge, Immunogenicity To evaluate the role of vaccine elicited antibodies in the protection against SHIV containing the envelope of a primary isolate of HIV.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name C4/89.6-V3 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular

Vaccine Name C4/89.6P-V3 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular

Challenge SHIV89.6, SHIV89.6P *Route:* Intravenous

Main Findings

- SHIV-89.6 not suitable to assess viral set point between vaccinees and controls.
- Both peptides (vaccine and mock) were immunogenic- the mock C4/scrbl-V3 was immunogenic due to the presence of C4 fragment in the peptide.
- Immunization with the C4/89.6-V3 peptide generated 10-fold-higher titre of V3-specific antibodies than infection with SHIV-89.6.
- Neutralization of immunogens (C4/89.6-V3, C4/89.6P) induced Ab were virus specific (SHIV-89.6 and SHIV-89.6P, respectively).

NHP.8 (10655111) **Protection of macaques against vaginal transmission of a pathogenic HIV-1/SIV chimeric virus by passive infusion of neutralizing antibodies**

Authors Mascola JR, Stiegler G, VanCott TC, Katinger H, Carpenter CB, Hanson CE, Beary H, Hayes D, Frankel SS, Birx DL, Lewis MG

Journal Nat Med 2000 Feb;6(2):207-10

Objectives Challenge, Passive Immunization To evaluate the protective effect of HIV-1 specific antibodies using the SHIV-macaque vaginal challenge model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV89.6PD *Route:* Vaginal or perivaginal

Main Findings

- 14 antibody-treated macaques were either completely protected against infection or against pathogenic manifestations of SHIV-infection
- Some types of antibody response could play a role in protection against mucosal transmission of HIV-1
- 5/5 control animals were viremic upon SHIV challenge and had decline CD4+ T cells

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NHP.9.1 (11017146) **Viremia control following antiretroviral treatment and therapeutic immunization during primary SIV251 infection of macaques**

Authors Hel Z, Venzon D, Poudyal M, Tsai WP, Giuliani L, Woodward R, Chougnet C, Shearer G, Altman JD, Watkins D, Bischofberger N, Abimiku A, Markham P, Tartaglia J, Franchini G

Journal Nat Med 2000 Oct;6(10):1140-6

Objectives Challenge, Immunogenicity, Immunotherapy To explore the effect of therapeutic immunization in the context of ART during primary infection using the simian immunodeficiency virus (SIV251) macaque model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge SIVmac251 *Route:* Intravenous

Main Findings

- Vaccination of Rhesus macaques with the highly attenuated poxvirus-based NYVAC-SIV vaccine expressing structural genes elicited vigorous virus-specific CD4 + and CD8+ T cell responses in macaques that responded effectively to ART.
- Following discontinuation of a six-month ART regimen, viral rebound occurred in most animals, but was transient in six of eight vaccinated animals.
- Viral rebound was also transient in four of seven mock-vaccinated control animals.

NHP.9.2 (12890631) **Prior DNA immunization enhances immune response to dominant and subdominant viral epitopes induced by a fowlpox-based SIVmac vaccine in long-term slow-progressor macaques infected with SIVmac251**

Authors Radaelli A, Nacsa J, Tsai WP, Edghill-Smith Y, Zanotto C, Elli V, Venzon D, Tryniszewska E, Markham P, Mazzara GP, Panicali D, De Giuli Morghen C, Franchini G

Journal Virology 2003 Jul 20;312(1):181-95

Objectives Immunogenicity, Immunotherapy, Chemotherapy To investigate whether a combination of DNA and recombinant poxvirus vaccine can induce high level of virus-specific CD4+ T-cell response and broadens the cytolytic activity in SIVmac251-infected macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name FP-SIV-gp (FP74) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name SIV-pcDNA3gag/pol *Type:* DNA *Routes:* Intradermal, Intramuscular

Main Findings

- The combination of a DNA expressing the gag and pol genes (DNA-SIV-gp) of SIVmac239 followed by a recombinant fowlpox expressing the same SIVmac genes (FP-SIV-gp) was significantly more immunogenic than two immunizations of FP-SIV-gp in SIVmac251-infectedmacaques treated with ART.
- The DNA/FP combination significantly expanded and broadened Gag-specific T-cell responses.
- The combination of these vaccine modalities also induced a sizeable expansion in most macaques of Gag-specific CD8-(CD4+) T-cells able to produce TNF-alpha.

NHP.10 (11257382) **Expansion of HBV-specific memory CTL primed by dual HIV/HBV genetic immunization during SHIV primary infection in rhesus macaques**

Authors Borgne SL, Michel ML, Camugli S, Corre B, Le Grand R, Riviere Y

Journal Vaccine 2001 Mar 21;19(17-19):2485-95

Objectives Challenge, Immunogenicity To evaluate the humoral and cellular immune response to immunization with HIV/HBV vaccine and the protection against SHIV challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pCMV-V3.S (HBV-HIV vaccine) *Type:* DNA *Route:* Intradermal

Challenge SHIVsbg0.1 *Route:* Intravenous

Main Findings

- DNA-immunized primates and control challenged with SHIV were all infected.
- Peak viremia correlates with HBV envelop specific CTL precursor detected in primary infection.
- HBV or SHIV specific cytotoxicity corresponded in part to CD8 T cells presenting a memory phenotype.

NHP.11 (11160726) **Polyvalent envelope glycoprotein vaccine elicits a broader neutralizing antibody response but is unable to provide sterilizing protection against heterologous Simian/human immunodeficiency virus infection in pigtailed macaques**

Authors Cho MW, Kim YB, Lee MK, Gupta KC, Ross W, Plishka R, Buckler-White A, Igarashi T, Theodore T, Byrum R, Kemp C, Montefiori DC, Martin MA

Journal J Virol 2001 Mar;75(5):2224-34

Objectives Challenge, Immunogenicity To compare the breadth of NAb and protective immune response following vaccination of pigtailed macaques with envelope protein(s) derived from either single or multiple viral isolates against the challenge with SHIVDH12.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Recombinant vaccinia virus-HIVgp160 (cocktail) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name Poly-gp120H *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name Poly-gp120H (-DH12) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name Mono-gp120H (89.6) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name Mono-gp120H (DH12) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge SHIV.DH12 (MD1) *Route:* Intravenous

Main Findings

- Mixtures of HIV-1 envelope glycoproteins elicit broader immune responses than individual Env immunogens.
- 5/8 animals immunized with polyvalent vaccines made NAbs against three or more viral strains.
- NAb activity almost entirely homologous to strains used in the vaccine.
- No sterilizing protection against heterologous SHIV challenge.
- Protection of animals against SIV or HIV-1 infection correlates with the presence of NAbs, not gp120 binding activity.

NHP.12 (11145897) **DNA vaccination of macaques with several different Nef sequences induces multispecific T cell responses**

Authors Couillin I, Letourneur F, Lefebvre P, Guillet JG, Martinon F

Journal Virology 2001 Jan 5;279(1):136-45

Objectives Immunogenicity To study the ability of DNA vaccine to induce a wide spectrum of TCL responses to recognize several epitopes and multiple isolates.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pCI-Nef plasmid *Type:* DNA *Route:* Intradermal

Main Findings

- DNA immunization with several sequences elicits multispecific T cell responses that recognize several epitopes expressed in the different Nef immunogens.
- DNA immunization with Nef sequences induced interferon-gamma (IFN-gamma) secreting cell responses directed against several regions of Nef.
- CD8+ T cells were predominantly involved in anti-Nef IFN-gamma secreting cell responses.

NHP.13 (11462016) **Protection against simian immunodeficiency virus vaginal challenge by using Sabin poliovirus vectors**

Authors Crotty S, Miller CJ, Lohman BL, Neagu MR, Compton L, Lu D, Lu FX, Fritts L, Lifson JD, Andino R

Journal J Virol 2001 Aug;75(16):7435-52

Objectives Challenge, Immunogenicity To assess the immunogenicity and protection of a vector-based vaccine (polio Sabin 1 and 2) coupled with SIV genes against vaginal challenge with highly pathogenic SIVmac251.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name pSabRV1-SIV *Type:* DNA *Route:* Intranasal

Vaccine Name pSabRV2-SIV *Type:* DNA *Route:* Intranasal

Challenge SIVmac251 *Route:* Vaginal or perivaginal

Main Findings

- 4/7 vaccinated animals exhibited substantial protection against the vaginal SIV challenge.
- All 12 control monkeys became SIV positive (infection).
- No virological evidence of infection following challenge in 2/7 SabRV-SIV-vaccinated monkeys, indicating complete protection.
- Two additional SabRV-SIV-vaccinated monkeys exhibited a pronounced reduction in postacute viremia to $<10^3$ copies/ml, suggesting that the vaccine elicited an effective cellular immune response.
- 3/6 control animals developed clinical AIDS by 48 weeks postchallenge. In contrast, all seven vaccinated monkeys remained healthy as judged by all clinical parameters.

NHP.14 (11134278) **Immunogenicity and protective efficacy of oligomeric human immunodeficiency virus type 1 gp140**

Authors Earl PL, Sugiura W, Montefiori DC, Broder CC, Lee SA, Wild C, Lifson J, Moss B

Journal J Virol 2001 Jan;75(2):645-53

Objectives Challenge, Immunogenicity To test the immunogenicity and protective efficacy of oligomeric gp140 in the rhesus macaque model, against homologous challenge with SHIV-HXB2.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name HIV-1 IIIB gp140 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings

- Strong neutralizing antibodies against a homologous virus and modest neutralization of heterologous laboratory-adapted isolates were elicited.
- No neutralization of primary isolates.
- 3/4 vaccinated macaques exhibited no evidence of virus replication.
- Infected animals demonstrated high, sustained neutralizing antibody titers to the challenge strain, while those that were protected exhibited waning titers.

NHP.15 (11462019) **Postnatal passive immunization of neonatal macaques with a triple combination of human monoclonal antibodies against oral simian-human immunodeficiency virus challenge**

Authors Hofmann-Lehmann R, Vlasak J, Rasmussen RA, Smith BA, Baba TW, Liska V, Ferrantelli F, Montefiori DC, McClure HM, Anderson DC, Bernacky BJ, Rizvi TA, Schmidt R, Hill LR, Keeling ME, Katinger H, Stiegler G, Cavacini LA, Posner MR, Chou TC, Andersen J, Ruprecht RM

Journal J Virol 2001 Aug;75(16):7470-80

Objectives Challenge, Passive Immunization To develop prophylaxis against mother-to-child of SIV by postnatal passive immunization of neonatal macaques with a triple combination of human monoclonal antibodies.

Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous
Vaccine Name Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous
Vaccine Name IgG1 b12 *Type:* Passive Antibody *Route:* Intravenous
Vaccine Name Monoclonal antibody F105 *Type:* Passive Antibody *Route:* Intravenous
Challenge SHIV89.6, SHIV-vpu+ *Route:* Oral
Main Findings

- Two neonates macaques passively immunized with monoclonal antibodies (F105, 2G12, and 2F5), were protected from oral SHIV-vpu+ challenge, while four untreated control animals became persistently infected.
- Among SHIV89.6P-challenged animals, the MAb combination was partially successful in preventing infection.
- Half of the treated infants were protected from the acute, severe T-cell depletion.

NHP.16.1 (11257383) **Modulation of antigen-specific cellular immune responses to DNA vaccination in rhesus macaques through the use of IL-2, IFN-gamma, or IL-4 gene adjuvants**
Authors Kim JJ, Yang JS, Manson KH, Weiner DB
Journal Vaccine 2001 Mar 21;19(17-19):2496-505
Objectives Challenge, Immunogenicity To examine the effects of cytokine gene adjuvants to enhance the level of cell-mediated immune responses generated by a multicomponent DNA vaccine in the rhesus macaque primate model.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name HIV env_{MN}/rev(pCEnv) *Type:* DNA *Route:* Intramuscular
Vaccine Name pCSGag/Pol.SIV *Type:* DNA *Route:* Intramuscular
Challenge SHIV-IIIB/HXB2 *Route:* Intravenous
Main Findings

- Coadministration of Il-2 and IFN-gamma cDNA enhances antigen-specific T cell-mediated immune response.
- Antibody-specific responses can be driven to a higher level through the use of cytokine genetic adjuvants in rhesus macaques.
- Overall, low CTL response.
- The stimulated T cells from vaccinated rhesus macaques produced higher levels of IFN-gamma than the control animals.
- 3/8 immunized and challenged animals were protected from SHIV challenge.
- Protection to SHIV challenge was associated with CTL

NHP.16.2 (11437655) **Protection from immunodeficiency virus challenges in rhesus macaques by multicomponent DNA immunization**
Authors Kim JJ, Yang JS, Nottingham LK, Lee DJ, Lee M, Manson KH, Wyand MS, Boyer JD, Ugen KE, Weiner DB
Journal Virology 2001 Jul 5;285(2):204-17
Objectives Challenge, Immunogenicity To test the ability of rhesus macaques immunized with DNA vaccines enconding HIV env/rev and SIV gag/pol to control infection with SIVmac239.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name HIV env MN *Type:* –
Vaccine Name HIV env_{MN}/rev(pCEnv) *Type:* DNA *Route:* Intramuscular
Vaccine Name pCSGag/Pol.SIV *Type:* DNA *Route:* Intramuscular
Challenge SIVmac239, SHIV89.6P, SHIV-IIIB/HXB2 *Route:* Intravenous
Main Findings

- Following the pathogenic challenges, all three vaccinated animals were negative for viral coculture and antigenemia and were negative by PCR.
- The control animals exhibited antigenemia by 2 weeks postchallenge and exhibited greater than 10 logs of virus/10^6 cells in limiting dilution coculture.

NHP.17 (11145906) **Sequential immunization of macaques with two differentially attenuated vaccines induced long-term virus-specific immune responses and conferred protection against AIDS caused by heterologous simian human immunodeficiency Virus (SHIV(89.6)P)**

Authors Kumar A, Lifson JD, Li Z, Jia F, Mukherjee S, Adany I, Liu Z, Piatak M, Sheffer D, McClure HM, Narayan O

Journal Virology 2001 Jan 5;279(1):241-56

Objectives Challenge, Immunogenicity To investigate the immunological response and protection in rhesus macaques sequentially immunized with live vaccines ΔvpuΔnefSHIV-4 (vaccine-I) and Δvpu SHIVPPC (vaccine-II).

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SHIV-4 (Deltavpu-Deltanef)-I *Type:* Live Attenuated Virus *Route:* Subcutaneous

Vaccine Name SHIV-PPC (Deltavpu) *Type:* Live Attenuated Virus *Route:* Oral

Challenge SHIV89.6P *Route:* Intravenous

Main Findings

- The vaccine viruses did not replicate productively in the PBMCs of the vaccinated animals.
- 4/4 vaccinees developed binding antibodies against both vaccine envelope glycoproteins but neutralizing antibodies were elicited by only one vaccine; and virus-specific CTLs that recognized homologous as well as heterologous pathogenic SHIVs.
- 3 naive control animals were infected with the challenged strain and 2/3 controls were immunocompromised and succumbed to AIDS 6mpc.
- 4/4 vaccinees became infected with challenge virus but virus in these animals replicated approximately 200- to 60,000-fold less efficiently than in control animals and eventually, plasma viral RNA became undetectable in three of the four vaccinates

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NHP.18 (11581387) **Role of CD8(+) lymphocytes in control of simian immunodeficiency virus infection and resistance to rechallenge after transient early antiretroviral treatment**

Authors Lifson JD, Rossio JL, Piatak M Jr, Parks T, Li L, Kiser R, Coalter V, Fisher B, Flynn BM, Czajak S, Hirsch VM, Reimann KA, Schmitz JE, Ghrayeb J, Bischofberger N, Nowak MA, Desrosiers RC, Wodarz D

Journal J Virol 2001 Nov;75(21):10187-99

Objectives Challenge, Immunogenicity, Immunotherapy To study the role of CD8+ in the control of SIV infection and rechallenge after tansient early antiretroviral theratpy.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVsmE660 *Type:* Live Virus *Route:* Intravenous

Challenge SIVsmE660, SIVmac239 *Route:* Intravenous

Main Findings

- Animals that controlled plasma viremia following transient postinoculation treatment showed substantial resistance to subsequent intravenous rechallenge with homologous (SIVsmE660) and highly heterologous (SIVmac239) SIV isolates, up to more than 1 year later, despite the absence of measurable neutralizing antibody.

NHP.19 (11393868) **Control of a mucosal challenge and prevention of AIDS by a multiprotein DNA/MVA vaccine**

Authors Amara RR, Villinger F, Altman JD, Lydy SL, O

Journal Science 2001 Apr 6;292(5514):69-74

Objectives Challenge, Immunogenicity To assess the protective value of an immunization scheme consisting of DNA priming followed by a recombinant modified vaccinia Ankara (rMVA) booster.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIV-HIV89.6 DNA vaccine *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Challenge SHIV89.6P *Route:* Intrarectal

Main Findings

- Two DNA inoculations at 0 and 8 weeks and a single rMVA booster at 24 weeks effectively controlled an intrarectal challenge administered 7 months after the booster

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NHP.20 (11507204) **Evidence for early local viral replication and local production of antiviral immunity upon mucosal simian-human immunodeficiency virus SHIV(89.6) infection in Macaca nemestrina**

Authors Ambrose Z, Larsen K, Thompson J, Stevens Y, Finn E, Hu SL, Bosch ML

Journal J Virol 2001 Sep;75(18):8589-96

Objectives Immunogenicity, Immunotherapy To study the differences in viremia, CD4 T-cell percentages, and mucosal and systemic anti-SHIV humoral and cellular immune responses during primary infection of animals infected either intravenously or intravaginally.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Challenge SHIV89.6v *Route:* Intravenous, Vaginal or perivaginal

Main Findings

- SHIV Positive viral cocultures, peripheral blood mononuclear cell viral load peaks, and CD4 cell declines were delayed by 1 week in the intravaginally inoculated animals compared to the animals infected intravenously, demonstrating delayed viral spreading to the periphery.
- Mucosal anti-SHIV antibody levels were greater in magnitude and arose more rapidly and mucosal CD8(+) T-cell responses were enhanced in the intravaginally inoculated animals.

NHP.21 (11424009) **Protection from secondary human immunodeficiency virus type 1 infection in chimpanzees suggests the importance of antigenic boosting and a possible role for cytotoxic T cells**

Authors Balla-Jhagjhoorsingh SS, Mooij P, ten Haaft PJ, Bogers WM, Teeuwsen VJ, Koopman G, Heeney JL

Journal J Infect Dis 2001 Jul 15;184(2):136-43

Objectives Challenge, Immunogenicity To investigate correlates of protection against secondary and subsequent HIV infection.

Species/Subspecies Pan troglodytes verus (chimpanzee), Macaca (sp)

Vaccine Name HIV-1 W6.1D gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge HIV-1 Han2 *Route:* Intravenous

Main Findings

- After exposure to an infectious dose of heterologous primary isolate, 4/8 HIV-1 seropositive chimpanzees resisted secondary infection, whereas 2 naive controls became readily infected.
- Only animals who were immunologically boosted were protected.
- Protection from heterologous secondary exposure appeared to be related to the repertoire of the cytolytic CD8+ T cell responses to HIV-1.

NHP.22 (11356960) **The ability of an oligomeric human immunodeficiency virus type 1 (HIV-1) envelope antigen to elicit neutralizing antibodies against primary HIV-1 isolates is improved following partial deletion of the second hypervariable region**

Authors Barnett SW, Lu S, Srivastava I, Cherpelis S, Gettie A, Blanchard J, Wang S, Mboudjeka I, Leung L, Lian Y, Fong A, Buckner C, Ly A, Hilt S, Ulmer J, Wild CT, Mascola JR, Stamatatos L

Journal J Virol 2001 Jun;75(12):5526-40

Objectives Immunogenicity To investigate whether the modified, SF162V2-derived envelope may elicit higher titers of cross-reactive neutralizing antibodies than the unmodified SF162-derived envelope.

Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name Delta-V2 gp140 oligomeric *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name DNA (pCMVKm2) gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name pCMVKm2-Delta-V2 gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name gp140 oligomeric *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Main Findings

- Modified immunogen was more effective in eliciting potent binding and neutralizing antibodies, against homologous and several heterologous primary HIV-1 isolates.

NHP.23 (11595290) **Vaccine-elicited immune responses prevent clinical AIDS in SHIV(89.6P)-infected rhesus monkeys**

Authors Barouch DH, Fu TM, Montefiori DC, Lewis MG, Shiver JW, Letvin NL

Journal Immunol Lett 2001 Nov 1;79(1-2):57-61

Objectives Challenge, Immunogenicity To study the role of adjuvant IL-2/Ig, a fusion protein consisting of IL-2 and the Fc portion of IgG, in DNA vaccines encoding SIVmac239 Gag and HIV-189.6P Env.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name DNA-gag,env *Type:* DNA *Route:* Intramuscular

Challenge SHIV89.6P *Route:* Intravenous

Main Findings

- Animals immunized with DNA vaccines plus IL-2/Ig plasmid or protein developed significantly higher levels of p11C- and p41A-specific CTLs.
- No prevention of infection in vaccinees upon intravenous challenge with SHIV89.6.
- Control of viremia to nearly undetectable levels in vaccinees.
- Control monkeys developed high levels of viremia and exhibited a rapid loss of CD4+ T cells, significant clinical disease progression, and death in half of the animals by day 140 following challenge.

NHP.24.1 (11160750) **Elicitation of high-frequency cytotoxic T-lymphocyte responses against both dominant and subdominant simian-human immunodeficiency virus epitopes by DNA vaccination of rhesus monkeys**

Authors Barouch DH, Craiu A, Santra S, Egan MA, Schmitz JE, Kuroda MJ, Fu TM, Nam JH, Wyatt LS, Lifton MA, Krivulka GR, Nickerson CE, Lord CI, Moss B, Lewis MG, Hirsch VM, Shiver JW, Letvin NL

Journal J Virol 2001 Mar;75(5):2462-7

Objectives Immunogenicity To compare the CTL response to vaccination with plasmid DNA, live recombinant vector and infection with simian-human immunodeficiency virus (SHIV).

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name rMVASIV239gagpol.HIV89.6env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name SHIV89.6 *Type:* Live Virus *Route:* Intravenous

Vaccine Name SHIV89.6P *Type:* Live Virus *Route:* Intravenous

Vaccine Name SHIVIIIBc2 *Type:* Live Virus *Route:* Intravenous

Vaccine Name pV1P-SIVmac239 gag *Type:* DNA *Route:* Intramuscular

Vaccine Name pV1P-HIV-1.89.6P env *Type:* DNA *Route:* Intramuscular

Main Findings

- The p11C-specific CTL response was high frequency and dominant and the p41A-specific CTL response was low frequency and subdominant in both SHIV-infected monkeys and in monkeys vaccinated with recombinant modified vaccinia virus Ankara vectors expressingthese viral antigens.
- Vaccination with plasmid DNA, but not vaccination with a live recombinant vector or infection with SHIV, elicits potent CTL responses against both dominant and subdominant epitopes in rhesus monkeys.
- Plasmid DNA vaccination leads to high-frequency CTL responses specific for both of env p41A and Gag p11C epitopes.

NHP.24.2 (11333896) **Reduction of simian-human immunodeficiency virus 89.6P viremia in rhesus monkeys by recombinant modified vaccinia virus Ankara vaccination**

Authors Barouch DH, Santra S, Kuroda MJ, Schmitz JE, Plishka R, Buckler-White A, Gaitan AE, Zin R, Nam JH, Wyatt LS, Lifton MA, Nickerson CE, Moss B, Montefiori DC, Hirsch VM, Letvin NL

Journal J Virol 2001 Jun;75(11):5151-8

Objectives Challenge, Immunogenicity To study the immune responses elicited in rhesus monkeys by a recombinant poxvirus vaccine and the degree of protection afforded against a pathogenic simian-human immunodeficiency virus SHIV-89.6P challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name MVA-SIV gag-pol and HIV-1 89.6 env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Challenge SHIV89.6P *Route:* Intravenous
Main Findings

- Immunization with MVA vectors expressing SIVmac239 gag-pol and HIV-1 89.6 env elicited potent Gag-specific CTL responses but no detectable SHIV-specific NAb responses.
- MVA-vaccinated monkeys had high-frequency secondary CTL responses, high-titer secondary SHIV-89.6-specific NAb responses, rapid SHIV-89.6P-specific NAb responses, partial preservation of CD4+ T lymphocytes, reduced setpoint viral RNA levels, and no clinical disease or mortality by day 168 postchallenge (in contrast to control animals).

NHP.27 (10590126) **Vaccination of macaques against pathogenic simian immunodeficiency virus with Venezuelan equine encephalitis virus replicon particles**
Authors Davis NL, Caley IJ, Brown KW, Betts MR, Irlbeck DM, McGrath KM, Connell MJ, Montefiori DC, Frelinger JA, Swanstrom R, Johnson PR, Johnston RE
Journal J Virol 2000 Jan;74(1):371-8
Objectives Challenge, Immunogenicity To evaluate the immunogeneicity and protective value of an SIV vaccine in VEE vector against SIV challenge.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name VEE-SIVsm (SIV MA/CA-VRP and gp160-VRP) *Type:* DNA *Routes:* Intravenous, Subcutaneous
Challenge SIVsmE660 *Route:* Intravenous
Main Findings

- 4/4 vaccinees were protected against disease for at least 16 mpc (intravenous) with a pathogenic SIV swarm, while two of four controls required euthanasia at 10 and 11 weeks.
- Vaccination reduced the mean peak viral load 100-fold.

NHP.28 (10600597) **Protection of macaques against a SHIV with a homologous HIV-1 Env and a pathogenic SHIV-89.6P with a heterologous Env by vaccination with multiple gene-deleted SHIVs**
Authors Ui M, Kuwata T, Igarashi T, Ibuki K, Miyazaki Y, Kozyrev IL, Enose Y, Shimada T, Uesaka H, Yamamoto H, Miura T, Hayami M
Journal Virology 1999 Dec 20;265(2):252-63
Objectives Challenge, Immunogenicity To evaluate the potential of SHIVs as anti-HIV-1 live attenuated virus vaccines.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SHIV-drn *Type:* Live Attenuated Virus *Route:* Intravenous
Vaccine Name SHIV-dxrn *Type:* Live Attenuated Virus *Route:* Intravenous
Challenge SHIV-NM-3rN, SHIV89.6P *Route:* Intravenous
Main Findings

- In 4 macaques that had been vaccinated with SHIV-drn and challenged with SHIV-NM-3rN, no challenge virus was detected by DNA PCR in, or recovered from, two of the macaques. In the other two, challenge virus was detected once and twice, respectively.
- Plasma viral loads were much lower than those in unvaccinated controls.
- Another four macaques vaccinated with SHIV-dxrn, control of infection was evident but less than that of SHIV-drn-vaccinated macaques.
- When the two SHIV-drn-vaccinated macaques were challenged with pathogenic SHIV-89.6P, which has an HIV-1 Env that is antigenically different from that of SHIV-drn, replication of the challenge virus was restricted.
- Protection involved not only neutralizing antibodies and killer cell activity, but also other unknown specific and nonspecific immunity elicited by the infection

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NHP.29.1 (12584336) **Simian-Human Immunodeficiency Virus SHIV89.6-Induced Protection against Intravaginal Challenge with Pathogenic SIVmac239 Is Independent of the Route of Immunization and Is Associated with a Combination of Cytotoxic T-Lymphocyte and Alpha Interferon Responses**
Authors Abel K, Compton L, Rourke T, Montefiori D, Lu D, Rothaeusler K, Fritts L, Bost K, Miller CJ
Journal J Virol 2003 Mar 1;77(5):3099-3118

Objectives Challenge, Immunogenicity To compare the the mucosal (intranasal, intravaginal) vs. intravenous immunization with live nonpathogenic SHIV89.6 in rhesus macaques subsequently challenged intravaginally with SIVmac239.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SHIV89.6 *Type:* Live Virus *Routes:* Intravenous, Vaginal or perivaginal, Intranasal
Main Findings

- The route of immunization did not affect mucosal challenge outcome after a prolonged period of systemic infection with the nonpathogenic vaccine virus.
- Protection from the SIV challenge was associated with the induction of multiple host immune effector mechanisms: vaccinated-protected animals had higher frequencies of SIV Gag-specific cytotoxic T lymphocytes and gamma interferon-secreting cells during the acute phase postchallenge than the vaccinated unprotected ones.
- Vaccinated-protected animals had a more pronounced increase in peripheral blood mononuclear cell IFN-gamma mRNA levels than did the vaccinated-unprotected animals in the first few weeks after challenge.

NHP.29.2 (14694116) **Gamma interferon-mediated inflammation is associated with lack of protection from intravaginal simian immunodeficiency virus SIVmac239 challenge in simian-human immunodeficiency virus 89.6-immunized rhesus macaques**
Authors Abel K, La Franco-Scheuch L, Rourke T, Ma ZM, De Silva V, Fallert B, Beckett L, Reinhart TA, Miller CJ
Journal J Virol 2004 Jan;78(2):841-54
Objectives Challenge, Immunogenicity To determine the relationship between IFN-Γ-related host immune responses and challenge virus replication in lymphoid tissues of SHIV89.6-vaccinated and unvaccinated rhesus macaques after challenge with SIVmac239.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Vaccinated-protected monkeys had low tissue viral RNA (vRNA) levels.
- Vaccinated-unprotected animals had moderate tissue vRNA levels.
- Unvaccinated animals had high tissue vRNA levels.
- Vaccinated-protected monkeys had slightly increased tissue IFN-Γ mRNA levels and a high frequency of IFN-Γ secreting T cells responding to in vitro SIVgag peptide stimulation.

NHP.30 (11739694) **ALVAC-SIV-gag-pol-env-based vaccination and macaque major histocompatibility complex class I (A*01) delay simian immunodeficiency virus SIVmac-induced immunodeficiency**
Authors Pal R, Venzon D, Letvin NL, Santra S, Montefiori DC, Miller NR, Tryniszewska E, Lewis MG, VanCott TC, Hirsch V, Woodward R, Gibson A, Grace M, Dobratz E, Markham PD, Hel Z, Nacsa J, Klein M, Tartaglia J, Franchini G
Journal J Virol 2002 Jan;76(1):292-302
Objectives Challenge, Immunogenicity To assess whether immunization with an ALVAC-based vaccine expressing the SIVmac251 Gag, Pol, and Env and subsequent boosting with subunit gp120 could confer immunity and prevent or contain SIVmac251 replication following a mucosal exposure to SIVmac251.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name ALVAC-SIV-gpe (vcp180) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intramuscular, Intranasal
Vaccine Name SIVmac251-gp120 *Type:* Purified Viral Products *Routes:* Intrarectal, Intramuscular, Intranasal
Challenge SIVmac251 (561) *Route:* Intrarectal
Main Findings

- MHC-I Mamu-A*01 genotype and vaccination of rhesus macaques with ALVAC-SIV-gag-pol-env (ALVAC-SIV-gpe) restrict SIVmac251 replication, preserve CD4+ T cells, and delay disease progression following intrarectal challenge exposure of the animals to SIVmac251.
- ALVAC-SIV-gpe immunization induced CTL responses cumulatively in 67% of the immunized animals.
- Significant delay in CD4+ T-cell loss was observed in Mamu-A*01-positive macaques.
- Neither boosting the ALVAC-SIV-gpe with gp120 immunizations nor administering the vaccine by the combination of mucosal and systemic immunization routes increased significantly the protective effect of the ALVAC-SIV-gpe vaccine.

- In the case of intravenous or intrarectal challenge with the chimeric SIV/HIV strains SHIV(89.6P) or SHIV(KU2), respectively, MHC-I Mamu-A*01-positive macaques did not significantly restrict primary viremia.

NHP.31 (11017793) **DNA vaccination of macaques by a full genome HIV-1 plasmid which produces noninfectious virus particles**

Authors Akahata W, Ido E, Shimada T, Katsuyama K, Yamamoto H, Uesaka H, Ui M, Kuwata T, Takahashi H, Hayami M

Journal Virology 2000 Sep 15;275(1):116-24

Objectives Challenge, Immunogenicity To evaluate the humoral and cell-mediated immune response to a DNA vaccine containing full genome of HIV-1.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name DNA Vaccine pNL432-ZF1* *Type:* DNA *Route:* Intramuscular

Challenge SHIV-NM-3rN *Route:* Intravenous

Main Findings

- Immunological responses against HIV-1 were elicited in all of the vaccinated monkeys: stable anti-HIV-1 Env antibodies were raised in two monkeys and CTL activities were induced in the other monkeys. After holomogous challenge of the macaques intravenously 54 weeks with 100 TCID50 of SHIV-NM-3rN, in all of the vaccinated macaques, the peak plasma viral loads were two to three orders of magnitude lower than those of the naive controls

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NHP.32 (10233957) **Highly attenuated vaccine strains of simian immunodeficiency virus protect against vaginal challenge: inverse relationship of degree of protection with level of attenuation**

Authors Johnson RP, Lifson JD, Czajak SC, Cole KS, Manson KH, Glickman R, Yang J, Montefiori DC, Montelaro R, Wyand MS, Desrosiers RC

Journal J Virol 1999 Jun;73(6):4952-61

Objectives Challenge, Immunogenicity To compare 3 levels of attenuation of SIV-based vaccine and their ability to protect against mucosal challenge with pathogenic SIV.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239Δ3 *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name SIVmac239Δ3x *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name SIVmac239Δ4 *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVmac251 *Route:* Intravenous, Vaginal or perivaginal

Main Findings

- All three vaccines elicited strong protective effect up to 1 year from immunization to challenge.
- Degree of protection correlated inversely with the level of attenuation.
- Protection against vaginal challenge was easier to achieve than protection against intravenous challenge.
- Protection associated with high antibody avidity indices.
- Protection in absence of detectable serum Nab was associated with CTL response in immunized animals. No vaccine virus recovered in 11 of 12 vaccinees.

NHP.33 (11085585) **Enhanced safety and efficacy of live attenuated SIV vaccines by prevaccination with recombinant vaccines**

Authors Jones L, Ahmad S, Chan K, Verardi P, Morton WR, Grant R, Yilma T

Journal J Med Primatol 2000 Aug;29(3-4):231-9

Objectives Challenge, Immunogenicity To evaluate the safety of a live attenuated vaccine (delta nef) in macaques pre-immunized with a recombinant DNA vaccine.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name vSIVgp120 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name CHO-SIVgp120 *Type:* DNA *Route:* Intramuscular

Vaccine Name vSIVgp160 *Type:* DNA *Route:* Intradermal

Vaccine Name bSIVgp120 *Type:* DNA *Route:* Intramuscular

Challenge SIVmac251 *Route:* Intravenous

Main Findings

- Preimmunized macaques advanced to disease SLOWER than controls after challenge with virulent SIV.
- 5 animals survived for 3 years without disease and only the vaccine virus (SIVΔnef) could be isolated at this time.
- In another experiment, preimmunized animals had lower virus loads and no disease compared to controls.

NHP.34 (9882330) **Limited protection from a pathogenic chimeric simian-human immunodeficiency virus challenge following immunization with attenuated simian immunodeficiency virus**

Authors Lewis MG, Yalley-Ogunro J, Greenhouse JJ, Brennan TP, Jiang JB, VanCott TC, Lu Y, Eddy GA, Birx DL

Journal J Virol 1999 Feb;73(2):1262-70

Objectives Challenge, Immunogenicity To test the ability of two live attenuated SIV constructs with single deletion to stimulate protective immunity in macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca nemestrina (pigtailed macaque)

Vaccine Name SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name SIV-PBJ6.6Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SHIV89.6PD *Route:* Intravenous

Main Findings

- Each construct generated high levels of specific immunity in all of the immunized animals.
- SIV239Δnef grew to high levels in all immunized animals. The SIVPBj6.6Δnef was effectively controlled by all of the immunized animals.
- Challenge strain: SIV89.6PD.
- Vaccination with attenuated SIV can protect macaques from disease and in some cases from infection by a highly pathogenic SHIV. Inability to control the immunizing virus may result in rapid disease progression.

NHP.35 (10593491) **Protective immunity of gene-deleted SHIVs having an HIV-1 Env against challenge infection with a gene-intact SHIV**

Authors Ui M, Kuwata T, Igarashi T, Miyazaki Y, Tamaru K, Shimada T, Nakamura M, Uesaka H, Yamamoto H, Hayami M

Journal J Med Primatol 1999 Aug-Oct;28(4-5):242-8

Objectives Challenge, Immunogenicity To assess the level of immunogenicity and protection of a SHIV-deleted live attenuated vaccine virus against a gene-intact SHIV challenge virus.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SHIV-dn *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name SHIV-drn *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name SHIV-dxrn *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SHIV-NM-3rN *Route:* Intravenous

Main Findings

- Protective immunity of live attenuated SHIV vaccine is inversely dependent upon the level of attenuation of the virus.
- Most immunized macaques had HIV-1 env and/or SIV gag-specific CTL responses.
- 10/12 vaccinated macaques had NK cell activities higher than those of normal macaques (<10%): NK cells may be involved in protection against challenge.

NHP.36 (11112494) **Induction of long-term protective effects against heterologous challenge in SIVhu-infected macaques**

Authors Villinger F, Switzer WM, Parekh BS, Otten RA, Adams D, Shanmugam V, Bostik P, Mayne AE, Chikkala NF, McClure HM, Novembre F, Yao Q, Heneine W, Folks TM, Ansari AA

Journal Virology 2000 Dec 5;278(1):194-206

Objectives Challenge, Immunogenicity To measure the immunogenicity and protective effect of a live attenuated vaccine SIVhu (isolated from a human accidentally exposed) against challenge with SHIV89.6P.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVhu *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVsmB670, SHIV89.6P *Route:* Intravenous

Main Findings

- SIVhu which accidentally infected human had a truncated nef which failed to repair itself and added additional stop codons post-infection.
- Infection with SIVhu was associated with minimal acute viral replication, followed by undetectable plasma viral loads and only intermittent PCR detection up to 5 ypi.
- 3/3 animals infected with SIVhu remained healthy and with stable CD4(+) lymphocyte levels and undetectable plasma viral loads at >20 months post-SHIV89.6p challenge.

NHP.37 (10482586) **Protection by live, attenuated simian immunodeficiency virus against heterologous challenge**

Authors Wyand MS, Manson K, Montefiori DC, Lifson JD, Johnson RP, Desrosiers RC

Journal J Virol 1999 Oct;73(10):8356-63

Objectives Challenge, Immunogenicity To examine the ability of a live, attenuated deletion mutant (SIVmac2393), which is missing nef and vpr genes, to protect against challenge by heterologous strains SHIV89.6p and SIVsmE660.

Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name SIVmac239Δ3 *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVsmE660, SHIV89.6P *Route:* Intravenous

Main Findings

- By the criteria of CD4+ cell counts and disease, strong protection against the SHIV89.6p challenge was observed in 4/4 vaccinated monkeys (group 1).

NHP.38 (11152522) **Persistence of pathogenic challenge virus in macaques protected by simian immunodeficiency virus SIVmacDeltanef**

Authors Khatissian E, Monceaux V, Cumont MC, Kieny MP, Aubertin AM, Hurtrel B

Journal J Virol 2001 Feb;75(3):1507-15

Objectives Challenge, Immunogenicity To investigate virological and immunological characteristics of five rhesus macaques immunized with a nef-inactivated SIVmac251 molecular clone (SIVmac251nef) and challenged 15 months later with the pathogenic SIVmac251 isolate.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac251ΔNef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVmac251 *Route:* Intravenous

Main Findings

- No total protection against homologous virus challenge but control of infection with challenge virus in the absence of a secondary immune response.
- Challenge and vaccine viruses may persist in a replication-competent form for long periods after the challenge, possibly resulting in recombination between the two viruses.

NHP.39 (11287551) **Quintuple deglycosylation mutant of simian immunodeficiency virus SIVmac239 in rhesus macaques: robust primary replication, tightly contained chronic infection, and elicitation of potent immunity against the parental wild-type strain**

Authors Mori K, Yasutomi Y, Ohgimoto S, Nakasone T, Takamura S, Shioda T, Nagai Y

Journal J Virol 2001 May;75(9):4023-8

Objectives Challenge, Immunogenicity To assess the immunogenicity and protection effect of a deglycosylated SIVmac239 mutant vaccine.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239Delta5G *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVmac239 *Route:* Intravenous

Main Findings

- Monkeys infected with the mutant tolerated a challenge infection with wild-type SIV very well.
- Analyses of host responses following challenge revealed no neutralizing antibodies against the challenge virus but strong secondary responses of cytotoxic T lymphocytes against multiple antigens, including Gag-Pol, Nef, and Env.
- Quintuple deglycosylation mutant appeared to represent a novel class of SIV live attenuated vaccine.

NHP.40 (10191194) **Long-lasting protection by live attenuated simian immunodeficiency virus in cynomolgus monkeys: no detection of reactivation after stimulation with a recall antigen**

Authors Sernicola L, Corrias F, Koanga-Mogtomo ML, Baroncelli S, Di Fabio S, Maggiorella MT, Belli R, Michelini Z, Macchia I, Cesolini A, Cioe L, Verani P, Titti F

Journal Virology 1999 Apr 10;256(2):291-302

Objectives Challenge, Immunogenicity To determine the breadth of the protection after repeated challenges of monkeys with SIV.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVmac251BK28, SIVmac251,32H.spl *Route:* Intravenous

Main Findings

- Monkeys immunized with live attenuated C8 vaccine were protected from consecutive challenge with SIVmac251, SIVmac32H.
- The C8 virus remained genotypically stable, and depletion of CD4+ cells was not observed during 3 years of follow-up.

NHP.41 (10998338) **Replication of simian immunodeficiency virus (SIV) in ex vivo lymph nodes as a means to assess susceptibility of macaques in vivo**

Authors Margolis L, Glushakova S, Chougnet C, Shearer G, Markham P, Robert-Guroff M, Benveniste R, Miller CJ, Cranage M, Hirsch V, Franchini G

Journal Virology 2000 Sep 30;275(2):391-7

Objectives Challenge, Immunogenicity To investigate whether infectability of ex vivo lymph nodes could predict resistance and/or susceptibility to SIV infection.

Species/Subspecies Macaca (sp)

Vaccine Name SIVmac251 *Type:* Live Virus *Route:* Mucosal

Vaccine Name SIVsmE660 *Type:* Live Virus *Route:* Mucosal

Challenge SIVmne clone A2-clone 5, SIVmac251(32H) *Route:* Mucosal

Main Findings

- Six macaques, apparently uninfected, following low-dose exposure to the pathogenic SIV(mac251) and SIV(SME660) by the mucosal route, were re-exposed to a less pathogenic SIV(MNE): 4/6 macaques resisted viral infection.
- PBMC and lymph-node resistance or susceptibility to infection ex vivo correlate with in vivo infectivity.

NHP.42 (10593484) **Antigen-specific cytokine responses in vaccinated Macaca nemestrina**

Authors Mulvania T, Lynch JB, Robertson MN, Greenberg PD, Morton WR, Mullins JI

Journal J Med Primatol 1999 Aug-Oct;28(4-5):181-9

Objectives Challenge, Immunogenicity Macaca nemestrina vaccinated with a minimally pathogenic HIV-2 strain KR. Group 1 was then inoculated with a non-infectious stock of a pathogenic strain, HIV-2287.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Main Findings

- Both groups 1 and 2 were subsequently challenged with an infectious stock of HIV-2287.
- 5/6 group 1 animals were protected against CD4 decline.
- 3/6 animals in group 2 were protected.
- Analysis of CTL responses demonstrated strong activityagainst HIV-2(KR)-Gag in group 1.
- Strong correlation between CTL responses and antigen-specific T-helper (Th) type 1 responses.

NHP.43 (10593486) **An anti-HIV strategy combining chemotherapy and therapeutic vaccination**

Authors Rosenwirth B, Bogers WM, Nieuwenhuis IG, Haaft PT, Niphuis H, Kuhn EM, Bischofberger N, Erfle V, Sutter G, Berglund P, Liljestrom P, Uberla K, Heeney JL

Journal J Med Primatol 1999 Aug-Oct;28(4-5):195-205

Objectives Challenge, Immunogenicity, Immunotherapy .

Main Findings

- Chemotherapy/therapeutic vaccination regimen induced a significant reduction in the steady-state level of viremia in one out of two chronically infected rhesus macaques.
- Chemotherapeutic treatment alone did not achieve reduction of viremia in two chronically infected animals. The nature of the immune responses assumed to have been induced by vaccination in one out of the two monkeys remains to be elucidated.

NHP.44 (10684264) **Immunization with a modified vaccinia virus expressing simian immunodeficiency virus (SIV) Gag-Pol primes for an anamnestic Gag-specific cytotoxic T-lymphocyte response and is associated with reduction of viremia after SIV challenge**

Authors Seth A, Ourmanov I, Schmitz JE, Kuroda MJ, Lifton MA, Nickerson CE, Wyatt L, Carroll M, Moss B, Venzon D, Letvin NL, Hirsch VM

Journal J Virol 2000 Mar;74(6):2502-9

Objectives Challenge, Immunogenicity To explore the immunogenicity and protective efficacy of rMVA expressing the SIV gag-pol proteins in rhesus monkeys expressing the MHC class I allele, MamuA*01.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name MVAgagpol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intravenous

Challenge SIVsmE660 *Route:* Intravenous

Main Findings

- MVA-gag-pol-immunized macaques exhibited a rapid and substantial anamnestic CTL response specific for the p11C, C-M Gag epitopes.
- The level at which CTL stabilized after resolution of primary viremia correlated inversely with plasma viral load set point (P = 0.03).
- The magnitude of reduction in viremia in the vaccinees was predicted by the magnitude of the vaccine-elicited CTL response prior to SIV challenge.

NHP.45 (10684290) **Comparative efficacy of recombinant modified vaccinia virus Ankara expressing simian immunodeficiency virus (SIV) Gag-Pol and/or Env in macaques challenged with pathogenic SIV**

Authors Ourmanov I, Brown CR, Moss B, Carroll M, Wyatt L, Pletneva L, Goldstein S, Venzon D, Hirsch VM

Journal J Virol 2000 Mar;74(6):2740-51

Objectives Challenge, Immunogenicity To evaluate the protective effects of prior immunization with MVA-SIV recombinant vaccines as a sole immunogen without boosting with Env protein and to optimize expression of Gag-Pol.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name MVA-SIVsmH-4 -env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name MVA(SIVsmH-4)gag-pol-env *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name MVA SIVsmH4 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge SIVsmE660 *Route:* Intravenous

Main Findings

- Although all animals became infected post challenge, plasma viremia was significantly reduced in animals that received the MVA-SIV recombinant vaccines as compared with animals that received nonrecombinant MVA (P = 0.0011 by repeated-measures analysis ofvariance).
- Immunization significantly modifies viral load following SIV challenge.
- Recombinant MVA has considerable potential as a vaccine vector for human AIDS.

NHP.46 (9707609) **Recombinant modified vaccinia virus Ankara-simian immunodeficiency virus gag pol elicits cytotoxic T lymphocytes in rhesus monkeys detected by a major histocompatibility complex class I/peptide tetramer**

Authors Seth A, Ourmanov I, Kuroda MJ, Schmitz JE, Carroll MW, Wyatt LS, Moss B, Forman MA, Hirsch VM, Letvin NL

Journal Proc Natl Acad Sci U S A 1998 Aug 18;95(17):10112-6

Objectives Immunogenicity To explore the utility of MVA as a vector for eliciting AIDS virus-specific CTL in the SIV/rhesus monkey model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name MVA SIVsmH4 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Main Findings

- Intramuscular immunization with recombinant MVA-SIVSM gag pol elicited a Gag epitope-specific CTL response readily detected in peripheral blood lymphocytes by using a functional killing assay. Moreover, those immunizations also elicited a population of CD8+ T lymphocytes in the peripheral blood that bound a specific major histocompatibility complex class I/peptide tetramer.
- Tetramer staining may be a useful technology for monitoring CTL generation in vaccine trials in nonhuman primates and in humans.

NHP.47 (11101054) **Cross-protection in NYVAC-HIV-1-immunized/HIV-2-challenged but not in NYVAC-HIV-2-immunized/SHIV-challenged rhesus macaques**

Authors Patterson LJ, Peng B, Abimiku AG, Aldrich K, Murty L, Markham PD, Kalyanaraman VS, Alvord WG, Tartaglia J, Franchini G, Robert-Guroff M

Journal AIDS 2000 Nov 10;14(16):2445-55

Objectives Challenge, Immunogenicity To evaluate the immunization with attenuated poxvirus-HIV-1 recombinants followed by protein boosting in rhesus monkeys model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name vP991, NYVAC HIV-1IIIB gp120.gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name vP1047, NYVAC HIV-2.SBL-ISY gp160.gag-pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name HIV-1 gp160 *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name HIV-2 gp160 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge HIV-2.SBL6669, SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings

- Both immunization groups developed homologous binding antibodies.
- Homologous Nab only observed in NYVAC-HIV-2-immunized macaques.
- No cross-reactive neutralizing antibodies detected.
- Immunization groups displayed cross-reactive CTL.
- Significant CD8AA observed for only one NYVAC-HIV-2-immunized macaque.
- Both immunizations significantly reduced viral burdens and partially protected against HIV-2 challenge.
- Humoral antibody and/or CTL and CD8AA associated with protection against homologous HIV-2 challenge.
- No significant protection observed in the SHIV-challenged macaques, although NYVAC-HIV-1 immunization resulted in significantly lower viral burdens compared with controls.

NHP.48 (10717345) **A recombinant avipoxvirus HIV-1 vaccine expressing interferon-gamma is safe and immunogenic in macaques**

Authors Kent SJ, Zhao A, Dale CJ, Land S, Boyle DB, Ramshaw IA

Journal Vaccine 2000 Apr 28;18(21):2250-6

Objectives Immunogenicity, Immunotherapy To construct and assess FPVgag/pol-IFNgamma as a therapeutic vaccine for safety and immunogenicity in Macaca nemestrina previously infected with HIV-1.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name FPV.HIV-1.gag/pol-IFNgamma *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name FPV.HIV-1.gag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge HIV-1.LAI *Route:* Intravenous

Main Findings

- FPVgag/pol-IFNgamma vaccinations were safe and enhanced T cell proliferative responses to Gag antigens (but not control tetanus antigens).
- Enhanced CTL responses to gag/pol antigens were also observed following IFNgamma expressing vaccinations.
- Since cellular immunity may be critical to controlling or preventing HIV-1 infection, these observations suggest that avipox vectors co-expressing IFNgamma should be further evaluated as therapeutic or preventive HIV-1 vaccines

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NHP.49 (10418922) **Vaccination with Rev and Tat against AIDS**

Authors Osterhaus AD, van Baalen CA, Gruters RA, Schutten M, Siebelink CH, Hulskotte EG, Tijhaar EJ, Randall RE, van Amerongen G, Fleuchaus A, Erfle V, Sutter G

Journal Vaccine 1999 Jun 4;17(20-21):2713-4
Objectives Challenge, Immunogenicity A pilot study to investigate the role of cytotoxic T cell in the containment of primatate lentivirus infection.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name rSFV-SIVmac32H.rev.tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name rMVA.SIVmac32H.tat.rev *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Challenge SIVmac251(32H) *Route:* Intravenous

NHP.51 (11555138) **Effect of vaccination with recombinant modified vaccinia virus Ankara expressing structural and regulatory genes of SIV(macJ5) on the kinetics of SIV replication in cynomolgus monkeys**

Authors Negri DR, Baroncelli S, Michelini Z, Macchia I, Belli R, Catone S, Incitti F, ten Haaft P, Corrias F, Cranage MP, Polyanskaya N, Norley S, Heeney J, Verani P, Titti F
Journal J Med Primatol 2001 Aug;30(4):197-206
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name MVA-mac(J5) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Challenge SIVmac251 *Route:* Intravenous
Main Findings

- Vaccination with rMVA-J5 performed at week 0, 12, and 24 induced a moderate proliferative response to whole SIV, a detectable humoral response to all but Nef SIV antigens, and failed to induce neutralizing antibodies.
- All control monkeys were infected by week two and seroconverted by weeks four to eight.
- In contrast a sharp increase of both humoral and proliferative responses at two weeks post-challenge was observed in vaccinated monkeys compared to control monkeys.
- Although all vaccinated monkeys were infected, vaccination with rMVA-J5 appeared to partially control viral replication during the acute and late phase of infection as judged by cell- and plasma-associated viral load.

NHP.52 (12072518) **Immunization of rhesus macaques with a DNA prime/modified vaccinia virus Ankara boost regimen induces broad simian immunodeficiency virus (SIV)-specific T-cell responses and reduces initial viral replication but does not prevent disease progression following challenge with pathogenic SIVmac239**

Authors Horton H, Vogel TU, Carter DK, Vielhuber K, Fuller DH, Shipley T, Fuller JT, Kunstman KJ, Sutter G, Montefiori DC, Erfle V, Desrosiers RC, Wilson N, Picker LJ, Wolinsky SM, Wang C, Allison DB, Watkins DI
Journal J Virol 2002 Jul;76(14):7187-202
Objectives Challenge, Immunogenicity To test the immunogenicity and protective value of a DNA prime/modified vaccinia virus Ankara boost regimen immunization in rhesus macaques against intrarectal challenge with simian immunodeficiency virus (SIV) mac239.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pC-SIVrev *Type:* DNA *Route:* Intradermal
Vaccine Name rMVA-SIVmac251 32H *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intradermal
Vaccine Name pC-SIV17E-Fred (gagpolenv) *Type:* DNA *Route:* Intradermal
Vaccine Name SIVmac17E-Fr Nef *Type:* DNA *Route:* Intradermal
Challenge SIVmac239/nef-open *Route:* Intrarectal
Main Findings

- Immunization resulted in induction of virus-specific CD8+ and CD4+ responses in all vaccinees.
- Anamnestic nab responses against laboratory-adapted SIVmac251 developed after the challenge.
- No neutralizing antibodies against SIVmac239.
- Vaccinated animals had significantly reduced peak viremia compared with controls (P<0.01).

- Most animals had gradual CD4 depletion and progressed to disease despite the induction of virus-specific CTL responses and reduced peak viral loads.

NHP.53 (12192089) **Crosslinked HIV-1 envelope-CD4 receptor complexes elicit broadly cross-reactive neutralizing antibodies in rhesus macaques**

Authors Fouts T, Godfrey K, Bobb K, Montefiori D, Hanson CV, Kalyanaraman VS, DeVico A, Pal R.

Journal Proc Natl Acad Sci U S A. 2002 Aug 21

Objectives Immunogenicity To evaluate the immunogenicity of crosslinked gp120-CD4 complexes in rhesus monkeys.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Crosslinked gp120-CD4 *Type:* Other *Route:* Intramuscular

Vaccine Name Crosslinked gp140-CD4 *Type:* Other *Route:* Intramuscular

Vaccine Name HIV-1 IIIB gp120 *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name HIV-1 IIIB gp140 *Type:* Purified Viral Products *Route:* Intramuscular

Main Findings

- The animals immunized with anti-env-CD4 exhibited a broad pattern of neutralization of primary viruses regardless of coreceptor usage and genetic subtype.
- anti-env-CD4 neutralization more biased toward primary isolates than laboratory adapted strains, unlike anti-env which neutralized only laboratory adapted strains.
- anti-Env-CD4 antisera failed to neutralize SHIV89.6, SHIV89.6P, and SHIVKU2 in the human PBMC-based assays and SIVmac239 in assays with either human or macaque PBMCs.

NHP.54 (10933680) **Vaccine protection against simian immunodeficiency virus by recombinant strains of herpes simplex virus**

Authors Murphy CG, Lucas WT, Means RE, Czajak S, Hale CL, Lifson JD, Kaur A, Johnson RP, Knipe DM, Desrosiers RC

Journal J Virol 2000 Sep;74(17):7745-54

Objectives Challenge, Immunogenicity To develop and use replication-competent and replication-defective strains of recombinant herpes simplex virus (HSV) that express envelope and Nef antigens of SIV.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name K81 *Type:* DNA *Routes:* Subcutaneous, Intramuscular

Vaccine Name d81 *Type:* DNA *Routes:* Intradermal, Intramuscular

Challenge SIVmac239 *Route:* Intrarectal

Main Findings

- The HSV recombinants induced antienvelope antibody responses that persisted at relatively stable levels for months after the last administration.
- 2/7 rhesus vaccinated monkeys were solidly protected, and another showed a sustained reduction in viral load following rectal challenge with pathogenic SIVmac239 at 22 weeks following the last vaccine administration.

NHP.55 (11551502) **An effective AIDS vaccine based on live attenuated vesicular stomatitis virus recombinants**

Authors Rose NF, Marx PA, Luckay A, Nixon DF, Moretto WJ, Donahoe SM, Montefiori D, Roberts A, Buonocore L, Rose JK

Journal Cell 2001 Sep 7;106(5):539-49

Objectives Challenge, Immunogenicity To test live attenuated vesicular stomitits virus vectors expressing SIV ?env and gag genes in rhesus monkeys.

Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name VSV-(GI)-Env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular

Vaccine Name VSV(GCh)-Env+Gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular

Vaccine Name VSV(GNJ)-Env+Gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intramuscular

Challenge SHIV89.6P *Route:* Intravenous

Main Findings

- Vectors with glycoproteins from different VSV serotypes boosted response.
- 7/8 controls progressed to AIDS at about 148 dpc with severe loss of CD4+ T cells, high viral loads.

- 7/8 vaccinees infected with SHIV89.6P remained healthy up to 14 mpc (low or undetectable viral loads).

NHP.56 (10229229) **Neutralizing antibody-independent containment of immunodeficiency virus challenges by DNA priming and recombinant pox virus booster immunizations**

Authors Robinson HL, Montefiori DC, Johnson RP, Manson KH, Kalish ML, Lifson JD, Rizvi TA, Lu S, Hu SL, Mazzara GP, Panicali DL, Herndon JG, Glickman R, Candido MA, Lydy SL, Wyand MS, McClure HM

Journal Nat Med 1999 May;5(5):526-34

Objectives Challenge, Immunogenicity To compare 8 different protocols for their ability to protect against immunodeficiency virus challenges in rhesus macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pRS102 -SIVmac239 gag-pol proteins *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name pCMV/nef *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name pJW4303/HXB-2.dpol *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name pJW4303/HXB-2.gp140 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name pJW4303/HXB-2.gp120 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name Prt-env gp160 *Type:* Purified Viral Products *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal

Vaccine Name rFPV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular

Challenge SHIV89.6P, SHIV-IIIB/HXB2 *Route:* Intravenous

Main Findings

- Intradermal DNA priming followed by recombinant fowl pox virus booster immunizations was a more efficient protocol in inducing immune response and containment of challenge infection than the gene gun inoculation method.

NHP.57 (10438842) **Effective induction of simian immunodeficiency virus-specific cytotoxic T lymphocytes in macaques by using a multiepitope gene and DNA prime-modified vaccinia virus Ankara boost vaccination regimen**

Authors Hanke T, Samuel RV, Blanchard TJ, Neumann VC, Allen TM, Boyson JE, Sharpe SA, Cook N, Smith GL, Watkins DI, Cranage MP, McMichael AJ

Journal J Virol 1999 Sep;73(9):7524-32

Objectives Challenge, Immunogenicity To test multi-CTL epitope gene and a DNA prime-MVA boost vaccination regimen in rhesus macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)

Vaccine Name pTH.HW DNA *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads)

Vaccine Name MVA.HW *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Challenge SIVmac251 *Route:* Intrarectal

Main Findings

- High SIV gag specific-CTL response by immunization, capable of killing SIV-infected cells in vitro.
- After intrarectal challenge with pathogenic SIVmac251, 2/3 vaccinated animals were infected.
- Correlates of protective immunity not defined.
- DNA prime-MVA boost regimen is an effective protocol for induction of CTLs in macaques.

NHP.58 (11085589) **A vaccine strategy utilizing a combination of three different chimeric vectors which share specific vaccine antigens**

Authors Heeney JL, Koopman G, Rosenwirth B, Bogers W, van Dijk J, Nieuwenhuis I, Niphuis H, ten Haaft P, Hanke T, Rhodes G, Berglund P, Burny A, Bex F, Sutter G, Liljestrom P

Journal J Med Primatol 2000 Aug;29(3-4):268-73

Objectives Immunogenicity Overcomes an anti-vector immune response with chimeric vectors that have in common only the specific antigens for immunization.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name DNA.PTH.SIVmac.J5.gptnr *Type:* DNA *Route:* Intradermal

Vaccine Name DNA.pND14-G1.SIVmac251.env *Type:* DNA *Route:* Intradermal

Vaccine Name MVA.pUCII.SIVmac.J5 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name MVApIII-sp.SIVmac.J5.env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular
Vaccine Name SFVpSFVI.SIVmac.J5.gpetnr *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intradermal
Challenge SIVmac32H.IXc *Route:* Intravenous
Main Findings

- Anti-vector immune response to foreign genes of engineered vectors may preclude sufficient 'priming' or immunogenicity, or impair optimal 'boosting' upon repeated immunization.
- Describes a new strategy that avoids increased anti-vector responses,allows the use of combinations of vectors to present the same or related antigen differently to the immune system and at alternative sites.
- New strategy induces optimal type of immunity against the pathogen.

NHP.59 (10906202) **Simian immunodeficiency virus (SIV) gag DNA-vaccinated rhesus monkeys develop secondary cytotoxic T-lymphocyte responses and control viral replication after pathogenic SIV infection**

Authors Egan MA, Charini WA, Kuroda MJ, Schmitz JE, Racz P, Tenner-Racz K, Manson K, Wyand M, Lifton MA, Nickerson CE, Fu T, Shiver JW, Letvin NL
Journal J Virol 2000 Aug;74(16):7485-95
Objectives Challenge, Immunogenicity To use plasmid DNA construct to elicit protective immunity in SIV/macaque model.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name V1R-SIV gag *Type:* DNA *Route:* Intramuscular
Challenge SIVsmE660 *Route:* Intravenous
Main Findings

- Soluble major histocompatibility class I/peptide tetramers and peptide-specific killing assays are used to monitor CD8(+) T-lymphocyte responses to a dominant SIV Gag epitope in rhesus monkeys.
- Codon-optimized SIV gag DNA vaccine construct elicits high-frequency SIV-specific CTL response in peripheral blood and lymph node lymphocytes.
- After IV challenge with SIVsm E660, gag plasmid DNA-vaccinated monkeys have better containment of viral replication by 50 dpc.

NHP.60.1 (11039923) **Control of viremia and prevention of clinical AIDS in rhesus monkeys by cytokine-augmented DNA vaccination**

Authors Barouch DH, Santra S, Schmitz JE, Kuroda MJ, Fu TM, Wagner W, Bilska M, Craiu A, Zheng XX, Krivulka GR, Beaudry K, Lifton MA, Nickerson CE, Trigona WL, Punt K,Freed DC, Guan L, Dubey S, Casimiro D, Simon A, Davies ME, Chastain M, Strom TB, Gelman RS, Montefiori DC, Lewis MG, Emini EA, Shiver JW, Letvin NL
Journal Science 2000 Oct 20;290(5491):486-92
Objectives Challenge, Immunogenicity Reports the protective efficacy of vaccine-elicited immune responses against a pathogenic SHIV-89.6P challenge in rhesus monkeys.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular
Vaccine Name HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular
Challenge SHIV89.6P *Route:* Intravenous
Main Findings

- The monkeys that received the DNA vaccines plus IL-2/Ig protein or IL-2/Ig plasmid demonstrated markedly higher vaccine-elicited CTL responses than the animals that received the DNA vaccines alone.
- All monkeys that received DNA vaccines augmented with IL-2/Ig were infected, demonstrated potent secondary CTL responses, stable CD4+ T cell counts, preserved virus-specific CD4+ T cell responses, low to undetectable setpoint viral loads, and no evidence of clinical disease or mortality by 140 dpc
- After the final immunization at week 40, the vaccinated monkeys developed significant circulating p11C- and p41A-specific CD8+ T lymphocytes, in contrast with the control monkeys that had no detectable circulating tetramer-positive CD8+ T lymphocytes.

NHP.60.2 (11797012) **Eventual AIDS vaccine failure in a rhesus monkey by viral escape from cytotoxic T lymphocytes**

Authors Barouch DH, Kunstman J, Kuroda MJ, Schmitz JE, Santra S, Peyerl FW, Krivulka GR, Beaudry K, Lifton MA, Gorgone DA, Montefiori DC, Lewis MG, Wolinsky SM, Letvin NL
Journal Nature 2002 Jan 17;415(6869):335-9
Objectives Challenge .
Main Findings

- Viral escape from CTL recognition can result in the long-term failure of partial immune protection to challenge (i.e. to control viral replication and prevent clinical disease progression).
- In a cohort of rhesus monkeys that were vaccinated and subsequently infected with a pathogenic hybrid SHIV, the frequency of viral sequence mutations within CTL epitopes correlated with the level of viral replication.
- Viral escape from CTL recognition may be a major limitation of the CTL-based AIDS vaccines.

NHP.60.3 (12021371) **Prior vaccination increases the epitopic breadth of the cytotoxic T-lymphocyte response that evolves in rhesus monkeys following a simian-human immunodeficiency virus infection**

Authors Santra S, Barouch DH, Kuroda MJ, Schmitz JE, Krivulka GR, Beaudry K, Lord CI, Lifton MA, Wyatt LS, Moss B, Hirsch VM, Letvin NL
Journal J Virol 2002 Jun;76(12):6376-81
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac239 gag DNA *Type:* DNA
Vaccine Name HIV-1.89.6P env DNA *Type:* DNA
Challenge SHIV89.6P *Route:*
Main Findings

- rMVA vaccination elicited high-frequency CTL responses to dominant epitopes but with substantially lower frequency to subdominant epitopes.
- Animals immunized with DNA plus IL-2/Ig plasmid showed higher frequency p41A-specific CTL responses than animals immunized with DNA alone and controls.

NHP.61 (11044096) **Effective induction of simian immunodeficiency virus-specific systemic and mucosal immune responses in primates by vaccination with proviral DNA producing intact but noninfectious virions**

Authors Wang SW, Kozlowski PA, Schmelz G, Manson K, Wyand MS, Glickman R, Montefiori D, Lifson JD, Johnson RP, Neutra MR, Aldovini A
Journal J Virol 2000 Nov;74(22):10514-22
Objectives Challenge, Immunogenicity Reports a pilot evaluation of a DNA vaccine producing genetically inactivated SIV particles in primates, focuses on eliciting mucosal immunity.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pVacc1 DNA *Type:* DNA *Routes:* Intrarectal, Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular
Challenge SIVmac239 *Route:* Intrarectal
Main Findings

- IgA in rectal secretions of macaques that received the DNA vaccine intradermally and at the rectal mucosa are higher than in natural infection.
- CTL responses were low and sporadic.
- After rectal challenge with cloned SIVmac239, some animals with high SIV-specific IgA levels became infected.
- High levels of IgA alone are not sufficient to prevent the establishment of chronic infection, although mucosal IgA responses may reduce the infectivity of the initial viral inoculum.

NHP.62 (11152527) **DNA vaccination with the human immunodeficiency virus type 1 SF162DeltaV2 envelope elicits immune responses that offer partial protection from simian/human immunodeficiency virus infection to CD8(+) T-cell-depleted rhesus macaques**

Authors Cherpelis S, Shrivastava I, Gettie A, Jin X, Ho DD, Barnett SW, Stamatatos L
Journal J Virol 2001 Feb;75(3):1547-50

Objectives Challenge, Immunogenicity To conduct DNA immunization of macaques with the SF162V2 envelope, then challenge with SHIV162P4.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name DNA.SF162ΔV2 gp140 *Type:* DNA *Routes:* Intradermal, Intramuscular
Vaccine Name SF162ΔV2 gp140 protein *Type:* Recombinant Subunit Protein *Routes:* Intradermal, Intramuscular
Challenge SHIV162P4 *Route:* Intravenous
Main Findings

- Immunization elicited lymphoproliferative responses and potent neutralizing antibodies.
- Animals were depleted of their CD8+ T lymphocytes and then challenged intravenously with SHIV162P4.
- Compared to unvaccinated animals, vaccinated macaques had lower peak viremia levels, rapidly cleared plasma virus, and delayed seroconversion.

NHP.63 (11884556) **Induction of mucosal protection against primary, heterologous simian immunodeficiency virus by a DNA vaccine**
Authors Fuller DH, Rajakumar PA, Wilson LA, Trichel AM, Fuller JT, Shipley T, Wu MS, Weis K, Rinaldo CR, Haynes JR, Murphey-Corb M
Journal J Virol 2002 Apr;76(7):3309-17
Objectives Challenge, Immunogenicity To analyze immunogenicity and protective efficacy of a DNA vaccine containing SIV strain 17E-Fr (SIV/17E-Fr) gag-pol-env in rhesus macaques.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIV/17E-Fr gag-pol-env *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal
Challenge SIVDeltaB670 *Route:* Intrarectal
Main Findings

- First report of mucosal protection against a primary pathogenic, heterologous isolate of SIV using a commercially viable vaccine approach.
- Vaccinated and naive control monkeys were challenged intrarectally with SIV strain DeltaB670 (SIV/DeltaB670), whose env is 15% dissimilar to that of the vaccine strain.
- Postchallenge, in 4/7 vaccinees no SIV viral RNA or DNA sequences were found in the peripheral blood, and anamnestic antibody responses were absent.

NHP.64 (11085583) **Mucosal challenge of Macaca nemestrina with simian immunodeficiency virus (SIV) following SIV nucleocapsid mutant DNA vaccination**
Authors Gorelick RJ, Lifson JD, Yovandich JL, Rossio JL, Piatak M Jr, Scarzello AJ, Knott WB, Bess JW Jr, Fisher BA, Flynn BM, Henderson LE, Arthur LO, Benveniste RE
Journal J Med Primatol 2000 Aug;29(3-4):209-19
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca nemestrina (pigtailed macaque)
Vaccine Name SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Route:* Intramuscular
Vaccine Name S8-NCΔZF2 *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular
Challenge SIV(Mne) clone E11S *Route:* Intrarectal
Main Findings

- Challenged mucosally, all 12 macaques became infected, the 4 immunized animals greatly restricted their viral replication.
- One immunized animal that controlled replication remains antibody negative, no disease evident 46 wpc.

NHP.65.1 (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost**
Authors Gorelick RJ, Benveniste RE, Lifson JD, Yovandich JL, Morton WR, Kuller L, Flynn BM, Fisher BA, Rossio JL, Piatak M Jr, Bess JW Jr, Henderson LE, Arthur LO
Journal J Virol 2000 Dec;74(24):11935-49
Objectives Challenge, Immunogenicity To evaluate SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost.
Species/Subspecies Macaca nemestrina (pigtailed macaque)
Vaccine Name SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Route:* Intramuscular

Vaccine Name SIV(Mne) gp160Env protein *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name Gag-Pol particles *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge SIV(Mne) clone E11S *Route:* Intravenous
Main Findings

- Background: 11 pigtailed macaques were inoculated with nucleocapsid mutant SIV expressing DNA, intramuscularly (i.m.) in one study and i.m. and subcutaneously in another study. Six control animals received vector DNA lacking SIV sequences.
- Post IV challenge, all control animals became infected and 3/4 developed progressive SIV disease.
- 2 ypc, most immunized animals had low postacute levels of plasma SIV RNA, no CD4+ T-cell depletion or clinical evidence of progressive disease (see experiment 2 for additional information).

NHP.65.2 (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost**
Authors Gorelick RJ, Benveniste RE, Lifson JD, Yovandich JL, Morton WR, Kuller L, Flynn BM, Fisher BA, Rossio JL, Piatak M Jr, Bess JW Jr, Henderson LE, Arthur LO
Journal J Virol 2000 Dec;74(24):11935-49
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca nemestrina (pigtailed macaque)
Vaccine Name SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular
Vaccine Name S8-NCΔZF2 *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular
Challenge SIV(Mne) clone E11S *Route:* Intravenous
Main Findings

- The vaccine induced only modest and inconsistent humoral responses and no cellular immune responses prior to challenge.
- Following iv challenge with 20 animal infectious doses of the pathogenic SIV(Mne) in a long-term study, all control animals became infected and 3/4 animals developed progressive SIV disease leading to death.
- All 11 NC mutant SIV DNA-immunized animals became infected following challenge but decreased initial peak plasma SIV RNA levels compared to those of control animals.

NHP.66 (11689679) **Vaccination with attenuated simian immunodeficiency virus by DNA inoculation**
Authors Kent SJ, Dale CJ, Preiss S, Mills J, Campagna D, Purcell DF
Journal J Virol 2001 Dec;75(23):11930-4
Objectives Challenge, Immunogenicity To evaluate attenuated proviral DNA vaccine in macaques.
Species/Subspecies Macaca nemestrina (pigtailed macaque)
Vaccine Name SIVmac239 sbbvΔ3 DNA *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular
Vaccine Name SIVmac239 sbbvΔ3Delta5 DNA *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal, Intramuscular
Challenge SIVmac251 *Route:* Intrarectal
Main Findings

- Innoculated with wild-type simian immunodeficiency virus strain mac239 (SIV(mac239)) DNA or SIV(mac239) DNA containing a single deletion in the 3' nef-long terminal repeat overlap region (nef/LTR) led to sustained SIV infections and AIDS.
- Injectionof SIV(mac239) DNA containing identical deletions in both the 5' LTR and 3' nef/LTR resulted in attenuated SIV infections and substantial protection against subsequent mucosal SIV(mac251) challenge.

NHP.67 (10869776) **Induction of protective immunity against pathogenic simian immunodeficiency virus by a foreign receptor-dependent replication of an engineered avirulent virus**
Authors Matano T, Kano M, Odawara T, Nakamura H, Takeda A, Mori K, Sato T, Nagai Y
Journal Vaccine 2000 Aug 1;18(28):3310-8

Objectives Challenge, Immunogenicity To develop a chimeric (SIV,Friend Murine leukemia virus) DNA vaccine to induce restricted replication of an avirulent virus.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular
Challenge SIVmac239 *Route:* Intravenous
Main Findings

- A novel strategy: a vaccine consisting of a chimeric SIV and a Friend murine leukemia virus, in which the SIV env is replaced with ecotropic Friend murine leukemia virus (FMLV) env to confine its replication to FMLV receptor (mCAT1)-expressing cells.
- Macaques vaccinated with both the FMSIV DNA and the mCAT1-expression plasmid DNA generated SIV Gag-specific cellular immune responses and resistance against pathogenic SIVmac239 challenge.
- Vaccination with FMSIV DNA alone was insufficient to prevent the disease onset.

NHP.68 (11118363) **Induction of immune responses and break of tolerance by DNA against the HIV-1 coreceptor CCR5 but no protection from SIVsm challenge**
Authors Zuber B, Hinkula J, Vodros D, Lundholm P, Nilsson C, Morner A, Levi M, Benthin R, Wahren B
Journal Virology 2000 Dec 20;278(2):400-11
Objectives Challenge, Immunogenicity To explore genetic immunization to induce an immune response directed to CCR5 structures and break immunological tolerance toward endogenous CCR5.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name pcDNA3-CCR5 *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads)
Vaccine Name pcDNA3–tet.CCR5 *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads)
Vaccine Name CCR5 peptides *Type:* Synthetic Protein/Peptide *Route:* Intramuscular
Challenge SIVsm *Route:* Intrarectal
Main Findings

- Intramucosal immunization of cynomolgus macaques with CCR5 DNA followed by boosts with CCR5 peptides induced prominent IgG and IgA antibody responses.
- The CCR5-specific antibodies neutralized the infectivity of primary human R5 HIV-1 strains, and the macaque SIVsm.
- CCR5 gene and CCR5 peptide immunizations induced B- and T-cell responses.
- Tolerance was broken against endogenous macaque CCR5.
- Neither protection against nor enhancement of SIVsm infection was achieved.

NHP.69 (10894297) **Elicitation of protective immunity against simian immunodeficiency virus infection by a recombinant Sendai virus expressing the Gag protein**
Authors Kano M, Matano T, Nakamura H, Takeda A, Kato A, Ariyoshi K, Mori K, Sata T, Nagai Y
Journal AIDS 2000 Jun 16;14(9):1281-2
Objectives Challenge, Immunogenicity To use recombinant SeV expressing the Gag antigen of SIV, SeV/SIVgag, to elicit protective immunity.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name SeV-gag *Type:* DNA *Route:* Intranasal
Challenge SIVmac239 *Route:* Intravenous
Main Findings

- The vaccinated animals and controls were all infected by the challenge virus SIVmac239. Only animals immunized with SeV-SIV-gag were able to control infection by reducing the viral load to below detectable level

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NHP.70 (11689672) **Rapid appearance of secondary immune responses and protection from acute CD4 depletion after a highly pathogenic immunodeficiency virus challenge in macaques vaccinated with a DNA prime/Sendai virus vector boost regimen**
Authors Matano T, Kano M, Nakamura H, Takeda A, Nagai Y
Journal J Virol 2001 Dec;75(23):11891-6

Objectives Challenge, Immunogenicity To test the immunogenicity and protective effect of a SHIV-DNA prime vaccine followed by a single booster with a Gag-expressing Sendai virus (SeV-Gag).
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SeV-gag *Type:* DNA *Route:* Intranasal
Vaccine Name FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular
Challenge SHIV89.6PD *Route:* Intravenous
Main Findings

- All naive control macaques showed acute CD4(+) T-cell depletion at 2 wpc (iv SHIV89.6PD).
- All vaccinated macaques with prime/boost regimen were protected from depletion and showed greatly reduced peak viral loads.
- Vaccination with DNA alone or SeV-Gag alone did not confer protection.
- Differences in secondary responses between the protected and unprotected macaques was clear at 1 wpc.
- Rapid secondary responses reduce peak viral loads and protect from acute CD4(+) T-cell depletion.

NHP.71 (10983638) **Therapeutic immunization of HIV-infected chimpanzees using HIV-1 plasmid antigens and interleukin-12 expressing plasmids**
Authors Boyer JD, Cohen AD, Ugen KE, Edgeworth RL, Bennett M, Shah A, Schumann K, Nath B, Javadian A, Bagarazzi ML, Kim J, Weiner DB
Journal AIDS 2000 Jul 28;14(11):1515-22
Objectives Immunogenicity, Immunotherapy To assess HIV-1 DNA vaccination and co-immunization with interleukin (IL)-12 and IL-10 as immunotherapy in the HIV-1 infected chimpanzee model system.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Vaccine Name pCMN160 (HIV-1 MN env) *Type:* DNA *Route:* Intramuscular
Vaccine Name pCGag/Pol *Type:* DNA *Route:* Intramuscular
Challenge HIV-1 IIIB *Route:*
Main Findings

- No evidence of systemic toxicity associated with DNA immunization or the cytokine-expressing plasmids.
- IL-12/HIV-1 DNA vaccinated animals enhanced proliferative responses to multiple HIV-1 antigens at multiple time points.
- Animal co-immunized with HIV-1 and IL-10 did not have any changes in the proliferative responses.
- Control chimpanzee demonstrated moderate increases in the proliferative responses to HIV-1 antigens.

NHP.72 (9971763) **Acute effects of pathogenic simian-human immunodeficiency virus challenge on vaccine-induced cellular and humoral immune responses to Gag in rhesus macaques**
Authors Steger KK, Waterman PM, Pauza CD
Journal J Virol 1999 Mar;73(3):1853-9
Objectives Challenge, Immunogenicity To test immunization with recombinant Salmonella typhimurium (expressing Gag) or soluble Gag in adjuvant, by challenge with SHIV89.6PD (macaques).
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVhu *Type:* Live Attenuated Virus *Routes:* Intragastric, Intramuscular
Challenge SHIV89.6PD *Route:* Intrarectal
Main Findings

- Virus infection accompanied by rapid losses of lymphoproliferative responses to Gag or phytohemagglutinin.
- 8 wpc mitogen responses recovered to near normal levels but antigen-specific immunity remained low or undetectable.
- Serum antibody levelselevated initially but soon dropped well below levels achieved by immunization.
- Rapid depletion of preexisting Gag-specific CD4(+) T cells prevent or limit subsequent antiviral cellular and humoral immune responses during acute SHIV infection.

NHP.73 (10461832) **Combined systemic and mucosal immunization with microsphere-encapsulated inactivated simian immunodeficiency virus elicits serum, vaginal, and tracheal antibody responses in female rhesus macaques**

Authors Israel ZR, Gettie A, Ishizaka ST, Mishkin EM, Staas J, Gilley R, Montefiori D, Marx PA, Eldridge JH

Journal AIDS Res Hum Retroviruses 1999 Aug 10;15(12):1121-36

Objectives Challenge, Immunogenicity To determine the efficacy of immunization with microsphere-encapsulated whole inactivated SIV by combined systemic and mucosal administration to protect female rhesus macaques against vaginal challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac251.whole inactivated *Type:* Whole (killed) Inactivated Virus *Routes:* Intratracheal, Oral, Intramuscular

Vaccine Name vvrgp140 *Type:* DNA *Routes:* Oral

Challenge SIVmac251 *Route:* Vaginal or perivaginal

Main Findings

- Intramuscular priming resulted in strong IgG and modest IgA response.
- Intratracheal boosting following intramuscular priming resulted in high bronchial alveolar wash IgG and less pronounced IgA.
- IgG was present in the animals immunized intramuscularly boosted either intramuscularly or intratracheally.
- No neutralizing antibody to homologous SIVmac251 in response to the immunization with the whole inactivated SIV vaccine.
- On vaginal challenge none of the immunized groups was infected at a lesser frequency than the unimmunized controls.

NHP.74 (10438051) **Induction of mucosal antibody responses by microsphere-encapsulated formalin-inactivated simian immunodeficiency virus in a male urethral challenge model**

Authors Ishizaka ST, Israel ZR, Gettie A, Mishkin EM, Staas JK, Gilley RM, Dailey PJ, Montefiori DC, Marx PA, Eldridge JH

Journal Vaccine 1999 Jul 16;17(22):2817-25

Objectives Challenge, Immunogenicity To test use of microsphere-encapsulated formalin-inactivated SIV particles against mucosal SIV challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Whole inactivated SIVmac239 (encapsulated) *Type:* Whole (killed) Inactivated Virus *Routes:* Intratracheal, Intramuscular

Challenge SIVmac251 *Route:* Urethral

Main Findings

- Macaques, primed intramuscularly, boosted tracheally, had strong Iga response to SIV vaccine.
- The bulk of antibody response was against non-envelope epitopes.
- No neutralizing antibody observed.
- Intraurethral challenge with cell-free rhesus-grown virus showed no evidence of protection against challenge.
- Microsphere-based immunization raises local and system responses, but does not provide sufficient immunity to protect against mucosal challenge.

NHP.75 (10074183) **Comparison of immunity generated by nucleic acid-, MF59-, and ISCOM-formulated human immunodeficiency virus type 1 vaccines in Rhesus macaques: evidence for viral clearance**

Authors Verschoor EJ, Mooij P, Oostermeijer H, van der Kolk M, ten Haaft P, Verstrepen B, Sun Y, Morein B, Akerblom L, Fuller DH, Barnett SW, Heeney JL

Journal J Virol 1999 Apr;73(4):3292-300

Objectives Challenge, Immunogenicity To compare the kinetics of T-helper immune responses in rhesus monkeys by 3 HIV vaccine strategies: a rgp120SF2 expressed in vivo by DNA immunization or when it was delivered as a subunit protein vaccine formulated with the MF59 adjuvant or by ISCOMs.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pUCgp120SF2-gold particle *Type:* DNA *Route:* Intradermal (Gene Gun DNA-coated gold beads)

Vaccine Name HIV-1SF2 rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Main Findings

- Virus-neutralizing antibodies against HIV-1SF2 reached similar titers in the two rgp120SF2 protein-immunized groups, with different kinetics, while nab were delayed and low in the DNA-immunized animals.

- rgp120/ISCOM-immunized animals rapidly developed marked IL-2, IFN-gamma (type 1-like), and IL-4 responses that peaked after the second immunization.
- Protection challenge with SHIV was observed in the two groups receiving the rgp120 subunit vaccines. Half of the animals in the ISCOM group were completely protected from infection.

NHP.76 (1708168) **Recombinant virus vaccine-induced SIV-specific CD8+ cytotoxic T lymphocytes**

Authors Shen L, Chen ZW, Miller MD, Stallard V, Mazzara GP, Panicali DL, Letvin NL

Journal Science 1991 Apr 19;252(5004):440-3

Objectives Immunogenicity To determine whether a genetically restricted live recombinant virus, the vaccinia-simian immunodeficiency virus of macaques (SIVmac) could generate a T lymphocyte-mediated antiviral response in a primate.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name rVaccinia-SIVmac-env.gagpol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Main Findings

- Vaccinia-SIVmac vaccination elicited an SIVmac Gag-specific, CD8+ CTL response in rhesus monkeys.
- The rhesus monkey major histocompatibility complex (MHC) class I gene product restricting this CTL response was defined.
- Both the vaccinated and control SIVmac-infected monkeys that shared this MHC class I gene product developed CTLs with the same Gag epitope specificity.
- The findings support the use of recombinant virus vaccines for the prevention of HIV infections in humans.

NHP.77 (10506654) **Accelerated clearance of SHIV in rhesus monkeys by virus-like particle vaccines is dependent on induction of neutralizing antibodies**

Authors Notka F, Stahl-Hennig C, Dittmer U, Wolf H, Wagner R

Journal Vaccine 1999 Sep;18(3-4):291-301

Objectives Challenge, Immunogenicity To investigate efficacy of recombinant, insect cell derived SIV Pr56(gag) virus-like particles modified either by inserting HIV-1 Gp160 derived peptides into the Pr56(gag) precursor or by integrating the complete HIV-1 gp120 in the particle membrane.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIV Pr56gag VLP-type II *Type:* Virus-like Particle

Vaccine Name SFV- Pr56gag VLP-type II *Type:* Live Virus

Vaccine Name SFV-SIV Pr56gag VLP-type I *Type:* Virus-like Particle

Challenge SHIV-4.vpu+ *Route:* Intravenous

Main Findings

- All vaccinated monkeys became infected upon challenge with SHIV-4, but animals vaccinated with VLPs presenting the complete gp120 cleared virus faster than nonimmunized controls.
- Observed virus elimination significantly correlated with an anamnesticantibody response and accelerated appearance of neutralizing antibodies postchallenge.

NHP.78 (10725402) **Vaccination with tat toxoid attenuates disease in simian/HIV-challenged macaques**

Authors Pauza CD, Trivedi P, Wallace M, Ruckwardt TJ, Le Buanec H, Lu W, Bizzini B, Burny A, Zagury D, Gallo RC

Journal Proc Natl Acad Sci U S A 2000 Mar 28;97(7):3515-9

Objectives Challenge, Immunogenicity To study the role of tat by immunizing macaques with chemically inactivated tat toxoid and challenging animals intrarectally with SHIV89.6PD.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name inactivated Tat toxoid *Type:* Other *Routes:* Intradermal, Intramuscular

Vaccine Name rVaccinia-gp160 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name soluble gp160 *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name biologically active Tat protein *Type:* Purified Viral Products *Routes:* Intradermal, Intramuscular

Challenge SHIV89.6PD *Route:* Intrarectal
Main Findings

- Immune animals had significantly attenuated disease with lowered viral RNA, interferon-Alpha, and chemokine receptor expression (CXCR4 and CCR5) on CD4+ T cells, features linked to in vitro effects of Tat.
- Immunization with Tat toxoid inhibits key steps in viral pathogenesis.

NHP.79 (10936096) **Evaluation of immune responses induced by HIV-1 gp120 in rhesus macaques: effect of vaccination on challenge with pathogenic strains of homologous and heterologous simian human immunodeficiency viruses**
Authors Kumar A, Lifson JD, Silverstein PS, Jia F, Sheffer D, Li Z, Narayan O
Journal Virology 2000 Aug 15;274(1):149-64
Objectives Challenge, Immunogenicity To evaluate monomeric recombinant gp120 of HIV-1(LAI) (rgp120) vaccines against (SHIV(KU-2) and SHIV(89.6)P.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Monomeric rgp120 *Type:* Recombinant Subunit Protein *Route:* Intradermal
Challenge SHIV-KU2, SHIV89.6P *Route:* Intravenous
Main Findings

- All 8 vaccinated macaques developed high antibody titers against rgp120 that reacted efficiently with envelope proteins of homologous SHIVKU-2 and poorly with the SHIV89.6P envelope.
- Vaccinated macaques showed anamnestic antibody and T-helper cell responses, but T-helper responses were short-lived.
- After challenge, level of productive virus replication was indistinguishable between vaccine and control groups, suggesting that rgp120 did not confer protection against virus replication.

NHP.80 (10756013) **Evidence for viral virulence as a predominant factor limiting human immunodeficiency virus vaccine efficacy**
Authors Mooij P, Bogers WM, Oostermeijer H, Koornstra W, Ten Haaft PJ, Verstrepen BE, Van Der Auwera G, Heeney JL
Journal J Virol 2000 May;74(9):4017-27
Objectives Challenge, Immunogenicity Using vaccination with CCR5 binding envelope of HIV-1W6.1D to determine if virus virulence or genetic distance had a greater impact on HIV-1 vaccine efficacy against SHIV challenge (rhesus macaques).
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rgp120W6.1D *Type:* Recombinant Subunit Protein
Challenge SHIV.W6.1D, SHIV.SF13, SHIVHan2, SHIV89.6P *Route:*
Main Findings

- Protection from either of the divergent SHIVsf13 or SHIVhan2 challenges was demonstrated in the majority of the vaccinated animals.
- Second challenge with the virulent SHIV89.6p achieved protection in only one of the previously protected vaccinees.
- Immunization beneficial to viral load and CD4+ T-cell counts, but failed to protect from infection.

NHP.81 (11689887) **Protection of rhesus macaques against disease progression from pathogenic SHIV-89.6PD by vaccination with phage-displayed HIV-1 epitopes**
Authors Chen X, Scala G, Quinto I, Liu W, Chun TW, Justement JS, Cohen OJ, vanCott TC, Iwanicki M, Lewis MG, Greenhouse J, Barry T, Venzon D, Fauci AS
Journal Nat Med 2001 Nov;7(11):1225-31
Objectives Challenge, Immunogenicity To test an array of HIV-specific epitopes that behave as antigenic mimics (mimotopes) of conformational epitopes of gp120 and gp41 proteins for clades A-F.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name gp120/gp41 mimotopes *Type:* Synthetic Protein/Peptide *Route:* Intramuscular
Challenge SHIV89.6PD *Route:* Intravenous
Main Findings

- Upon intravenous challenge with 60 MID50 of pathogenic SHIV-89.6PD, phage-borne epitopes elicit envelope-specific antibody responses.

- 4/5 mimotope-immunized monkeys had lower levels of peak viremia, followed by viral set points of undetectable or transient levels of viremia, mild decline of CD4+ T cells, protection from progression to AIDS-like illness.

NHP.82.1 (10196297) **Protection of Macaques against pathogenic simian/human immunodeficiency virus 89.6PD by passive transfer of neutralizing antibodies**

Authors Mascola JR, Lewis MG, Stiegler G, Harris D, VanCott TC, Hayes D, Louder MK, Brown CR, Sapan CV, Frankel SS, Lu Y, Robb ML, Katinger H, Birx DL

Journal J Virol 1999 May;73(5):4009-18

Objectives Challenge, Immunogenicity Used a chimeric SHIV based on the envelope of a primary isolate (HIV-89.6) to perform passive-transfer experiments and study the role of anti-envelope antibodies in protection (rhesus macaques).

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV89.6PD *Route:* Intravenous

Main Findings

- 3/6 animals given HIVIG/2F5/2G12 were completely protected; the remaining 3 animals became SHIV infected but displayed reduced plasma viremia and near normal CD4(+)-cell counts.
- 1/3 monkeys given 2F5/2G12 exhibited only transient evidence of infection; 2/3 had marked reductions in viral load.
- All monkeys that received HIVIG, 2F5, or 2G12 alone became infected and developed high-level plasma viremia.
- General correlation between in vitro neutralization and protection.

NHP.82.2 (10196297) **Protection of Macaques against pathogenic simian/human immunodeficiency virus 89.6PD by passive transfer of neutralizing antibodies**

Authors Mascola JR, Lewis MG, Stiegler G, Harris D, VanCott TC, Hayes D, Louder MK, Brown CR, Sapan CV, Frankel SS, Lu Y, Robb ML, Katinger H, Birx DL

Journal J Virol 1999 May;73(5):4009-18

Objectives Challenge, Immunogenicity, Passive Immunization Used a chimeric SHIV based on the envelope of a primary isolate (HIV-89.6) to perform passive-transfer experiments and study the role of anti-envelope antibodies in protection.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name HIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV89.6PD *Route:* Intravenous

NHP.83 (10772996) **Passive infusion of immune serum into simian immunodeficiency virus-infected rhesus macaques undergoing a rapid disease course has minimal effect on plasma viremia**

Authors Binley JM, Clas B, Gettie A, Vesanen M, Montefiori DC, Sawyer L, Booth J, Lewis M, Marx PA, Bonhoeffer S, Moore JP

Journal Virology 2000 Apr 25;270(1):237-49

Objectives Immunotherapy, Passive Immunization To investigate the role of passive immunization in controling viremia and disease progression in infected macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVIG-1 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name SIVIG-2 *Type:* Passive Antibody *Route:* Intravenous

Main Findings

- Despite restoring anti-SIV titers to levels typical of macaques with a normal disease course, SIVIG had only a modest effect on plasma SIV RNA and cell-associated viral load.
- The kinetics of the viremia changes are inconsistent with neutralization of new cycles of infection. More likely, perhaps unexpectedly, is that infused antibodies killed SIV-infected cells, via an effector mechanism such as antibody-dependent cellular cytotoxicity

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NHP.84 (10468614) **Postexposure immunoprophylaxis of primary isolates by an antibody to HIV receptor complex**

Authors Wang CY, Sawyer LS, Murthy KK, Fang X, Walfield AM, Ye J, Wang JJ, Chen PD, Li ML, Salas MT, Shen M, Gauduin MC, Boyle RW, Koup RA, Montefiori DC, Mascola JR, Koff WC, Hanson CV

Journal Proc Natl Acad Sci U S A 1999 Aug 31;96(18):10367-72

Objectives Immunotherapy To evaluate neutralizing activity of mAb B4, a monoclonal antibody directed against HIV receptor complex.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Vaccine Name mAb B4 *Type:* Passive Antibody

Challenge HIV-1.DH12 *Route:* Intravenous

Main Findings

- mAb B4 preferentially neutralized primary HIV-1 isolates, including syncytium-inducing(si) and non-si phenotypes, for subtypes A-G and HIV-2, SIV, SHIV.
- Neutralization demonstrated in both pre- and postinfection models.
- Administration of mAb B4 after infectious challenge totally interrupted the infection of hu-PBL-severe combined immunodeficient mice by PBL-grown HIV-1 and the infection of chimpanzees by chimp-adapted HIV-1.

NHP.85 (10655110) **Human neutralizing monoclonal antibodies of the IgG1 subtype protect against mucosal simian-human immunodeficiency virus infection**

Authors Baba TW, Liska V, Hofmann-Lehmann R, Vlasak J, Xu W, Ayehunie S, Cavacini LA, Posner MR, Katinger H, Stiegler G, Bernacky BJ, Rizvi TA, Schmidt R, Hill LR, Keeling ME, Lu Y, Wright JE, Chou TC, Ruprecht RM

Journal Nat Med 2000 Feb;6(2):200-6

Objectives Challenge, Passive Immunization To evaluate triple combination of the human IgG1 monoclonal antibodies F105, 2G12 and 2F5, which neutralize SHIV-vpu+, a chimeric simian-human virus that encodes the env gene of HIV-IIIB, to develop immunoprophylaxis against intrapartum HIV-1 transmission.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name F105/2G12/2F5 mab *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV-vpu+ *Route:* Intravenous, Oral

Main Findings

- Four pregnant macaques treated with a triple combination of mab F105, 2G12 and 2F5 were protected from SHI-vpu+ challenge.
- Infants treated with the mab triple combination at birth and and challenged orally: no evidence of infection in any infant during 6 months of follow-up.
- Epitopes recognized by the three monoclonal antibodies are important determinants for achieving substantial protection.

NHP.86.1 (9930869) **Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys**

Authors Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA

Journal Nat Med 1999 Feb;5(2):204-10

Objectives Challenge, Passive Immunization To assess whether HIV-1 envelope-specific antibodies confer resistance against primate lentivirus infections (pigtailed macaques).

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Anti-HIV-1 ch4750 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Anti-HIV-1 ch1206 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Anti-HIV-1 ch911 *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV-MD14YE (DH12) *Route:* Intravenous

Main Findings

- In pigtailed macaques passively immunized with HIV-1 specific antibodies from chimpanzees, anti-SHIV neutralizing activity is the absolute requirement for antibody-mediated protection.
- Ti ter in plasma for complete protection of SHIV-challenged macaques in range of 1:5-1:8.

- HIV-1-specific nab studied are able to bind to native gp120 present on infectious virus particles.
- Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection

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NHP.86.2 (9930869) **Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys**

Authors Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA

Journal Nat Med 1999 Feb;5(2):204-10

Objectives Challenge, Immunogenicity, Passive Immunization .

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Anti-HIV-1 ch1206 *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV-MD14YE (DH12) *Route:* Intravenous

NHP.87 (10082123) **Passively administered neutralizing serum that protected macaques against infection with parenterally inoculated pathogenic simian-human immunodeficiency virus failed to protect against mucosally inoculated virus**

Authors Joag SV, Li Z, Wang C, Foresman L, Jia F, Stephens EB, Zhuge W, Narayan O

Journal AIDS Res Hum Retroviruses 1999 Mar 1;15(4):391-4

Objectives Challenge, Immunogenicity, Passive Immunization To determine whether passive immunization with neutralizing serum would protect macaques against infection with pathogenic SHIV following oral inoculation of the virus.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Anti-SHIV Plasma *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV.KU1 *Route:* Oral

Main Findings

- Ten pigtail macaques were inoculated orally with one animal infectious dose of SHIV(KU-1). Four of the 10 had been given pooled anti-SHIV plasma (15 ml/kg) 24 hr earlier, 4 others were given the same dose of anti-SHIV plasma 2 hr after virus challenge, and the 2 remaining animals were used as controls.
- The neutralizing antibodies failed to protect macaques against infection after mucosal challenge with SHIV(KU-1)

NHP.88 (11907251) **Tat-vaccinated macaques do not control simian immunodeficiency virus SIVmac239 replication**

Authors Allen TM, Mortara L, Mothe BR, Liebl M, Jing P, Calore B, Piekarczyk M, Ruddersdorf R, O'Connor DH, Wang X, Wang C, Allison DB, Altman JD, Sette A, Desrosiers RC, Sutter G, Watkins DI

Journal J Virol 2002 Apr;76(8):4108-12

Objectives Challenge, Immunogenicity To assess the role of Tat-specific CTL in controlling pathogenic SIVmac239 replication after using a DNA-prime, vaccinia virus Ankara-boost vaccine regimen.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name MVA-SIV239tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name MVA-SIVSL8-tat28-35 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal

Vaccine Name MVA-SIV251 32H tat *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intradermal

Challenge SIVmac239 *Route:* Intrarectal

Main Findings

- Despite the induction of Tat-specific CTL, there was no significant reduction in either peak or viral set point in animals immunized with a DNA-prime, vaccinia virus Ankara-boost vaccine regimen and challenged with SIVmac239 compared to controls.

NHP.89 (12021347) **Critical role for Env as well as Gag-Pol in control of a simian-human immunodeficiency virus 89.6P challenge by a DNA prime/recombinant modified vaccinia virus Ankara vaccine**

Authors Amara RR, Smith JM, Staprans SI, Montefiori DC, Villinger F, Altman JD, O'Neil SP, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McNicholl JM, McClure HM, Moss B, Robinson HL

Journal J Virol 2002 Jun;76(12):6138-46
Objectives Challenge, Immunogenicity To test Gag-Pol DNA priming and Gag-Pol rMVA boosting to evaluate the contribution of anti-Env immune responses to viral control.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pGA1-gag-pol DNA vaccine *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intradermal
Vaccine Name rMVA SIV239 gag-pol *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular
Challenge SHIV89.6P *Route:* Intrarectal
Main Findings

- Gag-specific T cell response to a gag-pol DNA vaccine was similar to those raised against the gag-pol-env vaccine and were capable of controlling challenge infection with SHIV89.6P.
- The control of the SHIV 89.6P challenge was delayed and inconsistent in the Gag-Pol-vaccinated group and all of the animals underwent severe and, in most cases, sustained loss of CD4(+) cells.
- Most of the lost CD4(+) cells in the Gag-Pol-vaccinated group were uninfected cells, suggesting that the rapid appearance of binding antibody for Env in Gag-Pol-Env-vaccinated animals helped protect uninfected CD4(+) cells from Env-induced apoptosis.

NHP.90.1 (12009868) **Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model**

Authors Earl PL, Wyatt LS, Montefiori DC, Bilska M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B
Journal Virology 2002 Mar 15;294(2):270-81
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rMVASIV239gagpol.HIV89.6env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name Oligomeric HIV-1.89.6 gp140 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge SHIV89.6 *Route:* Intravenous
Main Findings

- All control and vaccinated animals except one became infected. However, the levels of viremia were as follows: controls >rMVA alone > rMVA >protein. The differences were statistically significant between immunized and control groups but not between the two immunized groups.
- A relationship between vaccine-induced antibody titers and reduction in virus burden was observed.

NHP.90.2 (12009868) **Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model**

Authors Earl PL, Wyatt LS, Montefiori DC, Bilska M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B
Journal Virology 2002 Mar 15;294(2):270-81
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rMVASIV239gagpol.HIV89.6env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name Oligomeric HIV-1.89.6 gp140 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge SHIV89.6P *Route:* Intravenous
Main Findings

- All animals became infected.
- The vaccinated group exhibited a 5-fold reduction in peak viremia and a 10-fold reduction in the postacute phase viremia in comparison to the controls.
- All of the controls required euthanasia by 10 mpc. A relationship between vaccine-induced antibody titers and reduction in virus burden was observed in both studies.

- Immunization with MVA/SHIV89.6 alone or with a protein boost stimulated both arms of the immune system and resulted in significant control of viremia and delayed progression to disease after challenge with SHIV-89.6P

NHP.92 (12111421) **Characterization of simian and human immunodeficiency chimeric viruses re-isolated from vaccinated macaque monkeys after challenge infection**

Authors Kwofie TB, Miura T, Ibuki K, Enose Y, Suzuki H, Ui M, Kuwata T, Hayami M

Journal Arch Virol 2002 Jun;147(6):1091-104

Objectives Challenge, Immunogenicity To examine the biological properties of circulating viruses whose replication has been suppressed in vaccinated monkeys.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Monkeys vaccinated with nef-deleted SHIVs were either fully or partially protected against challenge with acute pathogenic SHIV-89.6 P
- Though the vaccination did not completely prevent the replication of the challenge virus in the monkeys it did contain the challenge virus by suppressing the pathogenic variants.

NHP.93 (12100017) **Spontaneous production of RANTES and antigen-specific IFN-gamma production in macaques vaccinated with SHIV-4 correlates with protection against SIVsm challenge**

Authors Ahmed RK, Makitalo B, Karlen K, Nilsson C, Biberfeld G, Thorstensson R

Journal Clin Exp Immunol 2002 Jul;129(1):11-8

Objectives Challenge, Immunogenicity To investigate the production of beta-chemokines in eight cynomolgus macaques vaccinated with non-pathogenic SHIV-4 in relation to protection against pathogenic SIVsm challenge.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name SHIV-4 *Type:* Live Virus *Route:* Intravenous

Challenge SIVsm *Route:* Intrarectal

Main Findings

- 2/8 vaccinated monkeys were completely protected and one was partially protected against the challenge virus.
- The monkeys that resisted infectious SIVsm virus challenge showed higher spontaneous beta-chemokine production by peripheral blood mononuclear cells and had higher numbers of antigen-induced IFN-gamma secreting cells compared to the non-protected animals
- The genetic background of the host and/or environmental factors are involved in the chemokine production and beta-chemokines contribute to protection against HIV/SIV infection.

NHP.94 (1281660) **Vaccination of macaques with SIV conserved envelope peptides suppressed infection and prevented disease progression and transmission**

Authors Shafferman A, Lewis MG, McCutchan FE, Benveniste RE, Jahrling PB, Hickman RL, Lai CY, Burke DS, Eddy GA

Journal AIDS Res Hum Retroviruses 1992 Aug;8(8):1483-7

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVenv-Bgal peptides *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge SIV(Mne) clone E11S *Route:* Intravenous

Main Findings

- Vaccinated macaques became transiently viremic following challenge with SIVmne.
- Lymph nodes from all vaccinated macaques remain SIV-PCR positive.
- Lymph nodes and whole blood from vaccinated macaques challenged with SIV could not transmit SIV to naive macaques.

NHP.95.1 (1433263) **Comparison of protection from homologous cell-free vs cell-associated SIV challenge afforded by inactivated whole SIV vaccines**

Authors Heeney JL, de Vries P, Dubbes R, Koornstra W, Niphuis H, ten Haaft P, Boes J, Dings ME, Morein B, Osterhaus AD

Journal J Med Primatol 1992 Feb-May;21(2-3):126-30

Objectives Challenge, Immunogenicity To determine if SIV vaccines could protect against challenge with PBMCs from an SIV infected rhesus monkeys.

Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- 100% SIV vaccinated animals challenged with the 11-88 cell-free stock of SIVmac32H were protected, whereas only 50% of the SIV vaccinated monkeys receiving the same infectious dose of the 1XC cell stock were protected

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NHP.95.2 (1466991) **Comparison of protection afforded by whole virus ISCOM versus MDP adjuvanted formalin-inactivated SIV vaccines from IV cell-free or cell-associated homologous challenge**
Authors Osterhaus A, de Vries P, Morein B, Akerblom L, Heeney J
Journal AIDS Res Hum Retroviruses 1992 Aug;8(8):1507-10
Objectives Challenge, Immunogenicity To test SIV-ISCOM and SIV-MDP adjuvanted vaccines for their potential to induce protection from intravenous homologous SIV challenge in rhesus monkeys.
Main Findings
- 7/7 monkeys vaccinated 4x over a 4-month period with the SIV-ISCOM or the SIV-MDP vaccine were protected from developing viremia during a three-month observation period since intravenous challenge with 10 MID50 cell-free SIVmac251(32H).
- 2/4 and 2/4 monkeys in 2 other groups of 4 monkeys vaccinated in the same way with either of these vaccines, then challenged (intravenously with 10 MID50 of SIVmac251(32H)-infected PBMC of a rhesus monkey) were protected.
- All the control animals vaccinated with measles virus ISCOMS or MDP adjuvanted measles virus antigen were infected upon challenge.
- Conclusion: vaccinated previously unchallenged nonhuman primates can be protected from infection with lentivirus-infected PBMC from another animal. Serological analysis indicated that SIV-specific serum antibody titers were considerably higher in SIV-ISCOM vaccinated animals than in the SIV-MDP vaccinated animals

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NHP.96 (1346285) **Intrarectal challenge of macaques vaccinated with formalin-inactivated simian immunodeficiency virus**
Authors Cranage MP, Baskerville A, Ashworth LA, Dennis M, Cook N, Sharpe S, Farrar G, Rose J, Kitchin PA, Greenaway PJ
Journal Lancet 1992 Feb 1;339(8788):273-4
Objectives Challenge, Immunogenicity To test the immunogenicity and efficacy of a formalin-inactivated SIV in rhesus macaques.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- 4 rhesus macaques vaccinated with a formalin-inactivated SIV given intramuscularly were protected from challenge up to 10 mpc.

NHP.97 (1466966) **Immunization of rhesus monkeys with high- and low-dose Tween-ether-disrupted SIVMAC**
Authors Voss G, Stahl-Hennig C, Petry H, Coulibaly C, Nick S, Fuchs D, Wachter H, Luke W, Hunsmann G
Journal AIDS Res Hum Retroviruses 1992 Aug;8(8):1397-400
Objectives Challenge, Immunogenicity To test the immunogenicity and protection from challenge induced by a low dose of tween-ether-disrupted SIVmac251.32H.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251/32H (Tween/Ether) *Type:* Whole (killed) Inactivated Virus
Challenge SIVmac251(32H) *Route:*
Main Findings
- 3/3 naive controls infected 14 dpc (increased neopterin levels correlated with infection).
- 4/7 protected from infection.

NHP.98 (10759543) **Augmentation of immune responses to HIV-1 and simian immunodeficiency virus DNA vaccines by IL-2/Ig plasmid administration in rhesus monkeys**
Authors Barouch DH, Craiu A, Kuroda MJ, Schmitz JE, Zheng XX, Santra S, Frost JD, Krivulka GR, Lifton MA, Crabbs CL, Heidecker G, Perry HC, Davies ME, Xie H, Nickerson CE, Steenbeke TD, Lord CI, Montefiori DC, Strom TB, Shiver JW, Lewis MG, Letvin NL
Journal Proc Natl Acad Sci U S A 2000 Apr 11;97(8):4192-7

Objectives Immunogenicity To investigate whether DNA vaccine-elicited immune responses in rhesus monkeys could be augmented by using either an IL-2/Ig fusion protein or a plasmid expressing IL-2/Ig.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular
Vaccine Name HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular
Main Findings

- The administration of both IL-2/Ig protein and IL-2/Ig plasmid induced a significant and sustained in vivo activation of peripheral T cells in the vaccinated monkeys.
- The monkeys that received IL-2/Ig plasmid generated 30-fold higher Env-specific antibody titers and 5-fold higher Gag-specific, tetramer-positive CD8+ T cell levels than the monkeys receiving the DNA vaccines alone.
- IL-2/Ig protein also augmented the vaccine-elicited immune responses, but less effectively than IL-2/Ig plasmid.
- Augmentation of the immune responses by IL-2/Ig was evident after the primary immunization and increased with subsequent boost immunizations.

NHP.99.1 (11713828) **Cytokine-induced augmentation of DNA vaccine-elicited SIV-specific immunity in rhesus monkeys**
Authors Barouch DH, Letvin NL
Journal Dev Biol (Basel) 2000;104:85-92
Objectives Immunogenicity To investigate the ability of an IL-2/lg cytokine fusion protein and a plasmid expressing IL-2/lg to augment immune responses in rhesus monkeys induced by DNA vaccines encoding SIV gag and HIV-1 env 89.6P.
Main Findings

- Both IL-2/lg protein and IL-2/lg plasmid augment DNA vaccine-elicited antibody and CTL responses.
- The most consistent and dramatic augmentation was observed using the IL-2/lg plasmid.

NHP.99.2 (1466966) **Immunization of rhesus monkeys with high- and low-dose Tween-ether-disrupted SIVMAC**
Authors Voss G, Stahl-Hennig C, Petry H, Coulibaly C, Nick S, Fuchs D, Wachter H, Luke W, Hunsmann G
Journal AIDS Res Hum Retroviruses 1992 Aug;8(8):1397-400
Objectives Challenge, Immunogenicity To test the immunogenicity and protection from challenge induced by a HIGH dose of tween-ether-disrupted SIVmac251.32H.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251/32H (Tween/Ether) *Type:* Whole (killed) Inactivated Virus
Challenge SIVmac251(32H) *Route:*
Main Findings

- 3/3 naive historic controls infected 14 dpc.
- 4/5 protected from infection.

NHP.100 (11085584) **Maturation of envelope-specific antibody responses to linear determinants in monkeys inoculated with attenuated SIV**
Authors Cole KS, Paliotti MJ, Murphey-Corb M, Montelaro RC
Journal J Med Primatol 2000 Aug;29(3-4):220-30
Objectives Immunogenicity To characterize the evolution of antibody responses to define linear determinants of the SIV envelope protein.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIV 17E-CL *Type:* Recombinant Live Attenuated Virus *Route:* Intravenous
Main Findings

- Antibodies to certains envelope peptide domains have different patterns of antibody maturation to distinct linear envelope antigenic determinants.
- Potential for domain-specific serology to produce a high-resolution characterization of SIV-specific antibody responses that can be used to evaluate experimental vaccine responses and to identify potential immune correlates of protection.

NHP.101 (10954580) **Induction of mucosal homing virus-specific CD8(+) T lymphocytes by attenuated simian immunodeficiency virus**

Authors Cromwell MA, Veazey RS, Altman JD, Mansfield KG, Glickman R, Allen TM, Watkins DI, Lackner AA, Johnson RP
Journal J Virol 2000 Sep;74(18):8762-6
Objectives Immunogenicity To determine if virus-specific CD8+ lymphocytes induced in rhesus macaques by immunization with attenuated SIV express the mucosa-homing receptor $\alpha 4\beta 7$ (and traffic to the intestinal mucosa).
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251ΔNef *Type:* Live Attenuated Virus *Route:* Intravenous
Main Findings

- Virus-specific CD8+ T cells are induced by immunization with attenuated SIV express $\alpha 4\beta 7$ and home to mucosal sites, whereas those induced by a DNA-MVA vaccine lack expression of the intestinal homing receptor.
- SIV-specific CD8+ T lymphocytes expressing $\alpha 4\beta 7$ by a vaccine approach that replicates in mucosal tissue suggest that induction of virus-specific lymphocytes that are able to home to mucosal sites may be an important characteristic of asuccessful AIDS vaccine

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NHP.102 (10856795) **Anti-major histocompatibility complex antibody responses in macaques via intradermal DNA immunizations**
Authors Dela Cruz CS, MacDonald KS, Barber BH
Journal Vaccine 2000 Jul 15;18(27):3152-65
Objectives Immunogenicity To determine if DNA immunization with class I and class II MHC-encoding plasmids elicite xenogeneic and allogeneic antibody response against conformationally intact MHC molecules in rhesus macaques.
Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca fascicularis (cynomolgus macaque)
Main Findings

- Intradermal immunizations of non-human primates with plasmid DNA encoding human MHC alleles can safely elicit xenogeneic anti-MHC antibody responses.
- DNA encoding a specific macaque allogeneic MHC induced anti-allogeneic MHC antibodies production.

NHP.103 (10763887) **Control of viral replication and disease onset in cynomolgus monkeys by HIV-1 TAT vaccine**
Authors Ensoli B, Cafaro A
Journal J Biol Regul Homeost Agents 2000 Jan-Mar;14(1):22-6
Objectives Challenge, Immunogenicity To test the hypothesis that humoral and cellular anti-Tat immunity have a protective role and may control disease progression.
Main Findings

- High titers of anti-Tat antibodies capable of neutralizing Tat activity and the in vitro infection with the SHIV89.6P, Tat-specific proliferation, CTLs, TNFalpha production and skin tests were detected in the vaccinated monkeys.
- Upon challenge with the highly pathogenic SHIV89.6P (10 MID50, i.v.), 5/7 of the vaccinated monkeys showed no signs of infection nor CD4+-T cell decline over 19 months of follow-up, whereas 3/3 controls were highly infected.

NHP.104 (10729127) **Evidence for recombination of live, attenuated immunodeficiency virus vaccine with challenge virus to a more virulent strain**
Authors Gundlach BR, Lewis MG, Sopper S, Schnell T, Sodroski J, Stahl-Hennig C, Uberla K
Journal J Virol 2000 Apr;74(8):3537-42
Objectives Challenge, Immunogenicity To increase the immunogenicity of the vaccine virus with IL-2 and to investigate whether a recombination event between the vaccine and challenge viruses could explain the negative effect of vaccination with live, attenuated immunodeficiency viruses.
Main Findings

- Detection of recombination between a live attenuated vaccine and the challenge strain resulting in a more adverse clinical outcome in vaccinated animals.
- 3 of the vaccinated macaques developed higher set point viral load levels than unvaccinated control monkeys. 2 of these vaccinated monkeys developed AIDS, while the control monkeys infected in parallel remained asymptomatic.
- Emergence of more-virulent recombinants of live, attenuated viruses and less-aggressive wild-type viruses is an additional risk of live, attenuated immunodeficiency virus vaccines

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NHP.105 (11713807) **DNA vaccine protection against challenge with simian/human immunodeficiency virus 89.6 in rhesus macaques**

Authors Habel A, Chanel C, Le Grand R, Martinon F, Couillin L, Moog C, Doms R, Gauduin MC, Hurtrel B, Guillet JG, Aubertin AM, Girard M

Journal Dev Biol (Basel) 2000;104:101-5

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- 6/6 control monkeys became infected with challenge strain (SHIV89.6, 750 TCID50).
- In monkeys immunized with DNA only: 5/6 had challenge virus recovered by co-cultivation; in the DNA-protein group 2/6 were culture positive.
- Rechallenge using 600TCID50 of pathogenic SHIV-89.6P. A rapid CD4 cell count decline in the 4 control monkeys as well as in the monkey vaccinated with DNA only, but not 4 animals immunized with DNA + protein.
- No virus was recovered from PBMC in two of these monkeys, and viral RNA loads in plasma were greatly reduced in three of them as compared with the controls. Absence of virus in PBMC was ascertained by whole blood transfusion to naive recipients. Altogether, this shows that the DNA prime-protein boost vaccine regimen could provide some protection against mucosal SHIV infection in rhesus monkeys, whereas DNA alone was ineffective.

NHP.106 (10792505) **Up-regulation of beta-chemokines and down-modulation of CCR5 co-receptors inhibit simian immunodeficiency virus transmission in non-human primates**

Authors Lehner T, Wang Y, Cranage M, Tao L, Mitchell E, Bravery C, Doyle C, Pratt K, Hall G, Dennis M, Villinger L, Bergmeier L

Journal Immunology 2000 Apr;99(4):569-77

Objectives Challenge, Immunogenicity To evaluate in vivo the mechanism of protection from SIV that involves up-regulation of chemokines, which bind and may down-modulate the CCR5 coreceptors, thereby preventing transmission.

Species/Subspecies -

Vaccine Name rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Route:* Subcutaneous

Vaccine Name Recombinant p27 *Type:* Recombinant Subunit Protein *Route:* Subcutaneous

Challenge SIVmac220 *Route:* Intrarectal

Main Findings

- Immunization induced significant increases in the concentrations of CD8 cell-derived suppressor factor (CD8SF), regulated on activation normal T cells expressed and secreted (RANTES), macrophage inflammatory protein (MIP)1 and MIP1, and down-modulation of the proportion of cells expressing CCR5 ($r = 0.737$, $P < 0.05$)
- In vivo immunization up-regulates chemokines, which may down-modulate CCR5 coreceptors, and both functions are significantly correlated with the viral load

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NHP.107 (12359422) **Immunization of Macaques with Live Simian Human Immunodeficiency Virus (SHIV) Vaccines Conferred Protection Against AIDS Induced by Homologous and Heterologous SHIVs and Simian Immunodeficiency Virus**

Authors Kumar A, Mukherjee S, Shen J, Buch S, Li Z, Adany I, Liu Z, Zhuge W, Piatak M, Lifson J, McClure H, Narayan O

Journal Virology 2002 Sep 30;301(2):189

Objectives Challenge, Immunogenicity To evaluate the vaccine potential of SHIVs attenuated by deletion of viral accessory genes.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name DeltavpuDeltaNefSHIV-4 *Type:* Live Attenuated Virus *Route:* Subcutaneous

Vaccine Name DeltavpuSHIV-ppc *Type:* Live Attenuated Virus *Routes:* Oral, Subcutaneous

Challenge SHIV-KU2, SIVmacR71, SHIV89.6P *Route:* Intrarectal

Main Findings

- No virological evidence of productive infection with the vaccine strains.
- 7/7 animals developed binding as well as neutralizing antibodies.

- Virus-specific CTLs that recognized homologous as well as heterologous pathogenic SHIVs and SIV, and also soluble inhibitory factors that blocked the in vitro replication of the vaccine strains and different challenge viruses.
- 2/2 control animals were infected, succomed to AIDS upon challenge.
- 7/7 vaccinees were also infected with challenge viruses, but peak VL were 2-5 lower than in the control and later plasma viral RNA became undetectable in vaccinees (in lymph nodes of 6/7 vaccinees, SHIV89.6P in 5/7, and SHIVKU in 3/7 animals).

NHP.108 (10839807) **Effects of in vivo CD8(+) T cell depletion on virus replication in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine**

Authors Metzner KJ, Jin X, Lee FV, Gettie A, Bauer DE, Di Mascio M, Perelson AS, Marx PA, Ho DD, Kostrikis LG, Connor RI

Journal J Exp Med 2000 Jun 5;191(11):1921-31

Objectives Challenge, Immunogenicity To investigate the role of CD8(+) T lymphocytes in controlling replication of live, attenuated simian immunodeficiency virus (SIV) as part of a vaccine study to examine the correlates of protection in the SIV/rhesus macaque model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac251Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVmac251 *Route:* Intravenous

Main Findings

- CD8+ T cell depletion was associated with a 1-2 log increase in SIVmac239-nef plasma viremia.
- Control of SIVmac239-nef replication was temporally associated with the recovery of CD8+ T cells between days 8 and 10. The challenge virus, SIVmac251, was not detectable in either the plasma or lymph nodes after depletion of CD8+ T cells.
- CD8+ T cells play an important role in controlling replication of live, attenuated SIV in vivo.

NHP.109 (10612675) **Simian immunodeficiency virus-specific cytotoxic T lymphocytes and protection against challenge in rhesus macaques immunized with a live attenuated simian immunodeficiency virus vaccine**

Authors Nixon DF, Donahoe SM, Kakimoto WM, Samuel RV, Metzner KJ, Gettie A, Hanke T, Marx PA, Connor RI

Journal Virology 2000 Jan 5;266(1):203-10

Objectives Challenge, Immunogenicity To examine the role of SIV-specific CTLs in macaques immunized with an attenuated strain of simian immunodeficiency virus (SIVmac239Deltanef) in protection against pathogenic challenge with SIVmac251.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239-Δnef *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SIVmac251 *Route:* Intravenous

Main Findings

- Attenuated SIVmac239Deltanef can elicit specific CTL precursor cells (CTLp), but no correlation was observed between breadth or strength of CTLp response to structural proteins SIV-Env, -Gamg or -Pol and protection against infection.
- The low level of Mamu-A*01/p11C, C-M-specific CTLs induced through attenuated SIVmac239Deltanef vaccination increased in the absence of detectable SIVmac251 or SIVmac239Deltanef proviral DNA.

NHP.110 (9371609) **Identification of the V1 region as a linear neutralizing epitope of the simian immunodeficiency virus SIVmac envelope glycoprotein**

Authors Jurkiewicz E, Hunsmann G, Schaffner J, Nisslein T, Luke W, Petry H

Journal J Virol 1997 Dec;71(12):9475-81

Objectives Immunogenicity To investigate the role of the V1 in neutralization.

Species/Subspecies Macaca mulatta (Rhesus macaque)

NHP.111 (10644340) **Antiretroviral therapy during primary immunodeficiency virus infection can induce persistent suppression of virus load and protection from heterologous challenge in rhesus macaques**

Authors Rosenwirth B, ten Haaft P, Bogers WM, Nieuwenhuis IG, Niphuis H, Kuhn EM, Bischofberger N, Heeney JL, Uberla K

Journal J Virol 2000 Feb;74(4):1704-11
Objectives Challenge, Immunogenicity To study rhesus macaques with the pathogenic simian/human immunodeficiency virus RT-SHIV and treat them with the antiretroviral drug (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA) for 8 weeks starting 7 or 14 days postinfection.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name RT-SHIV *Type:* Live Virus *Route:* Intravenous
Main Findings

- Rhesus macaques inoculated with the pathogenic RT-SHIV then treated with the antiretroviral drug (R)-9-(2-phosphonylmethoxypropyl)adenine (PMPA) for 8 weeks starting 7 or 14 days postinfection, showed suppressed viral replication efficiently.
- Suppression of viral replication was transient in 4/6 monkeys.
- The challenge of the monkeys with better out come with SIV(8980) shows that both monkeys proved to be protected against the heterologous virus.

NHP.112 (9765452) **Oral immunization of macaques with attenuated vaccine virus induces protection against vaginally transmitted AIDS**
Authors Joag SV, Liu ZQ, Stephens EB, Smith MS, Kumar A, Li Z, Wang C, Sheffer D, Jia F, Foresman L, Adany I, Lifson J, McClure HM, Narayan O
Journal J Virol 1998 Nov;72(11):9069-78
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)
Vaccine Name DeltavpuDeltaNefSHIV-4 *Type:* Live Attenuated Virus *Route:* Subcutaneous
Vaccine Name DeltavpuSHIV-ppc *Type:* Live Attenuated Virus *Route:* Oral
Challenge SHIV.KU1 *Route:* Oral, Vaginal or perivaginal
Main Findings

- 4/4 controls developed low CD4+ T-cell counts (<200/µl) and AIDS.
- 12/12 vaccinees became infected with SHIVKU-1, and two in group 1 developed a persistent productive infection followed by development of AIDS in one. The other 10 maintained almost complete control over virus replication
- First demonstration of protection against virulent SHIV administered by the intravaginal route. Thus, sexually transmitted HIV disease can be prevented by parenteral or oral immunization

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NHP.113 (11054270) **Characterization of immune escape viruses from a macaque immunized with live-virus vaccine and challenged with pathogenic SHIVKU-1**
Authors Stipp HL, Kumar A, Narayan O
Journal AIDS Res Hum Retroviruses 2000 Oct 10;16(15):1573-80
Objectives Challenge To characterize immune escape viruses (SHIV(KU-1/105w52) and SHIV(KU-1/105w98)) from a macaque immunized with DeltavpuDeltanef SHIV-4 and challenged with pathogenic SHIV(KU-1).
Main Findings

- The two newly identified escape variant viruses could not be neutralized by anti-SHIV(KU-1)-specific neutralizing antibodies and were poorly recognized by challenge virus-specific CTLs.
- Sequence analysis of the gene encoding gp120 revealed several mutations in the protein that might have contributed to the development of the immune-escape viruses.

NHP.114 (10888354) **Protective immune responses induced by a non-pathogenic simian/human immunodeficiency virus (SHIV) against a challenge of a pathogenic SHIV in monkeys**
Authors Yoshino N, Ami Y, Someya K, Ando S, Shinohara K, Tashiro F, Lu Y, Honda M
Journal Microbiol Immunol 2000;44(5):363-72
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name SHIV-NM3n *Type:* Live Attenuated Virus
Challenge SHIV89.6 *Route:* Intravenous

Main Findings

- After the heterologous virus challenge, all of the vaccinees were completely protected from SHIV challenge.
- The inhibition of CD4+ cell depletion was associated with maintaining the proliferative response of helper T-cells against SIV p27 in the vaccinated animals following the pathogenic virus challenge.
- Decline of CD28+ cells, the increase in CD95+ cells, and the enhancement of in vitro apoptosis in PBMC were inhibited in the non-pathogenic virus-inoculated animals.

NHP.115 (11348720) **Enhanced simian immunodeficiency virus-specific immune responses in macaques induced by priming with recombinant Semliki Forest virus and boosting with modified vaccinia virus Ankara**

Authors Nilsson C, Makitalo B, Berglund P, Bex F, Liljestrom P, Sutter G, Erfle V, ten Haaft P, Heeney J, Biberfeld G, Thorstensson R

Journal Vaccine 2001 May 14;19(25-26):3526-36

Objectives Challenge, Immunogenicity To investigate the the immunogenicity and protection from challenge of two vector-based vaccines, either given alone or in a prime-boost regimen.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Main Findings

- Generally, antibody responses, T-cell proliferative responses and cytotoxic T-cell responses remained low or undetectable in vaccinees receiving MVA-SIVmac or SFV-SIVmac alone, in contrast with monkeys who first received SFV-SIVmac twice and then were boosted with MVA-SIVmac.
- No evidence of protection was seen against an intrarectal heterologous SIVsm challenge given 3 months after the last immunization.

NHP.116 (11514733) **In situ hybridization and immunolabelling study of the early replication of simian immunodeficiency virus (SIVmacJ5) in vivo**

Authors Canto-Nogues C, Jones S, Sangster R, Silvera P, Hull R, Cook R, Hall G, Walker B, Stott EJ, Hockley D, Almond N

Journal J Gen Virol 2001 Sep;82(Pt 9):2225-34

Objectives Pathogenicity To determine the distribution of virus-infected cells in cynomolgus macaques following intravenous challenge with 1000 TCID50 of the wild-type simian immunodeficiency virus SIVmacJ5 (stock J5C).

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Challenge SIVmac251(32H) *Route:* Intravenous

Main Findings

- Following intravenous inoculation with SIVmacJ5, all macaques became infected, as determined by virus isolation and/or DNA PCR.
- At day 4 post-infection detection of the virus was sporadic. By 7 dpc significant SIV loads were detected in the blood and lymphoid tissues by DNA PCR and virus co-cultivation. Large numbers of cells expressing SIV RNA were detected in mesenteric lymph nodes by ISH and significantly fewer ($P<0.05$) in the spleen.
- A major site of the initial replication of SIV is gut-associated lymphoid tissue.

NHP.117 (11983253) **Passive immunization with human neutralizing monoclonal antibodies: correlates of protective immunity against HIV**

Authors Xu W, Hofmann-Lehmann R, McClure HM, Ruprecht RM

Journal Vaccine 2002 May 6;20(15):1956-60

Objectives Challenge, Immunogenicity, Passive Immunization To determine the value of passive immunization to protect rhesus macaque against SHIV challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name F105/2G12/2F5 mab *Type:* Passive Antibody

Challenge SHIV89.6P, SHIV-vpu+ *Route:* Intravenous, Oral

Main Findings

- Passive immunization with synergistic combinations of human monoclonal antibodies (mAbs) directed against conserved epitopes of the HIV envelope completely protected 13/16 rhesus monkeys challenged intravenously or orally with chimeric simian-humanimmunodeficiency virus (SHIV) strains; partial protection was seen in another 2.
- A high degree of protection was seen among orally challenged neonates.

NHP.118 (11752703) **A DNA/MVA-based candidate human immunodeficiency virus vaccine for Kenya induces multi-specific T cell responses in rhesus macaques**

Authors Wee EG, Patel S, McMichael AJ, Hanke T

Journal J Gen Virol 2002 Jan;83(Pt 1):75-80

Objectives Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pTHr.HIVA DNA *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name MVA.HIVA *Type:* DNA *Route:* Intradermal

Main Findings

- The very same vaccines that had entered clinical trials in Oxford and Nairobi (plasmid pTHr.HIVA DNA and recombinant modified vaccinia virus Ankara MVA.HIVA in a prime-boost protocol) induced cellular immune responses specific for multiple HIV-derived epitopes in rhesus macaques.

NHP.119 (11752704) **Induction of anti-simian immunodeficiency virus cellular and humoral immune responses in rhesus macaques by peptide immunogens: correlation of CTL activity and reduction of cell-associated but not plasma virus load following challenge**

Authors Vogel TU, Beer BE, zur Megede J, Ihlenfeldt HG, Jung G, Holzammer S, Watkins DI, Altman JD, Kurth R, Norley S

Journal J Gen Virol 2002 Jan;83(Pt 1):81-91

Objectives Challenge, Immunogenicity To test the ability of branched peptide constructs to induce humoral and celular response against SIV infection in rhesus macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name P3CSS CTL *Type:* Synthetic Protein/Peptide *Route:* Subcutaneous

Vaccine Name V2-P3CSS *Type:* Synthetic Protein/Peptide *Route:* Subcutaneous

Vaccine Name V2-MAP *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular

Vaccine Name V4.32-MAP *Type:* Synthetic Protein/Peptide *Routes:* Subcutaneous, Intramuscular

Challenge SIV mac251 (European) stock 5 *Route:* Intravenous

Main Findings

- Although none of the monkeys were protected from infection, most demonstrated an anamnestic CTL response with epitope-specific CTL precursor frequencies reaching as high as 1 in 20 total PBMC as measured by limiting dilution CTL assay or 25% of all CD8+ T-cells using tetrameric MHC-I/peptide complexes.
- A significant inverse correlation between the levels of CTLp and the number of infected cells in circulation. However, no such correlation with the plasma viral load (RNA copies/ml) was evident

NHP.120 (12009295) **Evaluation of SIV library vaccines with genetic cytokines in a macaque challenge**

Authors Sykes KF, Lewis MG, Squires B, Johnston SA

Journal Vaccine 2002 May 22;20(17-18):2382-95

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIV Random-GLV *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name SIV-Run-Cyt. GLV *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name SIV Diected GLV *Type:* DNA *Routes:* Intradermal, Intramuscular

Challenge SIVmac251 *Route:* Intravenous

Main Findings

- 8/12 animals in the three test groups showed some anti-SIV immune response, whereas the controls did not.
- Six months after priming, monkeys were intravenously challenged with virulent SIVmac251: All were infected but animals in two groups vaccinated with SIV libraries showed a trend toward lower viral-loads, mitigated clinical disease, and higher survival rates than controls.

- Significantly, co-administering the GMCSF and IL-12-encoding plasmids worsened the measures of protection.

NHP.121 (11907220) **Outcome of simian-human immunodeficiency virus strain 89.6p challenge following vaccination of rhesus macaques with human immunodeficiency virus Tat protein**

Authors Silvera P, Richardson MW, Greenhouse J, Yalley-Ogunro J, Shaw N, Mirchandani J, Khalili K, Zagury JF, Lewis MG, Rappaport J

Journal J Virol 2002 Apr;76(8):3800-9

Objectives Challenge, Immunogenicity To investigate whether vaccination with biologically active Tat or inactive Tat toxoid derived from HIV-1(IIIB) and SHIV strain 89.6p would induce protective immunity in rhesus macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name HIV-1 HXBc2 Tat Toxoid *Type:* Other *Route:* Intramuscular

Vaccine Name SHIV89.6P tat toxoid *Type:* Other *Route:* Intramuscular

Vaccine Name HIV-1 HXBc2 Tat *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name SHIV89.6P tat *Type:* Purified Viral Products *Route:* Intramuscular

Challenge SHIV89.6P *Route:* Intravenous

Main Findings

- Vaccination induced high titers of anti-Tat immunoglobulin G in all immunized animals by week 7, but titers were somewhat lower in the 89.6p Tat group.
- Tat-specific T-helper responses were detected in 50% of immunized animals.
- T-cell epitopes appeared to map within amino acids (aa) 1 to 24 and aa 37 to 66.
- Tat-specific gamma interferon responses were detected in CD4+ and/or CD8+ T lymphocytes in 11/16 immunized animals on the day of challenge.
- All animals became infected upon intravenous challenge with 30 AID50 of SHIV 89.6p, and there were no significant differences in viral loads or CD4+ T-cell counts between immunized and control animals

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NHP.123 (11823518) **Recombinant canarypox vaccine-elicited CTL specific for dominant and subdominant simian immunodeficiency virus epitopes in rhesus monkeys**

Authors Santra S, Schmitz JE, Kuroda MJ, Lifton MA, Nickerson CE, Lord CI, Pal R, Franchini G, Letvin NL

Journal J Immunol 2002 Feb 15;168(4):1847-53

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name ALVAC-SIV-gpe (vcp180) *Type:* Recombinant Vector (virus/bacteria)

Challenge SIVmac251 *Route:* Intrarectal

Main Findings

- Following a series of five immunizations, memory gag-specific (not pol) CTL responses specific were demonstrated in vaccinated monkeys.
- Following challenge with SIVmac251, the vaccinated animals developed high frequency CTL responses specific for the dominant Gag epitope, associated with the early containment of viral replication.
- The vaccinees, but not the control animals, developed CTL responses to the subdominant Pol epitope that were detectable only after containment of early viremia.

NHP.124 (12076047) **DNA prime/protein boost vaccine strategy in neonatal macaques against simian human immunodeficiency virus**

Authors Rasmussen RA, Hofmann-Lehman R, Montefiori DC, Li PL, Liska V, Vlasak J, Baba TW, Schmitz JE, Kuroda MJ, Robinson HL, McClure HM, Lu S, Hu SL, Rizvi TA, Ruprecht RM

Journal J Med Primatol 2002 Feb;31(1):40-60

Objectives Challenge, Immunogenicity .

Main Findings

- Following SHIV-vpu+ challenge, containment of infection was observed in 4/15 animals given DNA priming/protein boost vaccination and in 3/4 animals given gp160 boosts only.
- Rechallenge with homologous virus of 6 animals that contained the first challenge virus resulted in rapid viral clearance or low viral loads.

- Upon additional rechallenge with heterologous, pathogenic SHIV89.6P, 4/6 animals maintained normal CD4+ T-cell counts with no or limited SHIV89.6P infection.
- Humoral and cellular immune mechanisms may have contributed to the containment of SHIV89.6P; however, viral interference with SHIV-vpu+ could also have played a role.
- Immunogenicity and efficacy of candidate AIDS vaccines are not affected when vaccination is initiated during infancy as compared with later in life

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NHP.125 (11907330) **Immunization with recombinant modified vaccinia virus Ankara can modify mucosal simian immunodeficiency virus infection and delay disease progression in macaques**

Authors Nilsson C, Sutter G, Walther-Jallow L, ten Haaft P, Akerblom L, Heeney J, Erfle V, Bottiger P, Biberfeld G, Thorstensson R

Journal J Gen Virol 2002 Apr;83(Pt 4):807-18

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name rMVA (SIVsm) gagpolenv *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name Native SIV gp148 env *Type:* Purified Viral Products *Route:* Intramuscular

Vaccine Name SIVmac251 p27 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge SIVsm *Route:* Intrarectal

Main Findings

- At the time of challenge, antibody titers to SIV Env and lymphocyte proliferation responses to whole viral antigen were highest in vaccinees receiving MVA-SIVsm with protein immunizations.
- One immunized animal was completely protected from intrarectal challenge SIVsm.
- A prolonged survival time was observed in 2/4 monkeys in each of the groups immunized with MVA-SIVsm, in 2 monkeys given MVA-SIVsm followed by protein and in 3/4 monkeys given wild-type MVA, compared with naive controls.
- Immunization with MVA-SIVsm, as well as wild-type MVA alone, seemed to delay disease progression after mucosal SIV infection in a proportion of the monkeys.

NHP.126 (11751978) **Vaccine protection against functional CTL abnormalities in simian human immunodeficiency virus-infected rhesus monkeys**

Authors McKay PF, Schmitz JE, Barouch DH, Kuroda MJ, Lifton MA, Nickerson CE, Gorgone DA, Letvin NL

Journal J Immunol 2002 Jan 1;168(1):332-7

Objectives Challenge, Immunogenicity To assess cytokine production by virus-specific CTL in the rhesus monkey model for AIDS to determine its contribution to the functional impairment of CTL.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name HIV-1.89.6P env DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name SIVmac239 gag DNA *Type:* DNA *Route:* Intramuscular

Challenge SIVmac251 (J5), SHIV89.6, SHIV89.6P *Route:* Intravenous

Main Findings

- CTL from monkeys infected with nonpathogenic isolates of simian and simian-human immunodeficiency virus expressed high levels of IFN-gamma, TNF-alpha, and IL-2 after in vitro exposure to a nonspecific mitogen or the optimal peptide representing a dominantvirus-specific CTL epitope.
- CTL from vaccinated monkeys that effectively controlled the replication of a highly pathogenic simian-human immunodeficiency virus isolate following challenge demonstrated a preserved capacity to produce these cytokines.

NHP.127 (12743287) **Comparative immunogenicity in rhesus monkeys of DNA plasmid, recombinant vaccinia virus, and replication-defective adenovirus vectors expressing a human immunodeficiency virus type 1 gag gene**

Authors Casimiro DR, Chen L, Fu TM, Evans RK, Caulfield MJ, Davies ME, Tang A, Chen M, Huang L, Harris V, Freed DC, Wilson KA, Dubey S, Zhu DM, Nawrocki D, Mach H, Troutman R, Isopi L, Williams D, Hurni W, Xu Z, Smith JG, Wang S, Liu X, Guan L, Long R, Trigona W, Heidecker GJ, Perry HC, Persaud N, Toner TJ, Su Q, Liang X, Youil R, Chastain M, Bett AJ, Volkin DB, Emini EA, Shiver JW

Journal J Virol 2003 Jun;77(11):6305-13
Objectives Immunogenicity To evaluate an MVA vector and a replication-defective adenovirus serotype 5 (Ad5) vector, each expressing the same codon-optimized HIV-1 gag gene for immunogenicity in rhesus monkeys.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- The Ad5-gag vector was the most effective in eliciting anti-Gag CTL; the vaccine produced both CD4(+) and CD8(+) T-cell responses, with the latter consistently being the dominant component.
- Of the formulations tested, the DNA-CRL1005 vaccine primed T-cell responses most effectively and provided the best overall immune responses after boosting with Ad5-gag.
- Conclusion: An immunization strategy for humans that is based on the adenovirusvector and in which existing adenovirus immunity may be overcome by combined immunization with adjuvanted DNA and adenovirus vector boosting

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NHP.128 (11751749) **Prime-boost immunization generates a high frequency, high-avidity CD8(+) cytotoxic T lymphocyte population**
Authors Estcourt MJ, Ramsay AJ, Brooks A, Thomson SA, Medveckzy CJ, Ramshaw IA
Journal Int Immunol 2002 Jan;14(1):31-7
Objectives Challenge, Immunogenicity To study a 'prime-boost' immunization with DNA vaccines and recombinant poxvirus vectors that generates high frequencies of CTL.
Main Findings

- The 'prime-boost' immunization with DNA vaccines and recombinant poxvirus vectors generated high frequencies of cytotoxic T lymphocytes (CTL) that recognize target cells expressing very low levels of specific antigen; these cells persist for at least 6 months at levels representing approximately 10% of the CD8(+) T cell population.
- Prime-boost immunized animals were capable of eliminating target cells expressing 10- to 100-fold less immunogenic peptide than mice given either vector alone.
- Viral challenge led to rapid expansion of CTL effectors in prime-boost groups, to levels representing >30% of total CD8(+) T cell numbers

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NHP.129 (12208982) **Sustained Peptide-Specific Gamma Interferon T-Cell Response in Rhesus Macaques Immunized with Human Immunodeficiency Virus gag DNA Vaccines**
Authors Caulfield MJ, Wang S, Smith JG, Tobery TW, Liu X, Davies ME, Casimiro DR, Fu TM, Simon A, Evans RK, Emini EA, Shiver J
Journal J Virol 2002 Oct 1;76(19):10038-43
Objectives Immunogenicity To examine the influence of dose and method of antigen delivery on the dynamics and durability of T-cell responses to candidate human immunodeficiency virus (HIV) vaccines.
Main Findings

- Cell-mediated immune (CMI) response in rhesus macaques persisted for at least 18 months following a four-dose vaccination regimen.
- The plasmid vaccine, with or without CRL8623, was immunogenic in macaques; however, the form coadministered with adjuvant exhibited improved T-cell responses, with a bias toward more antigen-specific CD8(+) T cells.
- Broad and durable CMI response to HIV DNA vaccines can be induced in a relevant nonhuman primate model.

NHP.131 (12127792) **Protection by intranasal immunization of a nef-deleted, nonpathogenic SHIV against intravaginal challenge with a heterologous pathogenic SHIV**
Authors Enose Y, Ui M, Miyake A, Suzuki H, Uesaka H, Kuwata T, Kunisawa J, Kiyono H, Takahashi H, Miura T, Hayami M
Journal Virology 2002 Jul 5;298(2):306-16
Objectives Challenge, Immunogenicity To examine the possibility of using an attenuated virus for mucosal immunization, four female macaques were intranasally or intravenously administered with a chimeric simian-human immunodeficiency virus with a deleted nef gene (SHIV-dn).
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SHIV-dn *Type:* Live Attenuated Virus *Routes:* Intravenous, Intranasal
Challenge SHIV89.6P *Route:* Vaginal or perivaginal

Main Findings

- Although all the monkeys had anti-HIV-1 antibodies with neutralizing activity in the plasma, the intranasally immunized monkeys had much higher levels of HIV-1 Env-specific IgG and IgA antibodies in mucosal secretions compared with the intravenously immunized monkeys.
- 3/4 intranasally immunized monkeys were completely protected from intravaginal challenge with a pathogenic virus, SHIV-89.6P, whereas only 1 intravenously immunized monkey was protected.
- Intranasal immunization of an attenuated virus can induce the protective efficacy against intravaginal infection.

NHP.132 (12097576) **Different patterns of immune responses but similar control of a simian-human immunodeficiency virus 89.6P mucosal challenge by modified vaccinia virus Ankara (MVA) and DNA/MVA vaccines**

Authors Amara RR, Villinger F, Staprans SI, Altman JD, Montefiori DC, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McClure HM, Moss B, Robinson HL

Journal J Virol 2002 Aug;76(15):7625-31

Objectives Challenge, Immunogenicity To evaluate the ability of the MVA component of this vaccine to serve as both a prime and a boost for an AIDS vaccine.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIV-HIV89.6 DNA vaccine *Type:* DNA *Route:* Intradermal

Vaccine Name rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intravenous, Intramuscular

Challenge SHIV89.6P *Route:* Intrarectal

Main Findings

- Compared to the DNA/MVA vaccine, the MVA-only vaccine raised less than one-tenth the number of vaccine-specific T cells but 10-fold-higher titers of binding antibody for Env.
- Postchallenge, the animals vaccinated with MVA alone increased their CD8 cell numbers to levels that were similar to those seen in DNA/MVA-vaccinated animals.
- By 5 wpc, the MVA-only-vaccinated animals had achieved as good control of the viral infection as the DNA/MVA group.

NHP.133 (11085582) **SHIV89.6P pathogenicity in cynomolgus monkeys and control of viral replication and disease onset by human immunodeficiency virus type 1 Tat vaccine**

Authors Cafaro A, Caputo A, Maggiorella MT, Baroncelli S, Fracasso C, Pace M, Borsetti A, Sernicola L, Negri DR, Ten Haaft P, Betti M, Michelini Z, Macchia I, Fanales-Belasio E, Belli R, Corrias F, Butto S, Verani P, Titti F, Ensoli B

Journal J Med Primatol 2000 Aug;29(3-4):193-208

Objectives Challenge, Immunogenicity .

Main Findings

- A vaccine based on the Tat protein of HIV blocks primary infection with SHIV89.6P and prevents the CD4 T cell decline and disease onset in cynomolgus monkeys.
- No signs of virus replication were found in five out of seven vaccinated macaques for almost 1 year of follow-up.
- Since the inoculated virus is shown to be highly pathogenic in cynomolgus macaques, the results indicate efficacy of Tat vaccination in protection against highly pathogenic virus challenge.
- There was a correlation of protection with a cytotoxic T cell response.

NHP.134 (10482571) **Role of immune responses against the envelope and the core antigens of simian immunodeficiency virus SIVmne in protection against homologous cloned and uncloned virus challenge in Macaques**

Authors Polacino PS, Stallard V, Klaniecki JE, Pennathur S, Montefiori DC, Langlois AJ, Richardson BA, Morton WR, Benveniste RE, Hu SL

Journal J Virol 1999 Oct;73(10):8201-15

Objectives Challenge, Immunogenicity To examine (i) the effect of priming by recombinant vaccinia virus; (ii) the role of surface antigen gp130; and (iii) the role of core antigens (Gag and Pol) in eliciting protective immunity.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name Recombinant vaccinia virus vac-gp160 (v-SE5) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name Recombinant vaccinia gp130 (v-SE6) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification
Vaccine Name Recombinant vaccinia gagpol (v-SG11) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification
Vaccine Name Recombinant vaccinia gagpolenv (v-SGE14) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification
Vaccine Name rgp160 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name Recombinant gp130 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name Recombinant gagpol particles *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name Recombinant gagpolenv particles *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge SIV(Mne) clone E11S *Route:* Intravenous
Main Findings

- Priming with recombinant vaccinia virus was more effective than subunit antigen in eliciting protective responses.
- While both gp130 and gp160 elicited similar levels of SIV-specific antibodies, gp130 was not as effective as gp160 in protection, indicating a possible role for the transmembrane protein in presenting functionally important epitopes.
- Although animals immunized with core antigens failed to generate any neutralizing antibody and were infected upon challenge, their virus load was 50- to 100-fold lower than that of the controls.
- Complete protection against intravenous infection by the pathogenic uncloned SIVmne was achieved by immunization with both the envelope and the core antigens.

NHP.135 (10203053) **Protection from pathogenic SIV challenge using multigenic DNA vaccines**
Authors Haigwood NL, Pierce CC, Robertson MN, Watson AJ, Montefiori DC, Rabin M, Lynch JB, Kuller L, Thompson J, Morton WR, Benveniste RE, Hu SL, Greenberg P, Mossman SP
Journal Immunol Lett 1999 Mar;66(1-3):183-8
Objectives Challenge, Immunogenicity To compare the efficacy of DNA immunization alone and in combination with subunit protein boosts.
Main Findings

- Humoral immune responses were stronger in the macaques receiving subunit boosts.
- Significant Nab titers to SIVmne detected in one of the subunit-boosted animals and in none of the DNA-only animals prior to challenge.
- T-cell proliferative responses to gp160 and to Gag were detected in all immunized animals after three immunizations, and these responses increased after four immunizations.

NHP.136 (9930869) **Neutralizing antibody directed against the HIV-1 envelope glycoprotein can completely block HIV-1/SIV chimeric virus infections of macaque monkeys**
Authors Shibata R, Igarashi T, Haigwood N, Buckler-White A, Ogert R, Ross W, Willey R, Cho MW, Martin MA
Journal Nat Med 1999 Feb;5(2):204-10
Objectives Challenge, Immunogenicity, Passive Immunization To assess whether human immunodeficiency virus type 1 (HIV-1) envelope-specific antibodies confer resistance against primate lentivirus infections.
Main Findings

- Passive immunization of pig-tailed macaques with IgG purified from multiply infected HIV-1+ chimpanzees followed by intravenous challenge with a SHIV (env derived form HIV-1DH12).
- Anti-SHIV neutralizing activity is the absolute requirement for antibody-mediated protection in vivo.
- Administration of non-neutralizing anti-HIV IgG neither inhibited nor enhanced a subsequent SHIV infection.

NHP.137 (9863867) **Live attenuated simian immunodeficiency virus (SIV)mac in macaques can induce protection against mucosal infection with SIVsm**
Authors Nilsson C, Makitalo B, Thorstensson R, Norley S, Binninger-Schinzel D, Cranage M, Rud E, Biberfeld G, Putkonen P
Journal AIDS 1998 Dec 3;12(17):2261-70
Objectives Challenge, Immunogenicity To investigate whether vaccination of macaques with attenuated simian immunodeficiency virus (SIV)macC8 could induce long-term protective immunity against rectal exposure to SIVsm and intravenous exposure to the more divergent HIV-2.

Main Findings

- At the time of challenge, 8/10 vaccinees were PCR-positive for SIVmacC8 DNA but no virus could be isolated from peripheral blood mononuclear cells.
- After SIVsm challenge, 3/6 vaccinees were repeatedly SIVsm PCR-negative. In 1/3 infected monkeys, the challenge virus was initially suppressed but the monkey ultimately developed AIDS after increased replication of the pathogenic virus. Monkeys protected from initial challenge remained uninfected after rechallenge.
- Infection with SIV did not protect from challenge with HIV-2.
- All controls became infected with either SIVsm or HIV-2.
- At the time of challenge the vaccinees had neutralizing antibodies to SIVmac but no demonstrable cross-neutralizing antibodies to SIVsm or HIV-2.
- Titers of antigen-binding or neutralizing antibodies did not correlate with protection.
- Cytotoxic T-cell responses to SIV Gag/Pol and virus-specific T-cell proliferative responses were low.

NHP.138 (9747945) **Presence of circulating CTL induced by infection with wild-type or attenuated SIV and their correlation with protection from pathogenic SHIV challenge**

Authors Vogel TU, Fournier J, Sherring A, Ko D, Parenteau M, Bogdanovic D, Mihowich J, Rud EW

Journal J Med Primatol 1998 Apr-Jun;27(2-3):65-72

Objectives Challenge, Immunogenicity To evaluate the role of CTLs in the protection from challenge with pathogenic SHIV in macaques vaccinated with attenuated virus.

Main Findings

- SIVmacC8-vaccinated monkeys demonstrated a broader CTL response than the SIVmacJ5-infected animals.
- CTL against some proteins in SIVmacC8-vaccinated monkeys became progressively more difficult to detect through the day of challenge.
- Neither the presence of circulating CTL nor the CTL precursor frequency against any of the tested proteins correlated with the outcome of the challenge when SIVmacJ5- and SIVmacC8-infected animals were analyzed together.
- Only the protected animal had detectable CTL precursors with moderate frequencies against all three tested proteins at the day of challenge.

NHP.139 (9814958) **Prime-boost immunization strategies against HIV**

Authors Barnett SW, Klinger JM, Doe B, Walker CM, Hansen L, Duliege AM, Sinangil FM

Journal AIDS Res Hum Retroviruses 1998 Oct;14 Suppl 3:S299-309

Objectives Passive immunotherapy .

NHP.140 (14498984) **Comparison of virology and immunology in SHIV 89.6 proviral DNA and virus-inoculated rhesus macaques**

Authors Busch M, Lu D, Fritts L, Lifson JD, Miller CJ

Journal J Med Primatol 2003 Aug;32(4-5):240-6

Objectives Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SHIV89.6 *Type:* Live Virus *Routes:* Intravenous, Vaginal or perivaginal, Intranasal

Vaccine Name pMA SHIV89.6 *Type:* DNA *Routes:* Targeted Lymph node immunization, Intradermal, Intramuscular, Intranasal

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NHP.141 (9811775) **Vaccine protection against a heterologous, non-syncytium-inducing, primary human immunodeficiency virus**

Authors Robert-Guroff M, Kaur H, Patterson LJ, Leno M, Conley AJ, McKenna PM, Markham PD, Richardson E, Aldrich K, Arora K, Murty L, Carter L, Zolla-Pazner S, Sinangil F

Journal J Virol 1998 Dec;72(12):10275-80

Objectives Challenge, Immunogenicity Follow up study: to challenge the three previously protected chimpanzees a third time, with the heterologous primary isolate HIV-15016.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Vaccine Name AD4-gp160(MN) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal

Vaccine Name AD5-gp160(MN) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal
Vaccine Name AD7-gp160(MN) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal
Vaccine Name CHO cell-expressed HIV-1SF2 gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge HIV-1.SF2, HIV-1.5016 *Route:* Intravenous
Main Findings

- Following challenge with HIV-1.5016, complete protection in 1/3 chimpanzees previously protected against low- and high-dose HIV-1SF2 exposures after immunization with an adenovirus-HIV-1MN gp160 priming-HIV-1SF2 gp120 boosting regimen.
- At challenge, the protected chimpanzee exhibited broad humoral immunity, including neutralizing antibody activity

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NHP.142 (9811759) **Enhanced T-cell immunogenicity and protective efficacy of a human immunodeficiency virus type 1 vaccine regimen consisting of consecutive priming with DNA and boosting with recombinant fowlpox virus**
Authors Kent SJ, Zhao A, Best SJ, Chandler JD, Boyle DB, Ramshaw IA
Journal J Virol 1998 Dec;72(12):10180-8
Objectives Challenge, Immunogenicity To evaluate a consecutive immunization strategy involving priming with DNA and boosting with rFPV vaccines encoding common HIV-1 antigens.
Main Findings

- A dramatic boosting effect on DNA vaccine-primed HIV-1-specific helper and cytotoxic T-lymphocyte responses, but a decline in HIV-1 antibody titers, was observed following rFPV immunization.
- The vaccine regimen protected macaques from an intravenous HIV-1 challenge, with the resistance most likely mediated by T-cell responses.

NHP.143 (9765452) **Oral immunization of macaques with attenuated vaccine virus induces protection against vaginally transmitted AIDS**
Authors Joag SV, Liu ZQ, Stephens EB, Smith MS, Kumar A, Li Z, Wang C, Sheffer D, Jia F, Foresman L, Adany I, Lifson J, McClure HM, Narayan O
Journal J Virol 1998 Nov;72(11):9069-78
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca (sp)
Main Findings

- Six adult macaques immunized subcutaneously with DeltavpuDeltanefSHIV-4 (vaccine 1), and six were immunized orally with DeltavpuSHIVPPc (vaccine 2). Both viruses caused infection in all inoculated animals, but whereas vaccine 1 virus caused only a nonproductive type of infection, vaccine 2 virus replicated productively but transiently for a 6- to 10-week period.
- The 12/12 vaccinated animals became infected with the challenge virus SHIVKU-1, and two in group 1 developed a persistent productive infection followed by development of AIDS in one. The other 10 have maintained almost complete control over virus replication even though spliced viral RNA was detected in lymph nodes.

NHP.144 (1466990) **Inactivated whole SIV vaccine in macaques: evaluation of protective efficacy against challenge with cell-free virus or infected cells**
Authors Johnson PR, Montefiori DC, Goldstein S, Hamm TE, Zhou J, Kitov S, Haigwood NL, Misher L, London WT, Gerin JL, et al.
Journal AIDS Res Hum Retroviruses 1992 Aug;8(8):1501-5
Objectives Challenge, Immunogenicity To evaluate the protective efficacy against challenge with cell-free virus or infected cells.

NHP.146 (1466992) **Prevention of HIV-2 and SIVSM infection in cynomolgus monkeys by active or passive immunization**
Authors Biberfield G, Putkonen P, Thorstensson R, Norrby E
Journal AIDS Res Hum Retroviruses 1992 Aug;8(8):1511-3
Objectives Challenge, Immunogenicity, Passive Immunization .
Main Findings

- Protection against homologous HIV-2 infection was demonstrated in 2/2 monkeys immunized with a Triton-X100-treated whole HIV-2SBL-6669 vaccine in incomplete Freund's adjuvant and in 2/4 monkeys immunized with a formalin-inactivated whole HIV-2 vaccine in RIBI adjuvant.

- Monkeys preinfected with a live poorly replicating HIV-2 strain were shown to develop cross-protection against SIV-induced disease.
- HIV-2 and SIVsm infection in cynomolgus monkeys can be prevented by passive immunization

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NHP.147 (1470916) **Cellular proteins bound to immunodeficiency viruses: implications for pathogenesis and vaccines**

Authors Arthur LO, Bess JW Jr, Sowder RC 2nd, Benveniste RE, Mann DL, Chermann JC, Henderson LE

Journal Science 1992 Dec 18;258(5090):1935-8

Main Findings

- Retracted from public display.

NHP.148 (1470917) **Protective effects of a live attenuated SIV vaccine with a deletion in the nef gene**

Authors Daniel MD, Kirchhoff F, Czajak SC, Sehgal PK, Desrosiers RC

Journal Science 1992 Dec 18;258(5090):1938-41

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239ΔNef *Type:* Live Attenuated Virus *Route:* Intramuscular

Challenge SIVmac239, SIVmac251 *Route:* Intravenous

Main Findings

- Rhesus monkeys vaccinated with live SIV deleted in nef were completely protected against challenge by intravenous inoculation of live, pathogenic SIV.
- 2/2 naive controls infected 14 dpc and dead of SAIDS 252 dpc.
- 2/2 vaccinees protected from increased viral load and disease and remain healthy >208 wpc (>4 years).
- 2/2 vaccinees protected from infection >208 wpc (>4 years).

NHP.149.1 (1677743) **Prevention of HIV-2 and SIVsm infection by passive immunization in cynomolgus monkeys**

Authors Putkonen P, Thorstensson R, Ghavamzadeh L, Albert J, Hild K, Biberfeld G, Norrby E

Journal Nature 1991 Aug 1;352(6334):436-8

Objectives Challenge, Passive Immunization To determine whether a transfer of antibodies can prevent HIV-2 and SIVsm (SIV of sooty mangabey origin) infection in cynomolgus monkeys.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name Anti-HIV-2 *Type:* Passive Antibody *Route:* Intravenous

Challenge HIV-2.SBL6669 *Route:* Intravenous

Main Findings

- All 6 control animals treated with normal monkey serum or no serum (n = 39) became infected by the challenge virus.
- 5/7 animals pretreated with antibody-containing serum at a dose of 9 ml kg-1 resisted infection.
- Conclusion: passively transferred antibodies can protect against a low-dose lentivirus challenge in a nonhuman primate

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NHP.149.2 (1677743) **Prevention of HIV-2 and SIVsm infection by passive immunization in cynomolgus monkeys**

Authors Putkonen P, Thorstensson R, Ghavamzadeh L, Albert J, Hild K, Biberfeld G, Norrby E

Journal Nature 1991 Aug 1;352(6334):436-8

Objectives Challenge, Passive Immunization .

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name DNA Vaccine pNL432-ZF1* *Type:* DNA *Route:* Intravenous

Vaccine Name Anti-HIV-2 *Type:* Passive Antibody *Route:* Intravenous

Main Findings

- Antibody titers declined to undetectable level after challenge.
- Active infection did not occur during 6-10 months of follow up in 3/4 passively immunized monkeys.

NHP.150.1 (8986737) **Resistance of neonatal monkeys to live attenuated vaccine strains of simian immunodeficiency virus**

Authors Wyand MS, Manson KH, Lackner AA, Desrosiers RC

Journal Nat Med 1997 Jan;3(1):32-6

Objectives Challenge, Immunogenicity, Passive Immunization .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- High viral loads and disease were observed in only 2 of 18 neonatal monkeys infected with gene-deleted vaccine strains of simian immunodeficiency virus.
- Pathogenicity was restricted to neonates born to unvaccinated mothers and that received extremely high doses of vaccine virus orally.
- No in utero transmission of vaccine virus was observed in 4 neonates born to mothers vaccinated during the second trimester.
- Conclusion: Live attenuated vaccine approach should remain a viable option for preventing HIV infection and disease in high-risk human populations.

NHP.150.2 (8986737) **Resistance of neonatal monkeys to live attenuated vaccine strains of simian immunodeficiency virus**

Authors Wyand MS, Manson KH, Lackner AA, Desrosiers RC

Journal Nat Med 1997 Jan;3(1):32-6

Objectives Challenge, Passive Immunization .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Oral, Intraplacental

Main Findings

- 0/4 cases of vertical transmission of SIVmac239Δ3.
- Maternal antibody dd not prevent transmission of the autologous challenge in 3/4 neonates.

NHP.151 (1733103) **Immunization with tween-ether-treated SIV adsorbed onto aluminum hydroxide protects monkeys against experimental SIV infection**

Authors Stahl-Hennig C, Voss G, Nick S, Petry H, Fuchs D, Wachter H, Coulibaly C, Luke W, Hunsmann G

Journal Virology 1992 Feb;186(2):588-96

Objectives Challenge, Immunogenicity To study immunogenicity and protective values of tween-ether-disrupted SIVmac251/32H adsorbed onto aluminum hydroxide immunization in monkeys.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac251/32H (Tween/Ether) *Type:* Whole (killed) Inactivated Virus *Route:* Intravenous

Challenge SIVmac251(32H) *Route:* Intravenous

Main Findings

- 4/7 immunized animals did not show any signs of virus replication and therefore appeared to be protected.
- Nonvaccinated control animals and the vaccine failures showed a rise in their urinary neopterin concentrations 1 to 2 weeks after infection.
- After the challenge, control animals and infected vaccinees showed a primary or secondary antibody response while antibody titers declined in virus-negative animals.
- Specific cytotoxic T-lymphocytes were not present prior to challenge.

NHP.152.1 (1741059) **Prevention of HIV-1 infection in chimpanzees by gp120 V3 domain-specific monoclonal antibody**

Authors Emini EA, Schleif WA, Nunberg JH, Conley AJ, Eda Y, Tokiyoshi S, Putney SD, Matsushita S, Cobb KE, Jett CM, et al.

Journal Nature 1992 Feb 20;355(6362):728-30

Objectives Challenge, Passive Immunization To demonstrate the protective efficacy of anti-V3 domain antibody in vivo.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Vaccine Name Cβ1 anti-V3 *Type:* Passive Antibody *Route:* Intravenous

Challenge SIVmac251(32H) *Route:* Intravenous

Main Findings

- 1/1 control chimpanzee infected.

- 1/1 protected from infection >336 dpc.

NHP.152.2 (1741059) **Prevention of HIV-1 infection in chimpanzees by gp120 V3 domain-specific monoclonal antibody**

Authors Emini EA, Schleif WA, Nunberg JH, Conley AJ, Eda Y, Tokiyoshi S, Putney SD, Matsushita S, Cobb KE, Jett CM, et al.

Journal Nature 1992 Feb 20;355(6362):728-30

Objectives Challenge, Immunotherapy To demonstrate the protective efficacy of anti-V3 post challenge with live virus.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Vaccine Name Cβ1 anti-V3 *Type:* Passive Antibody *Route:* Intravenous

Challenge SIVmac251(32H) *Route:* Intravenous

Main Findings

- 1 OF 1 CONTROL CHIMPANZEE INFECTED 56 DPC.
- 1 OF 1 PROTECTED FROM INFECTION >224 DPC.

NHP.153 (9593009) **Passive immunization of newborn rhesus macaques prevents oral simian immunodeficiency virus infection**

Authors Van Rompay KK, Berardi CJ, Dillard-Telm S, Tarara RP, Canfield DR, Valverde CR, Montefiori DC, Cole KS, Montelaro RC, Miller CJ, Marthas ML

Journal J Infect Dis 1998 May;177(5):1247-59

Objectives Challenge, Passive Immunization To determine if passively acquired antiviral antibodies modulate virus transmission and disease progression in human pediatric AIDS.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Untreated neonates became infected after oral SIV inoculation and had high viremia, and most animals developed fatal AIDS within 3 months.
- In contrast, SIV hyperimmune serum given subcutaneously prior to oral SIV inoculation protected 6 newborns against infection.
- When SIV hyperimmune serum was given to 3 newborns 3 weeks after oral SIV inoculation, viremia was not reduced, and all 3 infants died within 3 months of age due to AIDS and immune-complex disease.
- Conclusion: passively acquired anti-HIV IgG may decrease perinatal HIV transmission

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NHP.154 (1871125) **Protection of macaques with a simian immunodeficiency virus envelope peptide vaccine based on conserved human immunodeficiency virus type 1 sequences**

Authors Shafferman A, Jahrling PB, Benveniste RE, Lewis MG, Phipps TJ, Eden-McCutchan F, Sadoff J, Eddy GA, Burke DS

Journal Proc Natl Acad Sci U S A 1991 Aug 15;88(16):7126-30

Objectives Challenge, Immunogenicity To evaluate envelope peptide vaccine based on conserved HIV-1 sequences.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVenv-Bgal peptides *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge SIV(Mne) clone E11S *Route:* Intravenous

Main Findings

- After challenge with virulent virus, controls became virus positive and developed gradually rising antibody titers to SIV over 63 weeks.
- Immunized macaques developed a postchallenge anamnestic response to SIVenv antigens within 3-6 weeks followed bya gradual, fluctuating decline in SIV antibody titers and partial or total suppression of detectable SIV.
- Virus suppression correlated with prechallenge neutralizing antibody titers.

NHP.155 (1883540) **Efficacy of SIV/deltaB670 glycoprotein-enriched and glycoprotein-depleted subunit vaccines in protecting against infection and disease in rhesus monkeys**

Authors Murphey-Corb M, Montelaro RC, Miller MA, West M, Martin LN, Davison-Fairburn B, Ohkawa S, Baskin GB, Zhang JY, Miller GB, et al.

Journal AIDS 1991 Jun;5(6):655-62

Objectives Challenge, Immunogenicity To define the role of virion components in the induction of protective immunity.

Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- Immunization with the glycoprotein-enriched preparation prevented infection in 2/4 monkeys, whereas the glycoprotein-depleted vaccine failed to prevent infection in all 4 vaccinates tested.
- Glycoprotein-depleted vaccine appeared to moderate the progression of SIV-induced disease compared with non-immunized infected control monkeys inoculated with the same challenge dose.
- Conclusion: subunit vaccines containing sufficient quantities of viral glycoproteins can protect against SIV infection, whereas subunit vaccines composed predominantly of viral core proteins cannot.

NHP.156 (1907354) **Prevention of HIV-1 IIIB infection in chimpanzees by CD4 immunoadhesin**
Authors Ward RH, Capon DJ, Jett CM, Murthy KK, Mordenti J, Lucas C, Frie SW, Prince AM, Green JD, Eichberg JW
Journal Nature 1991 Aug 1;352(6334):434-6
Objectives Challenge, Passive Immunization To evaluate the CD4 immunoadhesin (CD4-IgG) in the protection against HIV-1 infection in chimpanzees.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Vaccine Name CHO-SIVgp120 *Type:* DNA *Route:* Intravenous
Vaccine Name CD4 Immunoadhesin (CD4-IgG) *Type:* Other *Routes:* Intravenous, Intramuscular
Main Findings
- Pretreatment with CD4-IgG can prevent the infection of chimpanzees with HIV-1.

NHP.157.1 (1979369) **Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine**
Authors Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P
Journal Lancet 1990 Dec 22-29;336(8730):1538-41
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name Fixed inactivated SIVmac251 infected cells *Type:* Whole (killed) Inactivated Virus *Route:* Subcutaneous
Challenge SIVmac251 *Route:* –
Main Findings
- Upon challenged with 10 MID50 of SIVmac251, virus and proviral DNA were not found in any of the vaccinated cynomolgus macaques immunized with with inactivated SIV-infected cells and 'Quil-A' as adjuvant.
- Virus was repeatedly isolated from unvaccinated animals on at least 5 separate occasions and proviral DNA was detected in circulating lymphocytes by polymerase chain reaction amplification (Trials 1,2).
- In animals previously infected, vaccination regimen did not eliminate virus (Trial 3).

NHP.157.2 (1979369) **Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine**
Authors Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P
Journal Lancet 1990 Dec 22-29;336(8730):1538-41
Objectives Challenge, Immunogenicity see experiment 1 (except the challenge was carried out at week 18).
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name Fixed inactivated SIVmac251 infected cells *Type:* Whole (killed) Inactivated Virus *Route:* Subcutaneous
Challenge SIVmac251 *Route:* Subcutaneous
Main Findings
- See Experiment 1.

NHP.157.3 (1979369) **Preliminary report: protection of cynomolgus macaques against simian immunodeficiency virus by fixed infected-cell vaccine**
Authors Stott EJ, Chan WL, Mills KH, Page M, Taffs F, Cranage M, Greenaway P, Kitchin P

Journal Lancet 1990 Dec 22-29;336(8730):1538-41
Objectives Immunotherapy To evaluate whether a vaccine would reduce the course of SIV infection in animals already infected with the live virus and have active progressive infection.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name Fixed inactivated SIVmac251 infected cells *Type:* Whole (killed) Inactivated Virus *Route:* Subcutaneous
Challenge SHIV.DH12R-PS1 *Route:* –
Main Findings

- The vaccine that protected from challenge in Trial 1 and 2, did little to eliminate the virus in already infected animals

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NHP.158 (1979745) **Infection of cynomolgus monkeys with HIV-2 protects against pathogenic consequences of a subsequent simian immunodeficiency virus infection**
Authors Putkonen P, Thorstensson R, Albert J, Hild K, Norrby E, Biberfeld P, Biberfeld G
Journal AIDS 1990 Aug;4(8):783-9
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Main Findings

- At the time of SIV challenge the HIV-2-infected monkeys had neutralizing antibodies against HIV-2, but virus could no longer be recovered from their PBMCs and no clinical symptoms or decrease in CD4+ lymphocytes were observed.
- Protection from challenge with SIVsm including SIV-induced immunodeficiency (no decrease of CD4+ lymphocytes) and lymphadenopathy was observed in HIV-2-infected monkeys for 9 months post challenge.
- 4 naive control monkeys that were inoculated with the same dose of SIV became persistently infected and developed a decrease of the absolute numbers of CD4+ cells and showed a marked lymphadenopathy

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NHP.159 (1988952) **Immunization of chimpanzees confers protection against challenge with human immunodeficiency virus**
Authors Girard M, Kieny MP, Pinter A, Barre-Sinoussi F, Nara P, Kolbe H, Kusumi K, Chaput A, Reinhart T, Muchmore E, et al.
Journal Proc Natl Acad Sci U S A 1991 Jan 15;88(2):542-6
Objectives Challenge, Immunogenicity To evaluate protection against challenge with human immunodeficiency virus in immunized chimpanzees.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Main Findings

- After 6 months of follow-up, immunized chimpanzees appeared uninfected by serologic and virologic criteria, including polymerase chain reaction analysis and failure to isolate virus from peripheral blood lymphocytes, bone marrow, and lymph node tissue.
- Of 2 chimpanzees monitored for 1 yr, virus was isolated initially from 1 animal at 32 weeks, but the second chimpanzee was virus negative by all assays through 12 mo; the third animal has remained virus negative through 9 mo of follow-up.

NHP.160 (2078406) **Vaccine protection of rhesus macaques against simian immunodeficiency virus infection**
Authors Carlson JR, McGraw TP, Keddie E, Yee JL, Rosenthal A, Langlois AJ, Dickover R, Donovan R, Luciw PA, Jennings MB, et al.
Journal AIDS Res Hum Retroviruses 1990 Nov;6(11):1239-46
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque), Macaca (sp)
Main Findings

- Method: Rhesus macaques were immunized with an inactivated whole SIVmac vaccine and muramyl dipeptide (MDP), incomplete Freund's adjuvant (IFA), or aqueous suspension were challenged intravenously with 0.1 TCID50 of cell-free SIVmac.
- Virus was readily recovered from the PBMCs of 10/10 controls.
- 3/3 animals that received the vaccine with MDP were protected from challenge.
- 1/2 animals that received the vaccine with IFA were protected from challenge.
- 1/3 animals that received the aqueous vaccine were protected from challenge.

NHP.161 (2127681) **Yeast-expressed p55 precursor core protein of human immunodeficiency virus type 1 does not elicit protective immunity in chimpanzees**
Authors Emini EA, Schleif WA, Quintero JC, Conard PG, Eichberg JW, Vlasuk GP, Lehman ED, Polokoff MA, Schaeffer TF, Schultz LD, et al.
Journal AIDS Res Hum Retroviruses 1990 Nov;6(11):1247-50
Objectives Challenge, Immunogenicity .

NHP.162 (11282197) **Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P)**
Authors Cafaro A, Titti F, Fracasso C, Maggiorella MT, Baroncelli S, Caputo A, Goletti D, Borsetti A, Pace M, Fanales-Belasio E, Ridolfi B, Negri DR, Sernicola L, Belli R, Corrias F, Macchia I, Leone P, Michelini Z, ten Haaft P, Butto S, Verani P, Ensoli B
Journal Vaccine 2001 Apr 6;19(20-22):2862-77
Objectives Challenge .
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name pCV-tat *Type:* DNA *Route:* Intramuscular
Main Findings
- A Tat-expressing vector (pCV-tat), expressing the HIV-1 BH10 isolate Tat gene, and containing unmethylated CpG dinucleotides, induced an anti-Tat CTL response that was protective in containing primary infection with SHIV89.6P

NHP.163 (11282197) **Vaccination with DNA containing tat coding sequences and unmethylated CpG motifs protects cynomolgus monkeys upon infection with simian/human immunodeficiency virus (SHIV89.6P)**
Authors Cafaro A, Titti F, Fracasso C, Maggiorella MT, Baroncelli S, Caputo A, Goletti D, Borsetti A, Pace M, Fanales-Belasio E, Ridolfi B, Negri DR, Sernicola L, Belli R, Corrias F, Macchia I, Leone P, Michelini Z, ten Haaft P, Butto S, Verani P, Ensoli B
Journal Vaccine 2001 Apr 6;19(20-22):2862-77
Objectives Challenge, Immunogenicity To verify whether a DNA vaccine utilizing the tat gene expressed by a vector containing defined unmethylated CpG sequences would be capable of enhancing antigen-specific CTL responses against Tat and inducing an effective protection against AIDS.
Main Findings
- Intramuscular inoculation of the pCV-tat contained primary infection with the highly pathogenic SHIV89.6P virus preventing the CD4+ T cell decline in all the vaccinated monkeys.
- Undetectable virus replication and negative virus isolation correlatedin all cases with the presence of anti-Tat CTLs.
- CD8-mediated non cytolytic antiviral activity was present in all protected animals.
- CpG-rich tat DNA vaccine may represent a promising candidate for preventive and therapeutic vaccination against AIDS.

NHP.164 (9747943) **The role of type-1 and type-2 T-helper immune responses in HIV-1 vaccine protection**
Authors Heeney JL, van Gils ME, van der Meide P, de Giuli Morghen C, Ghioni C, Gimelli M, Raddelli A, Davis D, Akerblom L, Morein B
Journal J Med Primatol 1998 Apr-Jun;27(2-3):50-8
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name HIV-1.SF2 gp120/p24 Recombinant *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name V2.V3.HIV-1.SF2 Synth.peptides *Type:* Synthetic Protein/Peptide *Route:* Intramuscular
Challenge SHIV.SF13 *Route:* Intravenous

NHP.165 (9733821) **Env-independent protection induced by live, attenuated simian immunodeficiency virus vaccines**
Authors Gundlach BR, Reiprich S, Sopper S, Means RE, Dittmer U, Matz-Rensing K, Stahl-Hennig C, Uberla K
Journal J Virol 1998 Oct;72(10):7846-51
Objectives Challenge, Immunogenicity .
Main Findings

- In contrast to the results with naive control monkeys, no challenge virus could be isolated from the SIV-IL2- and SIVNU-infected macaques.
- Challenge virus sequences detected by nested PCR in some of the vaccinated macaques.
- 4 vaccinated macaques were rechallenged with an SIV-murine leukemia virus (MLV) hybrid were protected from productive infection with the SIV-MLV hybrid in the absence of measurable Nab, while 2 naive control monkeys were readily infected.
- Chemokine inhibition and receptor interference phenomena were not involved in protection.
- Conclusion: protective responses induced by live attenuated SIV vaccines can be independent of host immune reactions directed against Env

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NHP.166 (9718118) **Neutralizing antibodies administered before, but not after, virulent SHIV prevent infection in macaques**

Authors Foresman L, Jia F, Li Z, Wang C, Stephens EB, Sahni M, Narayan O, Joag SV

Journal AIDS Res Hum Retroviruses 1998 Aug 10;14(12):1035-43

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- 3/6 macaques inoculated with anti-SHIV plasma and challenged 24 hr later with approximately 300 AID of SHIV(KU-2), completely resisted infection with SHIV(KU-2). A fourth animal failed to yield infectious virus, but DNA extracted from its peripheral blood mononuclear cells (PBMC) and lymph nodes had viral sequences.
- 2/6 vaccinees had partial control of infection.
- 6/6 macaques given the same dose of anti-SHIV plasma 18 hr after exposure to virus became infected.
- 2/2 macaques given anti-SHIV plasma only 2 hr after exposure to virus became infected.

NHP.167 (9718117) **Fine specificity of anti-V3 antibodies induced in chimpanzees by HIV candidate vaccines**

Authors Coeffier E, Girard M, Barre-Sinoussi F, Meignier B, Muchmore E, Fultz PN, LeClerc C

Journal AIDS Res Hum Retroviruses 1998 Aug 10;14(12):1023-34

Objectives Challenge, Immunogenicity To assess the specificity of the anti-V3 antibody responses induced in chimpanzees immunized by various human immunodeficiency type 1 (HIV-1) candidate vaccines and challenged by heterologous strains of HIV-1.

Species/Subspecies Pan Troglodytes (Chimpanzee)

NHP.168 (8896498) **Immunogenicity and protective efficacy of a human immunodeficiency virus type 2 recombinant canarypox (ALVAC) vaccine candidate in cynomolgus monkeys**

Authors Andersson S, Makitalo B, Thorstensson R, Franchini G, Tartaglia J, Limbach K, Paoletti E, Putkonen P, Biberfeld G

Journal J Infect Dis 1996 Nov;174(5):977-85

Objectives Challenge, Immunogenicity To investigate the efficacy of a recombinant HIV-2 canarypox (ALVAC HIV-2) vaccine candidate given alone or in combination with HIV-2 envelope gp125 or HIV-2 V3 synthetic peptides in cynomolgus monkeys.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Main Findings

- High antibody titers to HIV-2 gp125 and significant lymphocyte proliferative responses to killed HIV-2 virions demonstrated in monkeys given booster immunizations with gp125.
- Neutralizing antibody titers were low.
- 3/12 monkeys generated HIV-2-specific cytotoxic T lymphocytes prior to viral challenge.
- 4/10 monkeys immunized with ALVAC HIV-2 plus HIV-2 gp125 or V3 peptides were protected

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NHP.169 (9714241) **In vivo resistance to simian immunodeficiency virus superinfection depends on attenuated virus dose**

Authors Cranage MP, Sharpe SA, Whatmore AM, Polyanskaya N, Norley S, Cook N, Leech S, Dennis MJ, Hall GA

Journal J Gen Virol 1998 Aug;79 (Pt 8):1935-44

NHP.170 (8892959) **Failure of a human immunodeficiency virus type 1 (HIV-1) subtype B-derived vaccine to prevent infection of chimpanzees by an HIV-1 subtype E strain**

Authors Girard M, Yue L, Barre-Sinoussi F, van der Ryst E, Meignier B, Muchmore E, Fultz PN

Journal J Virol 1996 Nov;70(11):8229-33

NHP.171 (8892046) **In vivo protective anti-HIV immune responses in non-human primates through DNA immunization**

Authors Boyer JD, Wang B, Ugen KE, Agadjanyan M, Javadian A, Frost P, Dang K, Carrano RA, Ciccarelli R, Coney L, Williams WV, Weiner DB

Journal J Med Primatol 1996 Jun;25(3):242-50

NHP.172 (9696847) **Temporal analyses of virus replication, immune responses, and efficacy in rhesus macaques immunized with a live, attenuated simian immunodeficiency virus vaccine**

Authors Connor RI, Montefiori DC, Binley JM, Moore JP, Bonhoeffer S, Gettie A, Fenamore EA, Sheridan KE, Ho DD, Dailey PJ, Marx PA

Journal J Virol 1998 Sep;72(9):7501-9

NHP.173 (8827215) **Protection against mucosal SIVsm challenge in macaques infected with a chimeric SIV that expresses HIV type 1 envelope**

Authors Quesada-Rolander M, Makitalo B, Thorstensson R, Zhang YJ, Castanos-Velez E, Biberfeld G, Putkonen P

Journal AIDS Res Hum Retroviruses 1996 Jul 20;12(11):993-9

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Main Findings

- 4/4 immunized monkeys were infected with the vaccine virus.
- All monkeys developed neutralizing antibodies to HIV-1 and high antibody titers to HIV-1 env glycoproteins, but no Nabs to SIVsm.
- After a follow-up period of 1 year, 2/4 SHIV-infected monkeys were completely protected against SIVsm infection.
- 2/2 SHIV-immunized and infected with the challenge virus, but were able to control this infection.
- CTL in 1/4 of the immunized animals.
- All 6 control animals yielded virus repeatedly after SIVsm challenge and 3 of them showed declining CD4 cell counts.

NHP.174 (8827214) **Multiple immunizations with attenuated poxvirus HIV type 2 recombinants and subunit boosts required for protection of rhesus macaques**

Authors Myagkikh M, Alipanah S, Markham PD, Tartaglia J, Paoletti E, Gallo RC, Franchini G, Robert-Guroff M

Journal AIDS Res Hum Retroviruses 1996 Jul 20;12(11):985-92

Objectives Challenge, Immunogenicity To study macaques immunized twice with NYVAC or ALVAC recombinants carrying HIV-2 env, gag, and pol genes, then boosted either with an additional recombinant immunization or an HIV-2 gp160 protein.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name ALVAC/vCP153 HIV-2 gag,pol,env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name HIV-2 gp160 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge HIV-2.SBL6669 *Route:* Intravenous

Main Findings

- Macaques primed with ALVAC recombinant exhibited sporadic T cell proliferative activity, and all but one failed to develop neutralizing antibodies.
- In contrast, macaques primed with NYVAC recombinants had no T cell proliferative activity but exhibited neutralizing antibody titers (highest in the three recombinant group) that declined by the time of challenge.
- None of the macaques exhibited significant CTL activity.
- Following challenge at 32 weeks with HIV-2SBL6669 all macaques became infected. Thus, immunization regimen was not sufficient to confer protective immunity in the HIV-2 rhesus macaque model.
- Delayed infection in macaques immunized with the NYVAC-HIV-2 recombinant may have been associated with the development of memory B cells capable of providing a neutralizing antibody response on challenge

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NHP.175 (9614868) **Cytotoxic T cells and neutralizing antibodies induced in rhesus monkeys by virus-like particle HIV vaccines in the absence of protection from SHIV infection**
Authors Wagner R, Teeuwsen VJ, Deml L, Notka F, Haaksma AG, Jhagjhoorsingh SS, Niphuis H, Wolf H, Heeney JL
Journal Virology 1998 May 25;245(1):65-74

NHP.176 (8811357) **Attenuated SIV imparts immunity to challenge with pathogenic spleen-derived SIV but cannot prevent repair of the nef deletion**
Authors Stahl-Hennig C, Dittmer U, Nisslein T, Pekrun K, Petry H, Jurkiewicz E, Fuchs D, Wachter H, Rud EW, Hunsmann G
Journal Immunol Lett 1996 Jun;51(1-2):129-35

NHP.177 (8811354) **Recombinant subunit vaccines as an approach to study correlates of protection against primate lentivirus infection**
Authors Hu SL, Polacino P, Stallard V, Klaniecki J, Pennathur S, Travis BM, Misher L, Kornas H, Langlois AJ, Morton WR, Benveniste RE
Journal Immunol Lett 1996 Jun;51(1-2):115-9
Objectives Challenge, Immunogenicity .

NHP.178 (8811353) **Passive immune globulin therapy in the SIV/macaque model: early intervention can alter disease profile**
Authors Haigwood NL, Watson A, Sutton WF, McClure J, Lewis A, Ranchalis J, Travis B, Voss G, Letvin NL, Hu SL, Hirsch VM, Johnson PR
Journal Immunol Lett 1996 Jun;51(1-2):107-14

NHP.179 (9543435) **A clinically relevant HIV-1 subunit vaccine protects rhesus macaques from in vivo passaged simian-human immunodeficiency virus infection**
Authors Mooij P, van der Kolk M, Bogers WM, ten Haaft PJ, Van Der Meide P, Almond N, Stott J, Deschamps M, Labbe D, Momin P, Voss G, Von Hoegen P, Bruck C, Heeney JL
Journal AIDS 1998 Mar 26;12(5):F15-22

NHP.180 (8806509) **Fetal or neonatal infection with attenuated simian immunodeficiency virus results in protective immunity against oral challenge with pathogenic SIVmac251**
Authors Otsyula MG, Miller CJ, Tarantal AF, Marthas ML, Greene TP, Collins JR, van Rompay KK, McChesney MB
Journal Virology 1996 Aug 1;222(1):275-8

NHP.181 (8794330) **Intrarectal transmission of simian immunodeficiency virus in rhesus macaques: selective amplification and host responses to transient or persistent viremia**
Authors Trivedi P, Horejsh D, Hinds SB, Hinds PW II, Wu MS, Salvato MS, Pauza CD
Journal J Virol 1996 Oct;70(10):6876-83

NHP.182 (8794312) **The consequence of passive administration of an anti-human immunodeficiency virus type 1 neutralizing monoclonal antibody before challenge of chimpanzees with a primary virus isolate**
Authors Conley AJ, Kessler JA II, Boots LJ, McKenna PM, Schleif WA, Emini EA, Mark GE III, Katinger H, Cobb EK, Lunceford SM, Rouse SR, Murthy KK
Journal J Virol 1996 Oct;70(10):6751-8

NHP.183 (9461191) **Reduction in SIV replication in rhesus macaques infused with autologous lymphocytes engineered with antiviral genes**
Authors Donahue RE, Bunnell BA, Zink MC, Metzger ME, Westro RP, Kirby MR, Unangst T, Clements JE, Morgan RA
Journal Nat Med 1998 Feb;4(2):181-6

NHP.184 (8676459) **Resistance of previously infected chimpanzees to successive challenges with a heterologous intraclade B strain of human immunodeficiency virus type 1**
Authors Shibata R, Siemon C, Cho MW, Arthur LO, Nigida SM Jr, Matthews T, Sawyer LA, Schultz A, Murthy KK, Israel Z, Javadian A, Frost P, Kennedy RC, Lane HC, Martin MA
Journal J Virol 1996 Jul;70(7):4361-9

NHP.185.1 (8673922) **Protective mucosal immunity elicited by targeted iliac lymph node immunization with a subunit SIV envelope and core vaccine in macaques**

Authors Lehner T, Wang Y, Cranage M, Bergmeier LA, Mitchell E, Tao L, Hall G, Dennis M, Cook N, Brookes R, Klavinskis L, Jones I, Doyle C, Ward R

Journal Nat Med 1996 Jul;2(7):767-75

Objectives Challenge, Immunogenicity To evaluate a novel route of immunization (the targeted iliac lymph node-TILN) aiming close to the iliac lymph nodes draining the genitorectal mucosa.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Route:* Targeted Lymph node immunization

Vaccine Name Recombinant p27 *Type:* Recombinant Subunit Protein *Route:* Targeted Lymph node immunization

Challenge SIVmac251(32H) *Route:* Intrarectal

Main Findings

- Rectal challenge with the SIVmac 32H J5 molecular clone induced total protection in 4/7 macaques immunized by targeted iliac lymph node (TILN), compared with infection in 13/14 unimmunized macaques or immunized by other routes (P = 0.025)(experiment 1 and experiment 2).
- Protection was associated with significant increase in the iliac lymph nodes of IgA antibody-secreting cells to p27 (P < 0.02), CD8-suppressor factor (P < 0.01), and the chemokines RANTES and MIP-1 beta (P < 0.01)

NHP.185.2 (8680896) **Protective mucosal immunity elicited by targeted iliac lymph node immunization with a subunit SIV envelope and core vaccine in macaques**

Authors Lu Y, Salvato MS, Pauza CD, Li J, Sodroski J, Manson K, Wyand M, Letvin N, Jenkins S, Touzjian N, Chutkowski C, Kushner N, LeFaile M, Payne LG, Roberts B

Journal J Acquir Immune Defic Syndr Hum Retrovirol 1996 Jun 1;12(2):99-106

Objectives Challenge, Immunogenicity To evaluate a novel route of immunization (the targeted iliac lymph node-TILN) aiming close to the iliac lymph nodes draining the genitorectal mucosa.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Targeted Lymph node immunization, Intradermal, Intramuscular

Vaccine Name Recombinant p27 *Type:* Recombinant Subunit Protein *Routes:* Intrarectal, Targeted Lymph node immunization, Intradermal, Intramuscular

Challenge SIVmac251 (J5) *Route:* Intrarectal

Main Findings

- Rectal challenge with the SIVmac 32H J5 molecular clone induced total protection in 4/7 macaques immunized by targeted iliac lymph node (TILN), compared with infection in 13/14 unimmunized macaques or immunized by other routes (P = 0.025)(experiment 1 and experiment 2).
- Protection was associated with significant increase in the iliac lymph nodes of IgA antibody-secreting cells to p27 (P < 0.02), CD8-suppressor factor (P < 0.01), and the chemokines RANTES and MIP-1 beta (P < 0.01)

NHP.186 (8648707) **Vaccine protection by a triple deletion mutant of simian immunodeficiency virus**

Authors Wyand MS, Manson KH, Garcia-Moll M, Montefiori D, Desrosiers RC

Journal J Virol 1996 Jun;70(6):3724-33

Objectives Challenge, Immunogenicity .

NHP.187 (9445041) **Selection of virus variants and emergence of virus escape mutants after immunization with an epitope vaccine**

Authors Mortara L, Letourneur F, Gras-Masse H, Venet A, Guillet JG, Bourgault-Villada I

Journal J Virol 1998 Feb;72(2):1403-10

NHP.188 (9449524) **Vaccine evaluation studies of replication-defective SIVsmB7**

Authors Kraiselburd EN, Salaman A, Beltran M, Rivera M, Oliver J, Kessler M, Knezevich M, Rodriguez A, Bilska M, Montefiori D, Torres-Bauza LJ, Martinez I

Journal Cell Mol Biol (Noisy-le-grand) 1997 Nov;43(7):915-24

NHP.189 (8648735) **Simian immunodeficiency virus DNA vaccine trial in macaques**

Authors Lu S, Arthos J, Montefiori DC, Yasutomi Y, Manson K, Mustafa F, Johnson E, Santoro JC, Wissink J, Mullins JI, Haynes JR, Letvin NL, Wyand M, Robinson HL
Journal J Virol 1996 Jun;70(6):3978-91

NHP.190 (8648204) **Vaccination of pregnant macaques protects newborns against mucosal simian immunodeficiency virus infection**
Authors Van Rompay KK, Otsyula MG, Tarara RP, Canfield DR, Berardi CJ, McChesney MB, Marthas ML
Journal J Infect Dis 1996 Jun;173(6):1327-35
Objectives Challenge, Immunogenicity .

NHP.191 (8642649) **Construction and characterization of replication-competent simian immunodeficiency virus vectors that express gamma interferon**
Authors Giavedoni LD, Yilma T
Journal J Virol 1996 Apr;70(4):2247-51

NHP.192 (8627782) **Vaginal transmission of chimeric simian/human immunodeficiency viruses in rhesus macaques**
Authors Lu Y, Brosio P, Lafaile M, Li J, Collman RG, Sodroski J, Miller CJ
Journal J Virol 1996 May;70(5):3045-50

NHP.193 (8605050) **Resistance of chimpanzees immunized with recombinant gp120SF2 to challenge by HIV-1SF2**
Authors el-Amad Z, Murthy KK, Higgins K, Cobb EK, Haigwood NL, Levy JA, Steimer KS
Journal AIDS 1995 Dec;9(12):1313-22
Objectives Challenge, Immunogenicity To determine whether vaccination with recombinant HIV-1SF2 gp120 in a novel oil-in-water adjuvant emulsion, MF59, protects chimpanzees against challenge with HIV-1SF2, the homologous virus isolate.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Vaccine Name CHO cell-expressed HIV-1SF2 gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge HIV-1.SF2 *Route:* Intravenous
Main Findings

- 1/2 vaccinated animals showed no serologic or virologic evidence of infection suggesting a complete sterilizing protection from challenge in 1 animal and a transient infection in the other animal.
- Both control animals showed evidence of seroconversion in ELISA and Western blot assays; virus was detected in the early, acute phase of infection of both control animals by plasma RNA PCR, virus culture and PBMC DNA PCR assays

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NHP.194.1 (8623530) **Protection from pathogenic SIVmac challenge following short-term infection with a nef-deficient attenuated virus**
Authors Norley S, Beer B, Binninger-Schinzel D, Cosma C, Kurth R
Journal Virology 1996 May 1;219(1):195-205
Objectives Challenge, Immunogenicity To determine if protection could be achieved against challenge with a "swarm" of SIVmac251-32H produced in monkey cells and if protection could be demonstrated after a short period of infection with the attenuated virus.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous
Challenge SIVmac251(32H) *Route:* Intravenous
Main Findings

- 3/4 monkeys challenged at 10 weeks and 3/4 challenged at 20 weeks were protected from productive superinfection.
- No apparent correlation between the levels of binding or neutralizing antibodies on the day of challenge and subsequent protection.

NHP.194.2 (8623530) **Protection from pathogenic SIVmac challenge following short-term infection with a nef-deficient attenuated virus**
Authors Norley S, Beer B, Binninger-Schinzel D, Cosma C, Kurth R
Journal Virology 1996 May 1;219(1):195-205

Objectives Challenge, Immunogenicity To determine the breadth of protection afforded by immunization with live attenuated virus.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251 *Type:* Live Virus *Route:* Intravenous
Vaccine Name SIVmac251, 32H, (C8) *Type:* Live Attenuated Virus *Route:* Intravenous
Challenge SIVsm *Route:* Intrarectal, Intravenous, Intravenous
Main Findings

- Animals previously immunized with live attenuated SIVmac251 then with the wild type SIVmac251 were protected from infection with SIVsm.
- The virus load was 2-3 orders of magnitude lower than the control animals.

NHP.195 (8680896) **Utility of SHIV for testing HIV-1 vaccine candidates in macaques**
Authors Lu Y, Salvato MS, Pauza CD, Li J, Sodroski J, Manson K, Wyand M, Letvin N, Jenkins S, Touzjian N, Chutkowski C, Kushner N, LeFaile M, Payne LG, Roberts B
Journal J Acquir Immune Defic Syndr Hum Retrovirol 1996 Jun 1;12(2):99-106

NHP.196 (8605046) **Protection from HIV-1 envelope-bearing chimeric simian immunodeficiency virus (SHIV) in rhesus macaques infected with attenuated SIV: consequences of challenge**
Authors Bogers WM, Niphuis H, ten Haaft P, Laman JD, Koornstra W, Heeney JL
Journal AIDS 1995 Dec;9(12):F13-8
Objectives Challenge, Immunogenicity .

NHP.197 (9444999) **Induction of neutralizing antibodies to T-cell line-adapted and primary human immunodeficiency virus type 1 isolates with a prime-boost vaccine regimen in chimpanzees**
Authors Zolla-Pazner S, Lubeck M, Xu S, Burda S, Natuk RJ, Sinangil F, Steimer K, Gallo RC, Eichberg JW, Matthews T, Robert-Guroff M
Journal J Virol 1998 Feb;72(2):1052-9

NHP.198 (8537682) **Protection of MN-rgp120-immunized chimpanzees from heterologous infection with a primary isolate of human immunodeficiency virus type 1**
Authors Berman PW, Murthy KK, Wrin T, Vennari JC, Cobb EK, Eastman DJ, Champe M, Nakamura GR, Davison D, Powell MF, Bussiere J, Francis DP, Matthews T, Gregory TJ, Obijeski JF
Journal J Infect Dis 1996 Jan;173(1):52-9
Objectives Challenge, Immunogenicity .
Species/Subspecies Pan Troglodytes (Chimpanzee)
Vaccine Name HIV-1.MN.rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name SIVsmE660 *Type:* Live Virus *Route:* Intravenous
Main Findings

- The control animal was infected by the challenge virus: viral infection was detected in the control animal by viral culture, PCR, and multiple serologic assays beginning 2 weeks after infection.
- 3/3 animals immunized with gp120 were not infected (during 12 months of follow-up).
- No neutralization activity in gp120 immunized animals.
- Conclusions: (1) Immunization with recombinant gp120 derived from a T cell-adapted isolate prevented infection by a heterologous primary isolate of HIV-1. (2) In vitro virus neutralization assays utilizing primary isolates cultured in PBMC may be imperfect indicators of protection in vivo.

NHP.199 (9420212) **Administration of an anti-CD8 monoclonal antibody interferes with the clearance of chimeric simian/human immunodeficiency virus during primary infections of rhesus macaques**
Authors Matano T, Shibata R, Siemon C, Connors M, Lane HC, Martin MA
Journal J Virol 1998 Jan;72(1):164-9

NHP.200 (8493576) **Protection against vaginal SIV transmission with microencapsulated vaccine**

Authors Marx PA, Compans RW, Gettie A, Staas JK, Gilley RM, Mulligan MJ, Yamshchikov GV, Chen D, Eldridge JH

Journal Science 1993 May 28;260(5112):1323-7

Objectives Challenge, Immunogenicity To study the immunogenicity and protection confered by formalin inactivated SIV macaques.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac251 (encapsulated) *Type:* Whole (killed) Inactivated Virus *Routes:* Intratracheal, Oral, Intramuscular

Challenge SIVmac251 *Route:* Vaginal or perivaginal

Main Findings

- 5/6 macaques immunized with formalin-treated SIV in biodegradable microspheres by the intramuscular plus oral or plus intratracheal route were protected against vaginal challenge.
- Oral immunization alone did not protect.
- After a second vaginal challenge, 3/4 intramuscularly primed and mucosally boosted macaques remained protected.

NHP.201.1 (9419166) **Induction of Th2 cytokine expression for p27-specific IgA B cell responses after targeted lymph node immunization with simian immunodeficiency virus antigens in rhesus macaques**

Authors Kawabata S, Miller CJ, Lehner T, Fujihashi K, Kubota M, McGhee JR, Imaoka K, Hiroi T, Kiyono H

Journal J Infect Dis 1998 Jan;177(1):26-33

Objectives Immunogenicity To determine if there is an association between the isotype of SIV-specific B cell responses and the profile of Th1 and Th2 cytokine expression.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Route:* Targeted Lymph node immunization

Vaccine Name Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Route:* Targeted Lymph node immunization

Vaccine Name Recombinant p27 *Type:* Recombinant Subunit Protein *Route:* Targeted Lymph node immunization

Main Findings

- In rhesus macaques immunized with SIV antigens, when CD4+ T cells purified from antigen-stimulated PBMCs were analyzed, the levels of Th2 cytokine production were gradually increased after the second and third immunizations with no change of interferon-gamma.
- The main isotype following the second and third immunization was IgG.
- Induction of Th2 type responses in TLN-immunized rhesus macaques reflects the sequence of initial induction of SIV-specific IgG-producing cells followed by IgA-secreting cells

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NHP.201.2 (9456249) **Targeted lymph-node immunization with whole inactivated simian immunodeficiency virus (SIV) or envelope and core subunit antigen vaccines does not reliably protect rhesus macaques from vaginal challenge with SIVmac251**

Authors Lu X, Kiyono H, Lu D, Kawabata S, Torten J, Srinivasan S, Dailey PJ, McGhee JR, Lehner T, Miller CJ

Journal AIDS 1998 Jan 1;12(1):1-10

Objectives Challenge, Immunogenicity To investigate protection from challenge by recombinant subunit protein inoculation targeting iliac lymph node.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name rSIV-gp120 protein *Type:* Recombinant Subunit Protein *Route:* Targeted Lymph node immunization

Vaccine Name Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Route:* Targeted Lymph node immunization

Vaccine Name Recombinant p27 *Type:* Recombinant Subunit Protein *Route:* Targeted Lymph node immunization

Challenge SIVmac251 *Route:* Vaginal or perivaginal

Main Findings

- High-titer SIV-specific IgG antibodies in serum in all animals immunized with recombinant subunit proteins inoculated by (targeted) iliac lymph node immunization.
- Upon intravaginal challenge with SIVmac251, all animals became virus isolation-positive, except 1 animal immunized with SIV p27 and gp120.

- Conclusion: Reliable protection from vaginal transmission of SIV was not achieved by the targeted lymph node immunization procedure.

NHP.202 (9395361) **DNA vaccination as anti-human immunodeficiency virus immunotherapy in infected chimpanzees**

Authors Boyer JD, Ugen KE, Chattergoon M, Wang B, Shah A, Agadjanyan M, Bagarazzi ML, Javadian A, Carrano R, Coney L, Williams WV, Weiner DB

Journal J Infect Dis 1997 Dec;176(6):1501-9

Objectives Immunogenicity, Immunotherapy To evaluate the role of DNA vaccine as anti-HIV immunotherapy in infected chimpanzees.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Vaccine Name pCMN160 HIV-1.MN env-rev *Type:* DNA *Route:* Intramuscular

Challenge HIV-1 IIIB *Route:* Intravenous

Main Findings

- Two HIV-1-infected chimpanzees were vaccinated with plasmid pCMN160-HIV-1.MN.env-rev demonstrated enhanced humoral responses, decrease in viral load to background levels from week 20.
- The control chimpanzee was subsequently vaccinated with pCMN160 following the inoculation with a control sham plasmid, had the antibody responses increased and, as in the first animal, and the virus load decreased.
- Conclusion: the immune response has a direct impact on HIV-1 replication in chimpanzees.

NHP.203 (8427714) **Studies on the specificity of the vaccine effect elicited by inactivated simian immunodeficiency virus**

Authors Cranage MP, Polyanskaya N, McBride B, Cook N, Ashworth LA, Dennis M, Baskerville A, Greenaway PJ, Corcoran T, Kitchin P, et al.

Journal AIDS Res Hum Retroviruses 1993 Jan;9(1):13-22

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac251, 32H, (C8) *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular

Vaccine Name HIV-1 GB8 *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular

Challenge SIVsmB670, SIVmac251(32H) *Route:* Intravenous

Main Findings

- Partially purified SIVmac protected macaques from intravenous challenge with homologous and heterologous SIV grown on human cells but not on monkey grown cells.
- HIV-1 grown on human C8166 T cell line protected macaques against challenge with human cell-grown SIVmac.
- All vaccinated macaques had anti-cell antibodies.

NHP.204 (8427039) **Immune response of chimpanzees after immunization with the inactivated whole immunodeficiency virus (HIV-1), three different adjuvants and challenge**

Authors Niedrig M, Gregersen JP, Fultz PN, Broker M, Mehdi S, Hilfenhaus J

Journal Vaccine 1993;11(1):67-74

Objectives Challenge, Immunogenicity .

Species/Subspecies Pan troglodytes troglodytes (chimpanzee)

Vaccine Name Whole inactivated HIV-1 IIIB *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular

Vaccine Name Recombinant HIV-1 gag core (p24,p15) antigen *Type:* Recombinant Subunit Protein *Route:* Subcutaneous

Vaccine Name Recombinant HIV-1 env gp160 antigen *Type:* Recombinant Subunit Protein *Routes:* Subcutaneous, Intramuscular

Challenge HIV-1.LAI *Route:* Intravenous

Main Findings

- Weak and inconsistent responses were observed in animals that received HIV-1 formulated with alum as adjuvant, whereas HIV-1 formulated with incomplete Freund's adjuvant or an experimental adjuvant (BWZL) induced good humoral and cellular immune responses to the virus.
- The 3 animals that received HIV-1 with the BWZL adjuvant generated overall the best immune responses.

- Upon challenge with infectious HIV-1, despite good humoral and cell-mediated immunity, all 3 immunized animals and a control animal became infected within 4 weeks.

NHP.205.1 (9343211) **An adenovirus-simian immunodeficiency virus env vaccine elicits humoral, cellular, and mucosal immune responses in rhesus macaques and decreases viral burden following vaginal challenge**

Authors Buge SL, Richardson E, Alipanah S, Markham P, Cheng S, Kalyan N, Miller CJ, Lubeck M, Udem S, Eldridge J, Robert-Guroff M

Journal J Virol 1997 Nov;71(11):8531-41

Objectives Challenge, Immunogenicity To investigate the immunogenicity of an adenovirus expressing SIV env and its ability to protect rhesus macaques against vaginal challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal

Vaccine Name Native SIV gp120 *Type:* Purified Viral Products *Route:* Intratracheal

Challenge SIVmac251 *Route:* Vaginal or perivaginal

Main Findings

- The vaccine induced SIV-specific neutralizing antibodies and HIV gp120 binding IgG and IgA detected in nasal and rectal secretions.
- SIV-specific IgGs were also observed in vaginal secretions and saliva.
- T-cell proliferative responses to SIV gp140 and T-helper epitopes were sporadically detected in all immunized macaques.
- Following vaginal challenge with SIVmac251, transient or persistent infection resulted in both immunized and control monkeys.
- Conclusion: Ad5hr-SIV env recombinant and gp120 subunit induces strong humoral, cellular, and mucosal immunity in rhesus macaques.

NHP.205.2 (12021334) **Rhesus macaque resistance to mucosal simian immunodeficiency virus infection is associated with a postentry block in viral replication**

Authors Peng B, Voltan R, Lim L, Edghill-Smith Y, Phogat S, Dimitrov DS, Arora K, Leno M, Than S, Woodward R, Markham PD, Cranage M, Robert-Guroff M

Journal J Virol 2002 Jun;76(12):6016-26

Objectives Challenge To investigate the mechanism of resistance to challenge of an unvaccinated control rhesus macaque.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Challenge SIVmac251(32H), SIVmac251 *Route:* Intrarectal, Vaginal or perivaginal

Main Findings

- Rhesus macaque 359, a vaccine control animal, resisted 2 successive intravaginal challenges with SIVmac251 (and failed to seroconvert) an additional intrarectal SIVmac32H challenge.
- Resistance of this macaque to SIV infection was not due to a highlevel of CD8+ suppressor activity but to an inherent resistance of its CD4+ T cells.
- Resistance is due to a postentry block in viral replication and implicates a cellular inhibitory mechanism in its CD4+ T cells

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NHP.205.3 (10438833) **Factors associated with slow disease progression in macaques immunized with an adenovirus-simian immunodeficiency virus (SIV) envelope priming-gp120 boosting regimen and challenged vaginally with SIVmac251**

Authors Buge SL, Murty L, Arora K, Kalyanaraman VS, Markham PD, Richardson ES, Aldrich K, Patterson LJ, Miller CJ, Cheng SM, Robert-Guroff M

Journal J Virol 1999 Sep;73(9):7430-40

Objectives Challenge .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal

Vaccine Name Native SIV gp120 *Type:* Purified Viral Products *Route:* Intratracheal

Challenge SIVmac251 *Route:* Vaginal or perivaginal

Main Findings

- Reboosting and re-challenge of macaques vaccinated and challenged in trials 205.1 and 205.2 again resulted in partial protection from pathogenicity of challenge

NHP.206 (8411103) **Immunization of Macaca fascicularis with inactivated SIV preparations: challenge with human- or monkey-derived SIV and the effects of a longer immunization schedule**

Authors Titti F, Koanga Mogtomo ML, Borsetti A, Geraci A, Sernicola L, Panzini G, Turillazzi GP, Baroncelli S, Giovannetti A, Zamarchi R, et al.

Journal J Med Primatol 1993 Feb-May;22(2-3):110-8

Objectives Challenge, Immunogenicity To compare two human-derived SIVmac251 whole virus vaccines, a long vs short immunization schedule, and two different challenge viruses.

Main Findings

- Both vaccines induced protection after challenge with human-derived SIVmac251/32H.
- No difference between the 2 schedules of immunization.
- 5/7 were protected following the first challenge (human-derived).
- No protection was observed in monkeys that were reboosted and rechallenged with monkey-derived SIVmac251.

NHP.207 (9343164) **Live, attenuated simian immunodeficiency virus vaccines elicit potent resistance against a challenge with a human immunodeficiency virus type 1 chimeric virus**

Authors Shibata R, Siemon C, Czajak SC, Desrosiers RC, Martin MA

Journal J Virol 1997 Nov;71(11):8141-8

Objectives Challenge, Immunogenicity To ask what protection live attenuated vaccines can provide against SHIVdh12 challenge. A long term follow up.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIMmac239Δ2 *Type:* Live Attenuated Virus *Route:* Intravenous

Vaccine Name SIVmac239Δ3 *Type:* Live Attenuated Virus *Route:* Intravenous

Challenge SHIV.MD1 *Route:* Intravenous

Main Findings

- 3 rhesus macaques, previously immunized with SIVΔ3 or SIVΔ2, then challenged with 30,000 TCID50 dose of SHIV.DH12 controlled the SHIV infection by reducing the viral load to barely detectable levels.
- Only SIV sequences, derived from the vaccine, could be amplified from numerous tissue samples collected at the conclusion of the experiment, 60 weeks postchallenge, but SHIV-specific sequences (viz., HIV-1 env) could not.
- Live attenuated SIV vaccines provide strong long-term protection even against challenge strains with highly divergent envelope sequences

NHP.208 (8363756) **Protection of monkeys by a split vaccine against SIVmac depends upon biological properties of the challenge virus**

Authors Stahl-Hennig C, Voss G, Dittmer U, Coulibaly C, Petry H, Makoschey B, Cranage MP, Aubertin AM, Luke W, Hunsmann G

Journal AIDS 1993 Jun;7(6):787-95

Objectives Challenge, Immunogenicity To investigate the role of the anti-cellular immune response in the protection of rhesus macaques against infection with SIVmac and to determine the biological differences between SIV challenge stocks grown either on human T-cell lines or on monkey PBMC.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Main Findings

- Protection from virus challenge with C8166-grown SIVmac251/32H or SIVmac251/MPBMC did not correlate with anti-cellular antibodies or proliferative T-cell reactivities.
- Control animals infected with SIVmac251/MPBMC showed high persistent antigenaemia and high plasma virus titres.
- Neither the antibody nor the proliferative T-cell response to SIVmac correlates with protection from virus challenge. In contrast to SIVmac251/32H grown on C8166 cells, the MPBMC-grown challenge virus SIVmac251 appears to belong to the 'rapid-high' phenotype, possibly explaining the lack of protection against this SIV.

NHP.209 (9333153) **Superinfection with human immunodeficiency virus type 2 can reactivate virus production in baboons but is contained by a CD8 T cell antiviral response**

Authors Locher CP, Blackbourn DJ, Barnett SW, Murthy KK, Cobb EK, Rouse S, Greco G, Reyes-Teran G, Brasky KM, Carey KD, Levy JA
Journal J Infect Dis 1997 Oct;176(4):948-59
Objectives Challenge, Immunogenicity To assess resistance to superinfection by human immunodeficiency virus.
Main Findings

- Background: Asymptomatic baboons previously infected with HIV-2, were first challenged with homologous virus (HIV-2UC2 or HIV-2UC14) and later with heterologous virus (HIV-2UC12).
- After both virus inoculations, either resistance to viral infection or a transient viremia was observed.
- The original virus was recovered in 3 baboons, suggesting that reactivation of a latent infection occurred on heterologous challenge and that HIV-2 superinfection is blocked by processes established during prior infection.
- Low antibody titers and low levels of virus neutralization.
- Suppression of HIV-1 replication was observed attributed to CD8 T cells.

NHP.210 (8312055) **In vitro spontaneous production of anti-SIV antibodies is a reliable tool in the follow-up of protection of SIV-vaccinated monkeys**
Authors Zamarchi R, Veronese ML, Titti F, Geraci A, Verani P, Rossi GB, Amadori A, Chieco-Bianchi L
Journal AIDS Res Hum Retroviruses 1993 Nov;9(11):1139-44
Objectives Challenge, Immunogenicity To assess the reliability of the spontaneous in vitro synthesis of simian immunodeficiency virus (SIV)-specific antibodies as a marker in the monitoring of protection in SIV-vaccinated animals.
Main Findings

- Backgound: Macaca fascicularis monkeys were immunized with formalin-inactivated SIVmac251 or SIVmac251/32H, and challenged with human-derived (SIVmac251/32H) or monkey-derived live SIV.
- Immunized animals were protected against human-derived SIV challenge.
- No spontaneous in vitro synthesis of anti-SIV antibody was observed in nonstimulated PBMC cultures over a 4-month follow-up.
- Human cell-grown SIVmac251 immunization did not afford protection against monkey-derived SIV, and all the animals became infected and showed spontaneous in vitro synthesis of anti-SIV antibodies.

NHP.211 (9315483) **Gene gun-based nucleic acid immunization alone or in combination with recombinant vaccinia vectors suppresses virus burden in rhesus macaques challenged with a heterologous SIV**
Authors Fuller DH, Simpson L, Cole KS, Clements JE, Panicali DL, Montelaro RC, Murphey-Corb M, Haynes JR
Journal Immunol Cell Biol 1997 Aug;75(4):389-96
Objectives Challenge, Immunogenicity To evaluate the ability of gene gun-based DNA immunization alone or in combination with recombinant vaccinia vectors to elicit protective immune responses in rhesus macaques challenged with a pathogenic heterologous SIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Geometric mean end-point IgG titres in the DNA + VAC and VAC + DNA groups were substantially higher than the responses seen in the VAC + VAC and DNA + DNA groups, demonstrating a synergistic relationship between DNA-based vaccines and recombinant vacciniavirus-based vaccines.
- The vaccines did not prevent infection.
- All vaccine groups showed significant virus load reductions from 7 to 56 days post challenge when compared to controls.
- DNA + DNA group developed the lowest prechallenge antibody responses and the most significant reduction (200-fold) in virus load was associated with this group. In addition, a significant delay in CD4+ T cell loss relative to controls was observed in the DNA + DNA group

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NHP.212 (9271187) **Mechanisms of protection induced by attenuated simian immunodeficiency virus. IV. Protection against challenge with virus grown in autologous simian cells**
Authors Almond N, Corcoran T, Hull R, Walker B, Rose J, Sangster R, Silvera K, Silvera P, Cranage M, Rud E, Stott EJ
Journal J Med Primatol 1997 Feb-Apr;26(1-2):34-43
Objectives Challenge, Immunogenicity To test the mechanism of protection provided by live attenuated SIV.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Main Findings

- Background: 8 animals infected with live attenuated SIV then challenged with wild-type grown in autologous and heterologous cells.
- Animals infected with attenuated SIV are protected against wild-type SIV grown in autologous or heterologous cells.
- Live attenuated SIV protects by the induction of allogeneic antibodies is not tenable.

NHP.213 (8217348) **Lymphoproliferative responses in macaques immunized with inactivated SIV vaccine**
Authors Teng XC, Ashworth LA, Sharpe SA, Dennis MJ, Cranage MP
Journal AIDS Res Hum Retroviruses 1993 Aug;9(8):799-801
Objectives Challenge, Immunogenicity To examine the lymphoproliferative response of macaques immunized with inactivated, partially purified SIVmac32H grown in C8166 cells.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Animals vaccinated with partially purified C8166 cell-grown SIVmac32H in alum adjuvant (Group 1) were protected from initial challenge with SIVmac32H but became infected when rechallenged with SIVmac251.
- No association could be demonstrated betweenprotection from challenge and lymphoproliferative response to one particular antigen tested against.

NHP.214 (9266989) **Macaques infected with attenuated simian immunodeficiency virus resist superinfection with virulence-revertant virus**
Authors Sharpe SA, Whatmore AM, Hall GA, Cranage MP
Journal J Gen Virol 1997 Aug;78 (Pt 8):1923-7
Objectives Challenge, Immunogenicity To examine the protective values of live attenuated virus vaccine to protect against revertant autologous strains.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- 3 macaques already infected with the attenuated molecular clone SIVmacC8 were resistant to superinfection with virulent virus that arose in vivo following repair of a 12 bp attenuating lesion in the nef/3' LTR.
- 4 naive animals became infected following inoculation with blood taken from the macaque in which virulent virus arose.

NHP.215 (9266988) **Mechanisms of protection induced by attenuated simian immunodeficiency virus. I. Protection cannot be transferred with immune serum**
Authors Almond N, Rose J, Sangster R, Silvera P, Stebbings R, Walker B, Stott EJ
Journal J Gen Virol 1997 Aug;78 (Pt 8):1919-22
Objectives Challenge, Passive Immunization To evaluate the role in protection induced by live attenuated SIVmacC8 against SIVmajJ5 challenge.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name Anti-SIVmacC8 *Type:* Passive Antibody *Route:* Intraperitoneal
Challenge SIVmacJ5M *Route:* ND
Main Findings

- 4/4 control animals were infected as indicated by the test at 14 dpc.
- 2 of passively immunized animals were protected from infection at 14 dpc but were shown to be infected thereafter.
- The failure of passive immunization to transfer protection indicates that serum components alone are not sufficient to mediate the potent protection obtained using live attenuated vaccines.

NHP.216 (8198872) **Reduced virus load in rhesus macaques immunized with recombinant gp160 and challenged with simian immunodeficiency virus**
Authors Ahmad S, Lohman B, Marthas M, Giavedoni L, el-Amad Z, Haigwood NL, Scandella CJ, Gardner MB, Luciw PA, Yilma T
Journal AIDS Res Hum Retroviruses 1994 Feb;10(2):195-204
Objectives Challenge, Immunogenicity To evaluate the potential of SIVmac239 gp160 expressed by recombinant vaccinia virus (vSIVgp160) and baculovirus (bSIVgp160) to protectively immunize rhesus macaques against intravenous infection with pathogenic SIVmac isolates.

Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Binding antibodies to gp130 were induced in all animals following immunization with SIVgp160.
- Immunization did not induce neutralizing antibodies up to 1 week prior to virus challenge.
- No protection from challenge: All animals became infected after i.v. inoculation with 1-10 AID50 of either challenge virus.

NHP.217 (8198871) **Passive immunization of cynomolgus macaques with immune sera or a pool of neutralizing monoclonal antibodies failed to protect against challenge with SIVmac251**

Authors Kent KA, Kitchin P, Mills KH, Page M, Taffs F, Corcoran T, Silvera P, Flanagan B, Powell C, Rose J, et al.
Journal AIDS Res Hum Retroviruses 1994 Feb;10(2):189-94
Objectives Passive Immunization .

NHP.218 (9256490) **Potent, protective anti-HIV immune responses generated by bimodal HIV envelope DNA plus protein vaccination**

Authors Letvin NL, Montefiori DC, Yasutomi Y, Perry HC, Davies ME, Lekutis C, Alroy M, Freed DC, Lord CI, Handt LK, Liu MA, Shiver JW
Journal Proc Natl Acad Sci U S A 1997 Aug 19;94(17):9378-83
Objectives Challenge, Immunogenicity To study prime-boost regimen using HIV-1 env DNA and synthetic protein and neutralizing antibodies in nonhuman primate species.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- HIV-1 Env protein as a boosting immunogen generates a high titer neutralizing antibody response in rehesus macaques.
- HIV-1 env DNA (multiple doses) followed by a final immunization with HIV-1 env DNA plus HIV-1 Env protein (env gene from HXBc2 cloneof HIV IIIB; Env protein from parental HIV IIIB) completely protects monkeys from infection after i.v. challenge with a chimeric virus expressing HIV-1 env (HXBc2) on a simian immmunodeficiency virusmac backbone (SHIV-HXBc2).

NHP.219 (8179961) **Immune responses induced by prototype vaccines for AIDS in rhesus monkeys**

Authors Ohkawa S, Wilson LA, Larosa G, Javaherian K, Martin LN, Murphey-Corb M
Journal AIDS Res Hum Retroviruses 1994 Jan;10(1):27-38
Objectives Challenge, Immunogenicity To profile humoral and cell mediated immune response induced by immunization with candidate vaccines consisting of recombinant SIV gp110 with SAF-M adjuvant or rgp140+FA adjuvant.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- All the monkeys were infected after intravenous challenge.
- 16 days following infection, viral antigenemia was reduced in both groups of vaccinates compared to controls.
- After 23 days antigenemia in the gp110 + SAF-M group remained at the same level as on day 16, whereas antigenemia in the gp140 + FA group was significantly reduced further than the level observed on day 16.
- Both vaccines induced high ELISA titers of IgG antibody against rgp140.
- gp110 +/- SAF-M (not gp140 + FA) induced high titers of neutralizing antibody.

NHP.220 (9223408) **Anti-major histocompatibility complex antibody responses to simian B cells do not protect macaques against SIVmac infection**

Authors Polyanskaya N, Sharpe S, Cook N, Leech S, Banks J, Dennis M, Hall G, Stott J, Cranage M
Journal AIDS Res Hum Retroviruses 1997 Jul 20;13(11):923-31
Objectives Challenge, Immunogenicity To investigate the efficacy of alloimmunization with simian B cells expressing high level of MHC class I and class II molecules to confer protection against systemic challenge with SIVmac.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Antibody responses to allogeneic MHC molecules do not protect against infection with immunodeficiency lentiviruses.

NHP.221 (8176640) **Long-standing protection of macaques against cell-free HIV-2 with a HIV-2 iscom vaccine**

Authors Putkonen P, Bjorling E, Akerblom L, Thorstensson R, Lovgren K, Benthin L, Chiodi F, Morein B, Biberfeld G, Norrby E, et al.

Journal J Acquir Immune Defic Syndr 1994 Jun;7(6):551-9

Objectives Challenge, Immunogenicity To investigate the capacity of two immunostimulating-complex (iscom) formulations including inactivated native HIV-2 viral proteins and selected peptides to induce protective immunity against HIV-2 in a nonhuman primate.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Main Findings

- 3/4 immunized macaques were protected from challenge.
- 4/4 control macaques became readily infected with challenge virus.
- 1/3 protected animals showed an anamnestic antibody response to a dominating antigenic site.
- The vaccine-protected monkeys were subsequently resistant to rechallenge infection at 12, 15, and 18 months after the first challenge, suggesting that a reasonable duration of protective immunity had been induced by the vaccine.

NHP.222 (9188572) **Evolution of envelope-specific antibody responses in monkeys experimentally infected or immunized with simian immunodeficiency virus and its association with the development of protective immunity**

Authors Cole KS, Rowles JL, Jagerski BA, Murphey-Corb M, Unangst T, Clements JE, Robinson J, Wyand MS, Desrosiers RC, Montelaro RC

Journal J Virol 1997 Jul;71(7):5069-79

Objectives Challenge, Immunogenicity .

Main Findings

- The establishment of long-term protective immunity in general parallels the absence of further detectable changes in antibody responses and a maintenance of relatively constant antibody titer, avidity, conformational dependence, and the presence of neutralizing antibody for at least 2 years postinoculation.
- Attenuated SIV vaccine and whole virus elicited mature antibody response.
- Envelope subunit vaccines elicited in general immature antibody response characterized by poor reactivity with native envelope proteins, low avidity, low conformational dependence, and the absence of neutralization activity against the challenge strain.

NHP.223 (8107246) **Incomplete protection, but suppression of virus burden, elicited by subunit simian immunodeficiency virus vaccines**

Authors Israel ZR, Edmonson PF, Maul DH, O'Neil SP, Mossman SP, Thiriart C, Fabry L, Van Opstal O, Bruck C, Bex F, et al.

Journal J Virol 1994 Mar;68(3):1843-53

Objectives Challenge, Immunogenicity To compare the efficacy of immunization with either SIV Env glycoprotein, Gag-Env, or whole inactivated virus, with or without recombinant live vaccinia vector priming, in protecting rhesus macaques from challenge with SIVmac251 clone BK28.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Sterilizing immunity was induced only by whole inactivated vaccine.
- Abortive infection (strong immunity) was observed in 2 animals (one VV-Env and one Gag-Env).
- Suppression of infection (incomplete or partial immunity) occurred in the 8/12 of subunit-vaccinated animals.
- Active infection developed in all controls and 2/3 VV-Gag-Env-immunized animals.

NHP.224 (8046353) **Major histocompatibility complex class I-associated vaccine protection from simian immunodeficiency virus-infected peripheral blood cells**

Authors Heeney JL, van Els C, de Vries P, ten Haaft P, Otting N, Koornstra W, Boes J, Dubbes R, Niphuis H, Dings M, et al.

Journal J Exp Med 1994 Aug 1;180(2):769-74

Objectives Challenge, Immunogenicity To evaluate the effectiveness of vaccine protection from infected cells from another individual of the same species.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- 50% of the SIV-vaccinated animals were protected from challenge.
- 50% SIV-vaccinees were unprotected and rapidly progressed to AIDS.
- Protection was unrelated to either total antibody titers to human cells, used in the production of the vaccine, to HLA antibodies, or to virus neutralizing activity.
- All animals protected against cell-associated virus challenge were those which were SIV vaccinated and which shared the MHC class I allele (Mamu-A26) with the donor of the infected cells.
- CTL specific for SIV envelope protein were detected in 3/4 protected animals vs. 1/4 unprotected animals, suggesting a possible role of MHC class I-restricted CTL in protection from infected blood cells

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NHP.225 (9185593) **Challenge of chimpanzees immunized with a recombinant canarypox-HIV-1 virus**

Authors Girard M, van der Ryst E, Barre-Sinoussi F, Nara P, Tartaglia J, Paoletti E, Blondeau C, Jennings M, Verrier F, Meignier B, Fultz PN

Journal Virology 1997 May 26;232(1):98-104

Objectives Challenge, Immunogenicity To evaluate the potential protective efficacy of a live recombinant HIV-1 canarypox vaccine candidate.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Main Findings

- Vaccination against HIV-1(IIIB(LAI)) or HIV-1(MN) did not protect animals from challenge with heterologous cell-free HIV-1(DH12).
- 1/2 chimpanzees vaccinated 5 times with ALVAC-HIV-1 vCP250 and challenged by iv injection of PBMC from an HIV-1(IIIB(LAI))-infected chimpanzee were protected.
- After booster inoculation 5 months post-challenge, both animals were re-challenged with HIV-1(DH12) and neither animal had neutralizing antibodies to HIV-1(DH12) and neither was protected from infection.
- ALVAC-HIV-1 vCP250 expresses HIV-1(IIIB(LAI))gp120/TM, gag and protease gene products.

NHP.226 (9142121) **Protection of chimpanzees from high-dose heterologous HIV-1 challenge by DNA vaccination**

Authors Boyer JD, Ugen KE, Wang B, Agadjanyan M, Gilbert L, Bagarazzi ML, Chattergoon M, Frost P, Javadian A, Williams WV, Refaeli Y, Ciccarelli RB, McCallus D, Coney L, Weiner DB

Journal Nat Med 1997 May;3(5):526-32

Objectives Challenge, Immunogenicity To examine the immunogenicity and efficacy of of an HIV-1 DNA vaccine encoding env, rev, gag/pol in a chimpanzee model system.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Main Findings

- The immunized animals developed specific cellular and humoral immune responses.
- The DNA constructs induced protection from the establishment of infection with a heterologous challenge (HIV-1 SF2).
- Control animal was infected.

NHP.227 (9135877) **Live attenuated SIV vaccines are not effective in a postexposure vaccination model**

Authors Linhart H, Gundlach BR, Sopper S, Dittmer U, Matz-Rensing K, Kuhn EM, Muller J, Hunsmann G, Stahl-Hennig C, Uberla K

Journal AIDS Res Hum Retroviruses 1997 May 1;13(7):593-9

Objectives Challenge, Immunogenicity, Immunotherapy To evaluate the value of live attenuated vaccine therapeutic immunization.

Species/Subspecies -

Main Findings

- 4/4 controls (vaccinated with delta nef only - i.e., without the SIV IL-2 construct) were infected.
- 0/4 vaccinees protected from increased viral loads.
- 0/4 vaccinees protected from infection.
- All coinfected macaques had a high viral load, and some of them developed AIDS-like symptoms and pathological alterations rapidly.
- In the presence of pathogenic SIV, both live attenuated SIV vaccines did not protect from disease in this postexposure vaccination model.

NHP.228 (7986590) **Induction of antigen-specific killer T lymphocyte responses using subunit SIVmac251 gag and env vaccines containing QS-21 saponin adjuvant**

Authors Newman MJ, Munroe KJ, Anderson CA, Murphy CI, Panicali DL, Seals JR, Wu JY, Wyand MS, Kensil CR

Journal AIDS Res Hum Retroviruses 1994 Jul;10(7):853-61

Objectives Challenge, Immunogenicity To increase the immunogenicity of recombinant subunit vaccine (SIVmac251 gag and env) with QS-21 adjuvant.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Antigen-specific killer cell responses could be induced by a subunit vaccine formulated with the QS-21 saponin adjuvant that was detected was mediated by both CD4+ and CD8+ lymphocytes.
- Despite the presence of these killer cells, all of the animals became infected with the SIVmac251 on experimental challenge.
- The characteristics of the responses suggested that the effector cells were T lymphocytes, expressing either CD4 or CD8.

NHP.229 (9123856) **Macaques infected with live attenuated SIVmac are protected against superinfection via the rectal mucosa**

Authors Cranage MP, Whatmore AM, Sharpe SA, Cook N, Polyanskaya N, Leech S, Smith JD, Rud EW, Dennis MJ, Hall GA

Journal Virology 1997 Mar 3;229(1):143-54

Objectives Challenge, Immunogenicity To determine if protection against systemic challenge in the SIVmac model of AIDS extends to intrarectal mucosal challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- 4 macaques previously infected with the attenuated SIVmacC8 resisted superinfection with SIVmacJ5, following intrarectal inoculation.
- Immunization with live attenuated SIV protected 4 macaques from intrarectal challenge with SHIV (composed of SIVmac239 expressing the HXBc2 env, tat, and rev genes).
- In protected animals, SIV-specific CTL were detected in gut-associated lymph nodes and may have a role in limiting superinfection following mucosal exposure.

NHP.230.1 (7986589) **High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection**

Authors Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

Journal AIDS Res Hum Retroviruses 1994 Jul;10(7):839-51

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Method: Monkeys primed with a recombinant vaccinia virus expressing SIV Gag, Pol, and Env polypeptides +/- SIV particles boost in adjuvant.
- Despite the induction of vigorous immune responses, 17/18 rhesus monkeys became infected on challenge with a low dose of virulent SIVmac.
- Vaccination may have diminished SIV burdens and rates of CD4+ cell declines in some of the animals.
- Vaccinated/challenged/infected animals eventually developed fatal disease similar to control animals.

NHP.230.2 (7986589) **High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection**

Authors Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC

Journal AIDS Res Hum Retroviruses 1994 Jul;10(7):839-51

Objectives Challenge, Immunogenicity To evaluate the ability of two different vaccinia virus recombinant to elicit immune response and to protect macaques against challenge.

NHP.230.3 (7986589) **High-titer immune responses elicited by recombinant vaccinia virus priming and particle boosting are ineffective in preventing virulent SIV infection**

Authors Daniel MD, Mazzara GP, Simon MA, Sehgal PK, Kodama T, Panicali DL, Desrosiers RC
Journal AIDS Res Hum Retroviruses 1994 Jul;10(7):839-51
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)

NHP.231 (7966239) **Efficacy of inactivated whole HIV-2 vaccines with various adjuvants in cynomolgus monkeys**
Authors Putkonen P, Nilsson C, Walther L, Ghavamzadeh L, Hild K, Broliden K, Biberfeld G, Thorstensson R
Journal J Med Primatol 1994 Feb-May;23(2-3):89-94

NHP.232 (9108105) **Vaccine effect using a live attenuated nef-deficient simian immunodeficiency virus of African green monkeys in the absence of detectable vaccine virus replication in vivo**
Authors Beer B, Baier M, zur Megede J, Norley S, Kurth R
Journal Proc Natl Acad Sci U S A 1997 Apr 15;94(8):4062-7
Objectives Challenge, Immunogenicity To test a live attenuated virus vaccine (SIVagm3-Delta nef)) in its natural host (African green monkey).
Species/Subspecies Cercopithecus aetiops (African Green monkeys)
Main Findings

- Preinoculated African green monkeys showed drastic decreases in virus load or were protected from challenge.
- Vaccine protection occurred in the absence of detectable vaccine virus replication and humoral immune response, suggesting a protective cellular immune response similar to that associated with subinfectious or abortive infections.
- SIVagm3(delta)nef replication was delayed marginally in vitro, but hightly attenuated in vivo.

NHP.233 (7966237) **Immunization with whole inactivated vaccine protects from infection by SIV grown in human but not macaque cells**
Authors Goldstein S, Elkins WR, London WT, Hahn A, Goeken R, Martin JE, Hirsch VM
Journal J Med Primatol 1994 Feb-May;23(2-3):75-82
Objectives Challenge, Immunogenicity To determine whether the species of origin of the cell line used to generate virus stock influenced the degree of protection mediated by WI-SIV vaccine.
Species/Subspecies Macaca (sp)
Main Findings

- Two groups of animals were vaccinated then challenged with either SIV-Human or SIV-Macaque virus.
- All SIV-Human vaccinees were protected from infection, and all SIV-Macaque vaccinees became infected.
- Difference between the two groups is due to cellular proteins in the virus preparation rather than the pathogenic or genetic properties of the virus<Immune responses of all vaccinees were indistinguishable from one another.
- No virus was isolated from PBMC of macaques challenged with SIV-Human during the course of the study.

NHP.234 (7966232) **Passive immunization of macaques against SIV infection**
Authors Gardner MB, Rosenthal A, Jennings M, Yee JA, Antipa L, MacKenzie M
Journal J Med Primatol 1994 Feb-May;23(2-3):164-74
Objectives Challenge, Passive Immunization To evaluate the mechanism responsible for protection achieved by an inactivated whole SIV vaccine and to test antiviral effect against SIV challenge of inactivated plasma or purified Ig.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Plasma from a monkey that had been protected by an inactivated-whole SIV(mac) vaccine conferred protection to animals challenged iv 4-18 hours later with 10 AID50 of homologous cell-free virus.
- Plasma or purified immunoglobulin (Ig) from SIVmac infected asymptomatic monkeys failed to protect any recipients, and may have enhanced infection and accelerated disease.

- Anti-SIV Ig administered 24 hours post challenge may have enhanced infection

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NHP.235 (7966226) **Cellular immune responses in rhesus macaques infected rectally with low dose simian immunodeficiency virus**

Authors Salvato MS, Emau P, Malkovsky M, Schultz KT, Johnson E, Pauza CD

Journal J Med Primatol 1994 Feb-May;23(2-3):125-30

Objectives Challenge, Immunogenicity To test hypothesis that cellular immune responses in previously-infected animals are a correlate of protection.

Species/Subspecies -

Main Findings

- Monkeys infected rectally with low dose of SIV were resistant to high dose challenge with SIV.
- PBMC from 2/4 challenged monkeys were unable to support SIV replication in vitro unless cultures were depleted of CD8+ lymphocytes.
- Monkeys that survived high dose rectal infection with SIV also suppressed virus replication in cultured PBMC.
- Virus-suppressive activity of PBMC may be an important correlate of protective immunity in AIDS.

NHP.236 (7887023) **Protection of rhesus macaques from SIV infection by immunization with different experimental SIV vaccines**

Authors de Vries P, Heeney JL, Boes J, Dings ME, Hulskotte EG, Dubbes R, Koornstra W, ten Haaft P, Akerblom L, Eriksson S, et al.

Journal Vaccine 1994 Nov;12(15):1443-52

Objectives Challenge, Immunogenicity To compare the immunogenicity and efficacy of an inactivated whole SIVmac (32H) preparation adjuvanted with muramyl dipeptide (SIV-MDP) and a gp120-enriched SIVmac (32H) ISCOM preparation (SIV-ISCOM).

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Higher SIV-specific serum antibody titres were found in the SIV-MDP-immunized monkeys than in the SIV-ISCOM-immunized ones.
- 4/4 SIV-MDP- and 4/4 SIV-ISCOM-immunized monkeys were protected against intravenous challenge.
- 2/2 in each control group were infected with the challenge virus.
- 0/4 in each vaccinee group were protected after reboost and rechallenge with 10 MID50 of the same virus produced in PBMC from a rhesus macaque
- SIV-ISCOM-immunized animals of PBMC-only (Group B) did not develop clinical symptoms during observation period, unlike most other animals in this trial.
- Both SIV preparations induced low VN antibody titres, possibly caused by denatured form of gp120after formaldehyde or acid treatment in both vaccine preparations

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NHP.237 (9032322) **Rhesus macaques previously infected with simian/human immunodeficiency virus are protected from vaginal challenge with pathogenic SIV-mac239**

Authors Miller CJ, McChesney MB, Lu X, Dailey PJ, Chutkowski C, Lu D, Brosio P, Roberts B, Lu Y

Journal J Virol 1997 Mar;71(3):1911-21

Objectives Challenge, Immunogenicity To determine if a previous infection with SHIV 89.6 by vaginal inoculation could protect animals from vaginal challenge with pathogenic SIV.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- 5 Rhesus macaques infected intravaginally with SHIV89.6 then challenged intravaginally with pathogenic SIV-mac239 had low or undetectable viral RNA levels in plasma compared to control animals.
- 3/5 of the SHIV-immunized animals remained virus isolation negative for more than 8 months, while 2 became virus isolation positive.
- The presence of SIV Gag-specific cytotoxic T lymphocytes in peripheral blood mononuclear cells and SIV-specific antibodies in cervicovaginal secretions at the time of challenge was associated with resistance to pathogenic SIV infection after vaginal challenge

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NHP.238 (9000087) **Rapid development of vaccine protection in macaques by live-attenuated simian immunodeficiency virus**

Authors Stahl-Hennig C, Dittmer U, Nisslein T, Petry H, Jurkiewicz E, Fuchs D, Wachter H, Matz-Rensing K, Kuhn EM, Kaup FJ, Rud EW, Hunsmann G

Journal J Gen Virol 1996 Dec;77 (Pt 12):2969-81
Objectives Challenge, Immunogenicity To investigate the efficacy the nature of the immune protection induced of a nef-deleted mutant of SIVmac32H called pC8.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- All monkeys infected with pC8 live attenuated virus became persistently infected, exhibiting low cell-associated viral loads, but strong cellular and strong humoral antiviral responses.
- 2/8 pC8-infected monkeys developed an immunodeficiency and were not challenged with complete replenishment of the deletion.
- 6 monkeys, 2 preinfected for 42 weeks and 4 for 22 weeks, were challenged with pathogenic spleen-derived SIV; complete protection was achieved in 4 vaccinees.
- Protection from challenge virus infection or a delayed disease development seemed to be associated with a sustained SIV-specific T helper cell response after challenge.
- Conclusion: sterilizing immunity against superinfection with pathogenic SIV can be induced even after a relatively short waiting period of 22 weeks.

NHP.239 (2157886) **Inactivated simian immunodeficiency virus vaccine failed to protect rhesus macaques from intravenous or genital mucosal infection but delayed disease in intravenously exposed animals**
Authors Sutjipto S, Pedersen NC, Miller CJ, Gardner MB, Hanson CV, Gettie A, Jennings M, Higgins J, Marx PA
Journal J Virol 1990 May;64(5):2290-7
Objectives Challenge, Immunogenicity To test efficacy of a whole-virus vaccine inactivated with psoralen and UV light.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac HUT-78 ((Psoralem-UV) *Type:* Whole (killed) Inactivated Virus
Challenge SIVmac (not detemined) *Route:* Urethral, Vaginal or perivaginal, Mucosal
Main Findings

- The vaccine elicited humoral immune response prior to challenge.
- All immunized animals became infected after challenge, but their clinical course was delayed compared with controls.
- Route of infection affected disease course, with animals infected by the iv route more likely to develop acute form of SIV than those infected by the genital mucosal route.
- Concentration of challenge did not affect outcome; vaccinated animals did not fare any better following minimal mucosal challenge than a much greater iv infection.

NHP.240 (2164591) **Immunization with a live, attenuated simian immunodeficiency virus (SIV) prevents early disease but not infection in rhesus macaques challenged with pathogenic SIV**
Authors Marthas ML, Sutjipto S, Higgins J, Lohman B, Torten J, Luciw PA, Marx PA, Pedersen NC
Journal J Virol 1990 Aug;64(8):3694-700
Objectives Challenge, Immunogenicity Tp test the potential of virulence-attenuated virus to protect against iv challenge with a pathogenic SIV(MAC) strain.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac1A11 *Type:* Live Attenuated Virus *Route:* Intravenous
Challenge SIVmac (not detemined) *Route:* Intravenous
Main Findings

- Live SIVmacIAII is immunogenic, did not induce disease, but failed to protect against moderately high dose of pathogenic virus.
- Immunization prevented severe, early disease and prolonged the lives of monkeys subsequently infected with pathogenic SIV.
- Within 1-6 weeks iv inoculated animals developed transient viremia without clinical disease and persistent humoral antibody response.
- Time until severe clinical symptoms: 267-304 days in immunized monkeys, 38-227 days PC in naive controls.

NHP.241 (2370678) **Antibody-mediated in vitro neutralization of human immunodeficiency virus type 1 abolishes infectivity for chimpanzees**
Authors Emini EA, Nara PL, Schleif WA, Lewis JA, Davide JP, Lee DR, Kessler J, Conley S, Matsushita S, Putney SD, et al.

Journal J Virol 1990 Aug;64(8):3674-8
Objectives Challenge, Immunogenicity To determine whether antibody against the HIV-1 V3 loop can abolish infectivity of HIV-1 in chimpanzees.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Main Findings

- Antibody to the gp120 prinicpal neutralization determinant (V3 loop) prevented HIV-1 infection in vitro and inhibited infection in vivo.

NHP.242 (2455898) **Human immunodeficiency virus type 1 challenge of chimpanzees immunized with recombinant envelope glycoprotein gp120**
Authors Berman PW, Groopman JE, Gregory T, Clapham PR, Weiss RA, Ferriani R, Riddle L, Shimasaki C, Lucas C, Lasky LA, et al.
Journal Proc Natl Acad Sci U S A 1988 Jul;85(14):5200-4
Objectives Challenge, Immunogenicity .
Species/Subspecies Pan troglodytes troglodytes (chimpanzee)
Vaccine Name rgp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Challenge HIV-1 IIIB *Route:* Intravenous
Main Findings

- The recombinant gp120 was effective in eliciting cellular and humoral immunity as well as immunologic memory.
- Anti-rgp120 antibodies reacted with authentic viral gp120 in immunological blot assays and were able to neutralize HIV-1 infectivity in vitro.
- Sera from the rgp120-immunized animals were able to neutralize HIV-1 pseudotypes of vesicular stomatitis virus prepared from the IIIB isolate, from which the gene encoding rgp120 was derived, as well as two heterologous isolates, ARV-2 and RF.
- The immune response elicited against the rgp120 was not effective in preventing viral infection after intravenous challenge with HIV-1.

NHP.243 (2370678) **Antibody-mediated in vitro neutralization of human immunodeficiency virus type 1 abolishes infectivity for chimpanzees**
Authors Emini EA, Nara PL, Schleif WA, Lewis JA, Davide JP, Lee DR, Kessler J, Conley S, Matsushita S, Putney SD, et al.
Journal J Virol 1990 Aug;64(8):3674-8
Objectives Challenge, Immunogenicity To determine whether antibody against the HIV-1 V3 loop can abolish infectivity of HIV-1 in chimpanzees.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Main Findings

- Antibody to the gp120 prinicpal neutralization determinant (V3 loop) prevented HIV-1 infection in vitro and inhibited infection in vivo.

NHP.244 (2470398) **Cell-mediated immune proliferative responses to HIV-1 of chimpanzees vaccinated with different vaccinia recombinant viruses**
Authors Van Eendenburg JP, Yagello M, Girard M, Kieny MP, Lecocq JP, Muchmore E, Fultz PN, Riviere Y, Montagnier L, Gluckman JC
Journal AIDS Res Hum Retroviruses 1989 Feb;5(1):41-50
Objectives Immunogenicity To compare proliferative responses to HIV and to vaccinia virus antigens of lymphocytes taken at various times from chimpanzees vaccinated with recombinant vaccinia virus expressing different HIV genes.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Main Findings

- Irrespective of the HIV gene utilized, lymphocyte proliferation to HIV was usually weak and rapidly decreased after each inoculation, contrasting with strong and sustained responses to vaccinia virus.
- IL-2-producing VV did not lead to increased responsiveness.
- Reactivity to soluble purified gp160, but not to p25, could be detected in PBL from animals that had received both VV160 and VV25, while immunization with VVF resulted in a significant response to this protein in 1/2 animals.

NHP.245.1 (2548210) **Vaccine protection against simian immunodeficiency virus infection**
Authors Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD
Journal Proc Natl Acad Sci U S A 1989 Aug;86(16):6353-7
Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular
Challenge SIVmac251 *Route:* Intravenous
Main Findings

- 2/6 vaccinated monkeys showed no evidence of infection following the live virus challenge.
- Transfusion of 10 ml of whole blood from these 2 into uninfected, naive rhesus monkeys did not result in infection of the recipients, providing further support for the lack of infection in the 2 previously vaccinated animals.
- 4/4 unvaccinated control monkeys inoculated with live SIV became infected and 3 of these died with AIDS 118-258 days after infection (in contrast with 1/6 vaccinated monkeys).
- 4/4 naive controls infected and developed SAIDS.
- 4/4 naive controls infected and diseased.
- 0/4 vaccinees protected from infection.
- 1/4 protected from increased viral load and disease to 930 dpc.

NHP.245.2 (2548210) **Vaccine protection against simian immunodeficiency virus infection**
Authors Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD
Journal Proc Natl Acad Sci U S A 1989 Aug;86(16):6353-7
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular
Challenge SIVmac251 *Route:* Intramuscular

NHP.245.3 (2548210) **Vaccine protection against simian immunodeficiency virus infection**
Authors Desrosiers RC, Wyand MS, Kodama T, Ringler DJ, Arthur LO, Sehgal PK, Letvin NL, King NW, Daniel MD
Journal Proc Natl Acad Sci U S A 1989 Aug;86(16):6353-7
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Whole inactivated SIVmac251 *Type:* Whole (killed) Inactivated Virus
Challenge SIVmac251 *Route:* Intramuscular

NHP.247 (2555541) **Challenge of chimpanzees (Pan troglodytes) immunized with human immunodeficiency virus envelope glycoprotein gp120**
Authors Arthur LO, Bess JW Jr, Waters DJ, Pyle SW, Kelliher JC, Nara PL, Krohn K, Robey WG, Langlois AJ, Gallo RC, et al.
Journal J Virol 1989 Dec;63(12):5046-53
Objectives Challenge, Immunogenicity To determine the efficacy of the immunization of a gp120 immunization to prevent infection from homologous HIV-1 IIIB challenge in chimpanzees.
Species/Subspecies Pan troglodytes troglodytes (chimpanzee)
Vaccine Name HIV-1 IIIB gp120 *Type:* Purified Viral Products
Challenge HIV-1 IIIB *Route:* Intravenous
Main Findings

- 2/2 animals became infected with HIV, indicating that the immune response elicited by immunization with gp120 formulated in alum was not effective in preventing infection with HIV-1.

NHP.248 (2555923) **A formalin-inactivated whole SIV vaccine confers protection in macaques**
Authors Murphey-Corb M, Martin LN, Davison-Fairburn B, Montelaro RC, Miller M, West M, Ohkawa S, Baskin GB, Zhang JY, Putney SD, et al.
Journal Science 1989 Dec 8;246(4935):1293-7

Objectives Challenge, Immunotherapy Evaluate capacity of formalin-inactivated whole virus vaccine to prevent infection and/or block development of SIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIV/Delta$_{B670}$ *Type:* Whole (killed) Inactivated Virus *Route:* Intramuscular
Challenge SIVDeltaB670 *Route:* Intravenous
Main Findings

- Immunization with formalin-inactivated whole SIV potentiated with either MDP or MDP combined with alum protected 9/9 juvenile rhesus monkeys against disease for at least 1 year after challenge
- A high dose of highly purified material was used for all immunizations
- The vaccine contained all major virion proteins
- A rest period sufficient to establish appropriate memory cells was allowed before exposure to live virus

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NHP.249 (3475581) **Effect of immunization with a vaccinia-HIV env recombinant on HIV infection of chimpanzees**
Authors Hu SL, Fultz PN, McClure HM, Eichberg JW, Thomas EK, Zarling J, Singhal MC, Kosowski SG, Swenson RB, Anderson DC, et al.
Journal Nature 1987 Aug 20-26;328(6132):721-3
Objectives Challenge, Immunogenicity .
Species/Subspecies Pan troglodytes troglodytes (chimpanzee)
Vaccine Name Chimp anti-HIV IgG *Type:* Passive Antibody
Challenge LAV-1 or NY5 *Route:* Intravenous
Main Findings

- Although HIV-specific antibody and T-cell responses were elicited by immunization, virus was isolated from lymphocytes of all challenged chimpanzees, indicating that immunization did not prevent infection by HIV.
- Among the animals that received a higher dose of LAV-1, 1/2 control chimpanzees, but none of the 4 v-env5-immunized chimpanzees developed substantial and persistent lymphadenopathy.

NHP.250 (7584989) **Early suppression of SIV replication by CD8+ nef-specific cytotoxic T cells in vaccinated macaques**
Authors Gallimore A, Cranage M, Cook N, Almond N, Bootman J, Rud E, Silvera P, Dennis M, Corcoran T, Stott J, et al.
Journal Nat Med 1995 Nov;1(11):1167-73
Objectives Challenge, Immunogenicity To evaluate potential of subunit vaccine (nef) to elicit protection with nef-specific CTLs.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Main Findings

- Strong CTL responses substantially reduce viral load and appear to clear infection.
- Early decline in viraemia, observed in both vaccinated and unvaccinated control animals was associated with the development of virus-specific CTL activity and not with the presence of virus-specific neutralizing antibodies.

NHP.251 (7585061) **HIV-1 recombinant poxvirus vaccine induces cross-protection against HIV-2 challenge in rhesus macaques**
Authors Abimiku AG, Franchini G, Tartaglia J, Aldrich K, Myagkikh M, Markham PD, Chong P, Klein M, Kieny MP, Paoletti E, et al.
Journal Nat Med 1995 Apr;1(4):321-9
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Background: Rhesus macaques immunized with attenuated vaccinia or canarypox HIV-1 recombinants and boosted with HIV-1 protein subunits formulated in alum, then challenged with HIV-2.SBL6669.
- Following challenge with HIV-2SBL6669, 3/8 immunized macaques resisted infection for 6 months and another exhibited significantly delayed infection, whereas all 3 naive controls became infected.
- Immunizations elicited both humoral and cellular immune responses with no clear correlation with protection.

NHP.252 (7585217) **Long-term protection against SIV-induced disease in macaques vaccinated with a live attenuated HIV-2 vaccine**

Authors Putkonen P, Walther L, Zhang YJ, Li SL, Nilsson C, Albert J, Biberfeld P, Thorstensson R, Biberfeld G

Journal Nat Med 1995 Sep;1(9):914-8

Objectives Challenge, Immunogenicity To test the ability of a live attenuated human immunodeficiency virus type 2 (HIV-2) vaccine to protect cynomolgus monkeys against superinfection with a pathogenic simian immunodeficiency virus (SIVsm).

Main Findings

- 3/4 monkeys vaccinated with live HIV-2 were protected against immunosuppression and SIV-induced disease during more than 5 years of follow-up.
- The quality of the immunity was permissive for infection, but monkeys that survived showed restricted viral replication in peripheral blood and lymph nodes.
- Protection against a pathogenic heterologous primate lentivirus is possible.
- Vaccine can prevent disease in vaccinated monkeys even if infection is not prevented.

NHP.253 (7625117) **Heterologous HIV-2 challenge of rhesus monkeys immunized with recombinant vaccinia viruses and purified recombinant HIV-2 proteins**

Authors Vogt G, le Grand R, Vaslin B, Boussin F, Auboyer MH, Riviere Y, Putkonen P, Sonigo P, Kieny MP, Girard M, et al.

Journal Vaccine 1995 Feb;13(2):202-8

Objectives Challenge, Immunogenicity To analyze the role of anti-envelope immunity in the protection of rhesus monkeys against an HIV-2 intravenous challenge.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- None of the animals was protected in spite of high humoral immune responses on day of challenge as determined by ELISA and Western Blot assays.

NHP.254 (7521918) **Vaccine-induced neutralizing antibodies directed in part to the simian immunodeficiency virus (SIV) V2 domain were unable to protect rhesus monkeys from SIV experimental challenge**

Authors Schlienger K, Montefiori DC, Mancini M, Riviere Y, Tiollais P, Michel ML

Journal J Virol 1994 Oct;68(10):6578-88

Objectives Challenge, Immunogenicity To analyze the role of an SIV V2 vaccine as an effective region to boost SIV-neutralizing antibodies and to protect against live SIV challenge.

Main Findings

- 2 rhesus macaques primed with vaccinia virus recombinants expressing the surface glycoprotein gp140 of SIVmac then given booster with the SIVmac V2 domain: The 2 vaccinated macaques exhibited SIV-neutralizing antibodies (part of which directed specifically to the V2 region) after primer injections that were enhanced by the V2/HBsAg injections.
- Animals not protected against homologous challenge with SIVmac251.BK28.
- Vaccinees had higher viral loads than control animals after challenge.

NHP.255 (7632466) **In vivo administration of CD4-specific monoclonal antibody: effect on provirus load in rhesus monkeys chronically infected with the simian immunodeficiency virus of macaques**

Authors Reimann KA, Cate RL, Wu Y, Palmer L, Olson D, Waite BC, Letvin NL, Burkly LC

Journal AIDS Res Hum Retroviruses 1995 Apr;11(4):517-25

Objectives Immunotherapy, Passive Immunization To study the potential role of monoclonal antibodies specific for CD4 as an AIDS therapy.

Main Findings

- 6 infected monkeys treated with anti-CD4 MAb demonstrated a significant decrease in SIVmac provirus level after 9 days (3 had >800 CD4 cell/microliter and developed strong antimouse Ig response that prevented further treatment; the remaining 3 monkeys had <800 CD4 cell/microliter and failed to develop antimouse Ig antibody response).
- 4 control monkeys that received a control MAb of irrelevant specificity for 9-22 days showed either no significant change or a transient increase in SIVmac provirus

NHP.256 (7666524) **Vaccine-induced protection of chimpanzees against infection by a heterologous human immunodeficiency virus type 1**
Authors Girard M, Meignier B, Barre-Sinoussi F, Kieny MP, Matthews T, Muchmore E, Nara PL, Wei Q, Rimsky L, Weinhold K, et al.
Journal J Virol 1995 Oct;69(10):6239-48

NHP.257 (7666529) **Vaccine-induced virus-neutralizing antibodies and cytotoxic T cells do not protect macaques from experimental infection with simian immunodeficiency virus SIVmac32H (J5)**
Authors Hulskotte EG, Geretti AM, Siebelink KH, van Amerongen G, Cranage MP, Rud EW, Norley SG, de Vries P, Osterhaus AD
Journal J Virol 1995 Oct;69(10):6289-96

NHP.258.1 (7707496) **Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus**
Authors Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.
Journal J Virol 1995 May;69(5):2737-44
Objectives Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- Rhesus macaques inoculated with an attenuated macrophage-tropic recombinant of SIVmac239 (SIV/17E-Cl) exhibited vigorous type-specific nab responses restricted to SIV/17E-Cl by 2 weeks postinfection.
- Cross-reactive neutralizing antibodies emerged by 7 months, which neutralized not only SIV/17E-Cl but also the heterologous primary isolate SIV/DeltaB670.
- Challenge of SIV/17E-Cl-infected monkeys with SIV/DeltaB670: protective responses associated with cross-reactive neutralizing antibodies.
- Passive transfer of sera from SIV/17E-Cl-infected animals passively protected 2/4 naive recipients

NHP.258.2 (7707496) **Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus**
Authors Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.
Journal J Virol 1995 May;69(5):2737-44
Objectives Challenge .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- Challenge of SIV/17E-Cl-infected monkeys with SIV/DeltaB670: protective responses associated with cross-reactive neutralizing antibodies.

NHP.258.3 (7707496) **Cross-protective immune responses induced in rhesus macaques by immunization with attenuated macrophage-tropic simian immunodeficiency virus**
Authors Clements JE, Montelaro RC, Zink MC, Amedee AM, Miller S, Trichel AM, Jagerski B, Hauer D, Martin LN, Bohm RP, et al.
Journal J Virol 1995 May;69(5):2737-44
Objectives Passive Immunization .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- Passive transfer of sera from SIV/17E-Cl-infected animals passively protected 2/4 naive recipients

NHP.259 (7707540) **Macaques immunized with HLA-DR are protected from challenge with simian immunodeficiency virus**
Authors Arthur LO, Bess JW Jr, Urban RG, Strominger JL, Morton WR, Mann DL, Henderson LE, Benveniste RE
Journal J Virol 1995 May;69(5):3117-24

Objectives Challenge, Immunogenicity To identify the potential antigens involved in protection induced by the immunization with uninfected human cells against the challenge with SIV propagated in human cells.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Main Findings

- All macaques immunized with beta 2M and HLA class I developed high antibody titers to beta 2M, BUT were not protected from a subsequent challenge with infectious SIV grown in human cells.
- The macaques immunized with class II protein (HLA-DR) and mock virus developed antibodies to class II protein and were protected from the intravenous infectious virus challenge.
- The protection seen with human class II protein did not extend to protection from infection with SIV containing macaque class II proteins.
- Immunization with a purified cellular protein can protect from virus infection.

NHP.260 (7752758) **Protection by attenuated simian immunodeficiency virus in macaques against challenge with virus-infected cells**
Authors Almond N, Kent K, Cranage M, Rud E, Clarke B, Stott EJ
Journal Lancet 1995 May 27;345(8961):1342-4

NHP.261 (7865285) **Vaccine protection and reduced virus load from heterologous macaque-propagated SIV challenge**
Authors Heeney JL, Holterman L, ten Haaft P, Dubbes R, Koornstra W, Teeuwsen V, Bourquin P, Norley S, Niphuis H
Journal AIDS Res Hum Retroviruses 1994;10 Suppl 2:S117-21

NHP.262 (7884874) **A vaccine-elicited, single viral epitope-specific cytotoxic T lymphocyte response does not protect against intravenous, cell-free simian immunodeficiency virus challenge**
Authors Yasutomi Y, Koenig S, Woods RM, Madsen J, Wassef NM, Alving CR, Klein HJ, Nolan TE, Boots LJ, Kessler JA, et al.
Journal J Virol 1995 Apr;69(4):2279-84

NHP.263 (7818809) **T-cell proliferation to subinfectious SIV correlates with lack of infection after challenge of macaques**
Authors Clerici M, Clark EA, Polacino P, Axberg I, Kuller L, Casey NI, Morton WR, Shearer GM, Benveniste RE
Journal AIDS 1994 Oct;8(10):1391-5

NHP.265 (11090194) **Protection of Macaca nemestrina from disease following pathogenic simian immunodeficiency virus (SIV) challenge: utilization of SIV nucleocapsid mutant DNA vaccines with and without an SIV protein boost**
Authors Gorelick RJ, Benveniste RE, Lifson JD, Yovandich JL, Morton WR, Kuller L, Flynn BM, Fisher BA, Rossio JL, Piatak M Jr, Bess JW Jr, Henderson LE, Arthur LO
Journal J Virol 2000 Dec;74(24):11935-49
Objectives Challenge, Immunogenicity To use molecular clones (that express nucleocapsid deletion mutant SIVs that are replication defective but capable of completing virtually all of the steps of a single viral infection cycle) in a vaccine challenge study.
Species/Subspecies Macaca nemestrina (pigtailed macaque)
Vaccine Name SIV(Mne)NCΔZF2 DNA *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular
Vaccine Name S8-NCΔZF2 *Type:* Live Attenuated Virus *Routes:* Subcutaneous, Intramuscular
Challenge SIV(Mne) clone E11S *Route:* Intravenous
Main Findings

- 11/11 animals immunized with nucelocapside mutant SIV DNA; immunized animals became infected following challenge but typically showed decreased initial peak plasma SIV RNA levels compared to those of control animals; all control animals became infected and 3/4 animals developed progressive SIV disease leading to death.
- Only modest and inconsistent humoral responses and no cellular immune responses were observed prior to challenge.
- Immunization of macaques with DNA that codes for replication-defective but structurally complete virions appears to protect from or at least delay the onset of AIDS after infection with a pathogenic immunodeficiency virus.

NHP.266 (12390544) **Protection by SIV VLP DNA prime/protein boost following mucosal SIV challenge is markedly enhanced by IL-12/GM-CSF co-administration**

Authors O'Neill E, Martinez I, Villinger F, Rivera M, Gascot S, Colon C, Arana T, Sidhu M, Stout R, Montefiori DC, Martinez M, Ansari AA, Israel ZR, Kraiselburd E

Journal J Med Primatol 2002 Aug;31(4-5):217-27

Objectives Challenge, Immunogenicity To induce and enhance antiviral responses using a DNA prime/virus-like particles (VLP) protein boost strategy adjuvanted with interleukin (IL)-12/GM-CSF in rhesus macaques challenged with simian immunodeficiency virus (SIV).

Main Findings

- All except 1 immunized monkey became infected.
- All immunized monkeys showed a marked reduction of acute viral peaks.
- Reduction of viral load set points was only achieved in groups whose prime-boost immunizations were supplemented with IL-12/GM-CSF (prime) and/or with IL-12 (boost).
- Control of viremia correlated with lack of disease progression and survival.
- Detection of virus in rectal washes at 1 year post-challenge was only successful in monkeys whose immunizations did not include cytokine adjuvant, but these loads did not correlate with plasma viral loads.

NHP.267 (2190095) **Protection of chimpanzees from infection by HIV-1 after vaccination with recombinant glycoprotein gp120 but not gp160**

Authors Berman PW, Gregory TJ, Riddle L, Nakamura GR, Champe MA, Porter JP, Wurm FM, Hershberg RD, Cobb EK, Eichberg JW

Journal Nature 1990 Jun 14;345(6276):622-5

Objectives Challenge, Immunogenicity To study chimpanzees that were immunized with recombinant forms of the HIV-1 glycoproteins gp120 and gp160 produced in Chinese hamster ovary cells, and then challenged with HIV-1.

Species/Subspecies Pan Troglodytes (Chimpanzee)

Vaccine Name rgp120 *Type:* Recombinant Subunit Protein

Vaccine Name rsgp160 *Type:* Recombinant Subunit Protein

Challenge HIV-1 IIIB *Route:*

Main Findings

- The control and the 2 animals immunized with the gp160 variant became infected within 7 weeks of challenge.
- The 2 animals immunized with the gp120 variant have shown no signs of infection after more than 6 months.
- Conclusion: recombinant gp120, formulated in an adjuvant approved for human use, can elicit protective immunity against a homologous strain of HIV-1.

NHP.268.1 (10812220) **Minimization of chronic plasma viremia in rhesus macaques immunized with synthetic HIV-1 Tat peptides and infected with a chimeric simian/human immunodeficiency virus (SHIV33)**

Authors Goldstein G, Manson K, Tribbick G, Smith R

Journal Vaccine 2000 Jun 15;18(25):2789-95

Objectives Challenge, Immunogenicity To study the effect of Tat on HIV-1 replication in vivo during acute, chronic asymptomatic and AIDS stages of infection by comparisons of plasma viremia in Tat-immunized or control monkeys challenged with SHIV33 or SHIV33A.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Synthetic tat *Type:* Synthetic Protein/Peptide *Route:* Intramuscular

Challenge SHIV33, SHIV33A *Route:* Intravenous

Main Findings

- Immunization of monkeys with tat affected the outcome of challenge: chronic plasma viremia became undetectable or minimized in Tat-immunized asymptomatic SHIV33-infected monkeys while the high viral loads of acute infection or SHIV33A-induced simian AIDS were unaffected by Tat immunization.
- Active or passive immunotherapies targeting Tat provide potential approaches to controlling chronic HIV-1 viremia and preventing AIDS.

NHP.268.2 (10812220) **Minimization of chronic plasma viremia in rhesus macaques immunized with synthetic HIV-1 Tat peptides and infected with a chimeric simian/human immunodeficiency virus (SHIV33)**

Authors Goldstein G, Manson K, Tribbick G, Smith R

Journal Vaccine 2000 Jun 15;18(25):2789-95

Objectives Challenge, Immunogenicity To study the effect of Tat on HIV-1 replication in vivo during acute, chronic asymptomatic and AIDS stages of infection by comparisons of plasma viremia in Tat-immunized or control monkeys challenged with SHIV33 or SHIV33A.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- See NHP.268.

NHP.269 (10074165) **Protection of macaques against intrarectal infection by a combination immunization regimen with recombinant simian immunodeficiency virus SIVmne gp160 vaccines**

Authors Polacino P, Stallard V, Montefiori DC, Brown CR, Richardson BA, Morton WR, Benveniste RE, Hu SL

Journal J Virol 1999 Apr;73(4):3134-46

Objectives Challenge, Immunogenicity To examine the protective efficacy of recombinant simian immunodeficiency virus SIVmne envelope (gp160) vaccines against mucosal challenge by the cloned homologous virus E11S clone and the uncloned SIVmne.

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

Vaccine Name Recombinant vaccinia virus vac-gp160 (v-SE5) *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification

Vaccine Name gp160/BSC-40 *Type:* Purified Viral Products *Route:* Intramuscular

Challenge SIV(Mne) clone E11S, SIV(Mne) Cell-free *Route:* Intrarectal

Main Findings

- Protection correlates with high levels of SIV-specific antibodies.
- 4/4 vaccinees developed low levels of SIV-specific antibody responses after the recombinant vaccinia virus immunization; level increased 10-30 fold by boost envelop subunit.
- After intrarectal challenge with E11S, all 3 control animals became persistently infected, whereas 3/4 immunized macaques were completely protected.

NHP.270.1 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity**

Authors Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M

Journal J Gen Virol 2001 Sep;82(Pt 9):2215-23

NHP.270.2 (11514732) **Induction of simian immunodeficiency virus (SIV)-specific CTL in rhesus macaques by vaccination with modified vaccinia virus Ankara expressing SIV transgenes: influence of pre-existing anti-vector immunity**

Authors Sharpe S, Polyanskaya N, Dennis M, Sutter G, Hanke T, Erfle V, Hirsch V, Cranage M

Journal J Gen Virol 2001 Sep;82(Pt 9):2215-23

NHP.274 (12490410) **Equivalent Immunogenicity of the Highly Attenuated Poxvirus-Based ALVAC-SIV and NYVAC-SIV Vaccine Candidates in SIVmac251-Infected Macaques**

Authors Hel Z, Nacsa J, Tsai WP, Thornton A, Giuliani L, Tartaglia J, Franchini G

Journal Virology 2002 Dec 5;304(1):125-34

Objectives Challenge, Immunogenicity, Immunotherapy To compare the immunogenicity of two vaccine candidates, the canarypox-based ALVAC-SIV-gag-pol-env and the vaccinia-based NYVAC-SIV-gag-pol-env, in rhesus macaques infected with SIVmac251 and treated with ART by 2 weeks postinfection.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name NYVAC-SIV-gag-pol-env (NYVAC-SIV-gpe) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name ALVAC-SIV-gpe (vcp180) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge SIVmac251 (561) *Route:* Intravenous

Main Findings

- Both ALVAC-SIV-gpe and NYVAC-SIV-gpe vaccine candidates induced and/or enhanced a virus-specific CD8+ T cell response to a similar extent, as demonstrated by tetramer staining of Gag-specific CD8+ T cells.
- Both vaccines elicited comparable lymphoproliferative responses (LPRs) to the SIV p27 Gag and gp120 Env proteins.
- The vaccine was given after infection and initiation of HAART, as a therapuetic vaccine, not as protection from infection

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NHP.275 (9234548) **SIV DNA vaccine trial in macaques: post-challenge necropsy in vaccine and control groups**

Authors Lu S, Manson K, Wyand M, Robinson HL

Journal Vaccine 1997 Jun;15(8):920-3

Objectives Challenge To study histopathologic findings from 9 macaques in a simian immunodeficiency virus (SIV) DNA vaccine trial evaluating the ability of a 5-plasmid DNA vaccine to protect against an uncloned SIVmac251 challenge (Lu et al., J. Virol. 1996, 70, 3978-3991).

Species/Subspecies Macaca (sp)

Vaccine Name DNA-SIV *Type:* DNA *Routes:* Intravenous, Intradermal (Gene Gun DNA-coated gold beads), Intramuscular

Main Findings

- 3 vaccinated and 1 control macaques developed disease and were sacrificed in the first year following challenge.
- Diseased and clinically "normal" animals had developed typical SIV-related lymphoid changes, inflammatory disorders and opportunistic infections (all but 1 vaccinated animal and both controls).
- The ability to contain challenge was superior in animals immunized by 3 routes (iv,im and gene gun) as compared to those that received the control DNA or DNA vaccine by gene gun only

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NHP.276 (12396607) **Evaluation in rhesus macaques of Tat and rev-targeted immunization as a preventive vaccine against mucosal challenge with SHIV-BX08**

Authors Verrier B, Le Grand R, Ataman-Onal Y, Terrat C, Guillon C, Durand PY, Hurtrel B, Aubertin AM, Sutter G, Erfle V, Girard M

Journal DNA Cell Biol 2002 Sep;21(9):653-8

Objectives Challenge, Immunogenicity To evaluate whether vaccination with Tat or Tat and Rev could significantly reduce viral load in nonhuman primates.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SFV-tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Subcutaneous

Vaccine Name SFV-rev *Type:* Recombinant Vector (virus/bacteria) *Route:* Subcutaneous

Vaccine Name MVA-tat *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name MVA-rev *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name DNA-pCI-tat *Type:* DNA *Routes:* Intradermal, Intramuscular

Vaccine Name DNA-pCI-rev *Type:* DNA *Routes:* Intradermal, Intramuscular

Challenge SHIV-BX08 *Route:* Intrarectal

Main Findings

- The immunization strategy by priming with either DNA or SFV seemed to be equivalent, but the additive or synergistic effect of a rev vaccine could not be clearly established.
- None of the animals was protected from infection.
- Peak viremia was reduced more than 200-fold compared to sham controls in one third (6/18) of vaccinated macaques.
- 4/6 protected animals did not seroconvert.

NHP.277 (12396606) **Immunogenicity of HIV-1 IIIB and SHIV 89.6P Tat and Tat toxoids in rhesus macaques: induction of humoral and cellular immune responses**

Authors Richardson MW, Mirchandani J, Silvera P, Regulier EG, Capini C, Bojczuk PM, Hu J, Gracely EJ, Boyer JD, Khalili K, Zagury JF, Lewis MG, Rappaport J

Journal DNA Cell Biol 2002 Sep;21(9):637-51

Objectives Challenge, Immunogenicity To compare immune responses in rhesus macaques immunized with unmodified HIV-1 IIIB Tat, SHIV89.6P Tat, and carboxymethylated IIIB and 89.6P Tat toxoids.

Main Findings

- Immunization with either IIIB or 89.6P preparation induced high titer and broadly cross-reactive serum anti-Tat IgG that recognized HIV-1 subtype-E and SIVmac251 Tat.
- Proliferative responses to Tat toxoids corresponding to the immunogen were evident in vitro in both IIIB and 89.6P groups.
- All animals were infected upon intravenous challenge with 30 MID(50) of SHIV89.6P and outcome of vaccine groups was not different from controls.
- Tat specific CD8+ T-cell responses may not appropriately recognize infected cells in vivo in rhesus macaque model.

NHP.278 (12477432) **Co-immunization of rhesus macaques with plasmid vectors expressing IFN-gamma, GM-CSF, and SIV antigens enhances anti-viral humoral immunity but does not affect viremia after challenge with highly pathogenic virus**

Authors Lena P, Villinger F, Giavedoni L, Miller CJ, Rhodes G, Luciw P

Journal Vaccine 2002 Dec 19;20 Suppl 4:A69-79

Objectives Challenge, Immunogenicity To investigate the adjuvant capacity of.

Main Findings

- Proliferative responses significantly enhanced by co-immunization with the cytokines GM-CSF and interferon-γ.
- 12 immunized monkeys and 6 naive controls, were challenged by the oral mucosal route with the uncloned and highly pathogenic SIVmac251 and became infected.
- Plasma viremia set points were not different in co-immunized group and the non-immunized control group.
- Monkeys vaccinated with equivalent amounts of empty vector plasmid (i.e. no cytokine inserts) along with plasmids expressing viral antigens demonstrated a slight but significant decrease in acute viremia compared to non-immunized controls (P<0.02).
- Conclusion: results underscore the need for further testing of cytokines as vaccine adjuvants in relevant animal models

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NHP.279 (12396605) **Potent, persistent cellular immune responses elicited by sequential immunization of rhesus macaques with Ad5 host range mutant recombinants encoding SIV Rev and SIV Nef**

Authors Patterson LJ, Malkevitch N, Zhao J, Peng B, Robert-Guroff M

Journal DNA Cell Biol 2002 Sep;21(9):627-35

NHP.280 (12396604) **Design and in vivo immunogenicity of a polyvalent vaccine based on SIVmac regulatory genes**

Authors Hel Z, Tryniszewska E, Tsai WP, Johnson JM, Harrod R, Fullen J, Kalyanaraman VS, Altman JD, McNally J, Karpova T, Felber BK, Tartaglia J, Franchini G

Journal DNA Cell Biol 2002 Sep;21(9):619-26

NHP.281 (12391256) **Vaccination of macaques with long-standing SIVmac251 infection lowers the viral set point after cessation of antiretroviral therapy**

Authors Tryniszewska E, Nacsa J, Lewis MG, Silvera P, Montefiori D, Venzon D, Hel Z, Parks RW, Moniuszko M, Tartaglia J, Smith KA, Franchini G

Journal J Immunol 2002 Nov 1;169(9):5347-57

Objectives Immunotherapy, Chemotherapy Tested ART, ART plus therapeutic vaccine, ART plus therapeutic vaccine plus IL-2, ART plus IL-2.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Therapeutic vaccines reduced average viral load at set point, but not peak viral load following cessation of ART. Addition of IL-2 to therapeutic vaccine produced virus-specific proliferative resopnses lower than therapeutic vaccine alone

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NHP.282 (12391187) **Containment of simian immunodeficiency virus infection in vaccinated macaques: correlation with the magnitude of virus-specific pre- and postchallenge CD4+ and CD8+ T cell responses**

Authors Hel Z, Nacsa J, Tryniszewska E, Tsai WP, Parks RW, Montefiori DC, Felber BK, Tartaglia J, Pavlakis GN, Franchini G

Journal J Immunol 2002 Nov 1;169(9):4778-87

NHP.283 (12388726) **Both mucosal and systemic routes of immunization with the live, attenuated NYVAC/simian immunodeficiency virus SIV(gpe) recombinant vaccine result in gag-specific CD8(+) T-cell responses in mucosal tissues of macaques**
Authors Stevceva L, Alvarez X, Lackner AA, Tryniszewska E, Kelsall B, Nacsa J, Tartaglia J, Strober W, Franchini G
Journal J Virol 2002 Nov;76(22):11659-76

NHP.284 (12388710) **Elicitation of simian immunodeficiency virus-specific cytotoxic T lymphocytes in mucosal compartments of rhesus monkeys by systemic vaccination**
Authors Baig J, Levy DB, McKay PF, Schmitz JE, Santra S, Subbramanian RA, Kuroda MJ, Lifton MA, Gorgone DA, Wyatt LS, Moss B, Huang Y, Chakrabarti BK, Xu L, Kong WP, Yang ZY, Mascola JR, Nabel GJ, Carville A, Lackner AA, Veazey RS, Letvin NL
Journal J Virol 2002 Nov;76(22):11484-90

NHP.285 (12388697) **Live, attenuated simian immunodeficiency virus SIVmac-M4, with point mutations in the Env transmembrane protein intracytoplasmic domain, provides partial protection from mucosal challenge with pathogenic SIVmac251**
Authors Shacklett BL, Shaw KE, Adamson LA, Wilkens DT, Cox CA, Montefiori DC, Gardner MB, Sonigo P, Luciw PA
Journal J Virol 2002 Nov;76(22):11365-78

NHP.286 (12359453) **Systemic infection and limited replication of SHIV vaccine virus in brains of macaques inoculated intracerebrally with infectious viral DNA**
Authors Smith MS, Niu Y, Li Z, Adany I, Pinson DM, Liu ZQ, Berry T, Sheffer D, Jia F, Narayan O
Journal Virology 2002 Sep 15;301(1):130-5

NHP.287 (12359438) **A simian immunodeficiency virus nef peptide is a dominant cytotoxic T lymphocyte epitope in Indian-origin rhesus monkeys expressing the common MHC class I allele mamu-A*02**
Authors Newberg MH, Kuroda MJ, Charini WA, Miura A, Lord CI, Schmitz JE, Gorgone DA, Lifton MA, Kuus-Reichel K, Letvin NL
Journal Virology 2002 Sep 30;301(2):365-73

NHP.288 (12239328) **Effects of cytotoxic T lymphocytes (CTL) directed against a single simian immunodeficiency virus (SIV) Gag CTL epitope on the course of SIVmac239 infection**
Authors Allen TM, Jing P, Calore B, Horton H, O Connor DH, Hanke T, Piekarczyk M, Ruddersdorf R, Mothe BR, Emerson C, Wilson N, Lifson JD, Belyakov IM, Berzofsky JA, Wang C, Allison DB, Montefiori DC, Desrosiers RC, Wolinsky S, Kunstman KJ, Altman JD, Sette A, McMichael AJ, Watkins DI
Journal J Virol 2002 Oct;76(20):10507-11

NHP.289 (12239289) **Slowly declining levels of viral RNA and DNA in DNA/recombinant modified vaccinia virus Ankara-vaccinated macaques with controlled simian-human immunodeficiency virus SHIV-89.6P challenges**
Authors Tang Y, Villinger F, Staprans SI, Amara RR, Smith JM, Herndon JG, Robinson HL
Journal J Virol 2002 Oct;76(20):10147-54

NHP.290 (12111423) **Infection of macaques with chimeric simian and human immunodeficiency viruses containing Env from subtype F**
Authors Kuwata T, Takemura T, Takehisa J, Miura T, Hayami M
Journal Arch Virol 2002 Jun;147(6):1121-32

NHP.291 (12502824) **Nonneutralizing antibodies to the CD4-binding site on the gp120 subunit of human immunodeficiency virus type 1 do not interfere with the activity of a neutralizing antibody against the same site**
Authors Herrera C, Spenlehauer C, Fung MS, Burton DR, Beddows S, Moore JP
Journal J Virol 2003 Jan;77(2):1084-91
Objectives Passive Immunization To investigate whether nonneutralizing monoclonal antibodies to the gp120 subunit of env glycoprotein complex of HIV-1 can interfere with HIV-1 neutralization by another anti-gp120 MAb.
Main Findings
- REMOVE THIS.

NHP.293 (1708168) **Recombinant virus vaccine-induced SIV-specific CD8+ cytotoxic T lymphocytes**
Authors Shen L, Chen ZW, Miller MD, Stallard V, Mazzara GP, Panicali DL, Letvin NL
Journal Science 1991 Apr 19;252(5004):440-3

NHP.294 (12477823) **Immunization of newborn rhesus macaques with simian immunodeficiency virus (SIV) vaccines prolongs survival after oral challenge with virulent SIVmac251.*****
Authors Van Rompay KK, Greenier JL, Cole KS, Earl P, Moss B, Steckbeck JD, Pahar B, Rourke T, Montelaro RC, Canfield DR, Tarara RP, Miller C, McChesney MB, Marthas ML
Journal J Virol 2003 Jan;77(1):179-90
Objectives Challenge, Immunogenicity To evaluate immunization of infant macaques at birth and 3 weeks of age with either MVA-SIV Gag, Pol, and Env or live-attenuated SIVmac1A11.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rMVA SIVmac239 gagpolenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intramuscular, Intranasal
Vaccine Name SIVmac1A11 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intranasal
Vaccine Name Anti-SIVmac251 *Type:* Passive Antibody *Route:* Intraplacental
Challenge SIVmac251 *Route:* Oral
Main Findings
- Upon challenge with virulent SIVmac251, all animals became infected.
- The immunized animals mounted better antiviral antibody responses, controlled virus levels more effectively, and had a longer disease-free survival than the unvaccinated infected monkeys.
- Maternal antibodies did not significantly reduce the efficacy of the MVA-SIVgpe vaccine.

NHP.295 (11000207) **Intrinsic susceptibility of rhesus macaque peripheral CD4(+) T cells to simian immunodeficiency virus in vitro is predictive of in vivo viral replication**
Authors Goldstein S, Brown CR, Dehghani H, Lifson JD, Hirsch VM
Journal J Virol 2000 Oct;74(20):9388-95
Main Findings
- Following intravenous infection of macaques with SIVsmE543-3, the wide range in plasma viremia followed the same rank order as the relative susceptibility established by in vitro studies.
- Significant correlation between plasma viremia at 2-8 wpi and in vitro susceptibility ($P < 0.05$).
- Simian T-lymphotropic virus type 1 appears to enhance susceptibility to SIV infection.
- Intrinsic susceptibility of CD4+ target cells influences early virus replication patterns in vivo.

NHP.296 (12502820) **Prevention of Disease Induced by a Partially Heterologous AIDS Virus in Rhesus Monkeys by Using an Adjuvanted Multicomponent Protein Vaccine**
Authors Voss G, Manson K, Montefiori D, Watkins DI, Heeney J, Wyand M, Cohen J, Bruck C
Journal J Virol 2003 Jan;77(2):1049-58
Objectives Challenge To assess the efficacy of a recombinant human immunodeficiency virus type 1 (HIV-1) gp120, NefTat fusion protein, and simian immunodeficiency virus (SIV) Nef formulated in the clinically tested adjuvant AS02A.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Recombinant gp120 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name Nef-Tat *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name SIV Nef *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Main Findings
- Multiantigen subunit protein vaccine was able to prevent the development of disease induced in rhesus monkeys by a partially heterologous AIDS virus.

- Upon challenge of genetically unselected rhesus monkeys with the highly pathogenic and partially heterologous SIV/HIV strain SHIV89.6p, the vaccine was able to reduce virus load and protect the animals from a decline in CD4-positive cells.
- Vaccination prevented the development of AIDS for more than 2.5 years.

NHP.297 (12502815) **Increased mucosal transmission but not enhanced pathogenicity of the CCR5-tropic, simian AIDS-inducing simian/human immunodeficiency virus SHIV(SF162P3) maps to envelope gp120**

Authors Hsu M, Harouse JM, Gettie A, Buckner C, Blanchard J, Cheng-Mayer C

Journal J Virol 2003 Jan;77(2):989-98

Objectives Pathogenicity To determine whether envelope glycoprotein gp120 is responsible for increased pathogenesis and transmissibility of the SHIV-SF162P3.

Main Findings

- See NHP.312.

NHP.298 (12477842) **Importance of B-cell responses for immunological control of variant strains of simian immunodeficiency virus**

Authors Johnson WE, Lifson JD, Lang SM, Johnson RP, Desrosiers RC

Journal J Virol 2003 Jan;77(1):375-81

Objectives Immunogenicity, Pathogenicity To compare the pathogenicity of three variants of cloned simian immunodeficiency virus strain 239 (SIV239).

Main Findings

- All 3 cloned strains (M5, DeltaV1-V2 and 316) of SIVmac239 were capable of significant levels of fusion independent of CD4, and all 3 were considerably more sensitive to antibody-mediated neutralization than the parent strain from which they were derived.
- The 3 clones induce viral loads at peak height around day 14 that are indistinguishable from or only slightly less than those observed in monkeys infected with the parental SIV239 strain.
- Viral loads at the set point 20 to 50 weeks after infection, however, were more than 400- to 10,000-fold lower with the variant strains.
- Depletion of B cells around the time of infection with M5 resulted in less effective immunological control and much higher viral loads at the set point in 2/3 monkeys

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NHP.299 (12496959) **Therapeutic dendritic-cell vaccine for simian AIDS**

Authors Lu W, Wu X, Lu Y, Guo W, Andrieu JM

Journal Nat Med 2003 Jan;9(1):27-32

Objectives Immunogenicity, Immunotherapy To investigate the ability of a vaccination with chemically inactivated SIV-pulsed dendritic cells to induce cellular and humoral immunity in SIV infected rhesus monkey model.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name AT-2 inactivated SIV-loaded DC *Type:* Cell/Tissue *Route:* Subcutaneous

Main Findings

- Chemically inactivated SIV-pulsed dendritic cells induced an effective and durable SIV-specific cellular and humoral immunity in SIV-infected rhesus monkeys.
- After 3 immunizations made at 2-week intervals, the animals exhibited a 50-fold decrease of SIV DNA and a 1,000-fold decrease of SIV RNA in peripheral blood with reduced viral load levels maintained over the remaining 34 weeks.

NHP.300 (12531331) **A Gag-Pol/Env-Rev SIV239 DNA vaccine improves CD4 counts, and reduce viral loads after pathogenic intrarectal SIV(mac)251 challenge in Rhesus Macaques**

Authors Muthumani K, Bagarazzi M, Conway D, Hwang DS, Manson K, Ciccarelli R, Israel Z, Montefiori DC, Ugen K, Miller N, Kim J, Boyer J, Weiner DB

Journal Vaccine 2003 Jan 30;21(7-8):629-37

Objectives Challenge, Immunogenicity To study plasmid vaccines supplemented by IL-2 Ig cytokine gene adjuvants or boosted by recombinant MVA vectors expressing relevant SIV and HIV antigens.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pGagpol/EnvRev SIV239 DNA *Type:* DNA *Route:* Intramuscular
Challenge SIVmac251 *Route:* Intrarectal
Main Findings

- The immunization strategy employed in this study prevented CD4(+) T-cell loss and lowered viral loads following pathogenic challenge.
- Using a pathogenic SIV251 rhesus mucosal challenge model, pGag/Pol+pEnv/Rev plasmid vaccines could not prevent SIVinfection: vaccinated animals exhibited significant improvement in control of viral challenge and protection against CD4(+) T-cell loss compared to control animals

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NHP.301 (12526038) **Human and simian immunodeficiency virus-infected chimpanzees do not have increased intracellular levels of beta-chemokines in contrast to infected humans**
Authors Ondoa P, Vereecken C, Fransen K, Colebunders R, Van Der Groen G, Heeney JL, Kestens L
Journal J Med Virol 2003 Mar;69(3):297-305
Objectives Immunogenicity, Pathogenicity To explain why chimpanzees infected with HIV-1 or SIVcpz are relatively resistant to AIDS.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Main Findings

- In humans, the percentage of B-chemokine-positive cells was significantly higher in CD8+ T and natural killer (NK) cells than in CD4+ T cells in both uninfected and HIV-1-infected individuals.
- In the presence of HIV-1 infection, however, both CD8+ and CD4+ T cell subsets contained significantly more B-chemokine-positive cells than in the absence of infection.
- In chimpanzees, the percentage of B-chemokine-positive CD8+ T and NK cells was significantly higher than in uninfected humans.
- In contrast to humans, infection of chimpanzees with either HIV-1 or with SIVcpz was not associated with increased numbers of B-chemokine-positive cells.

NHP.302 (12393472) **Impact of simian immunodeficiency virus (SIV) infection on lymphocyte numbers and T-cell turnover in different organs of rhesus monkeys**
Authors Sopper S, Nierwetberg D, Halbach A, Sauer U, Scheller C, Stahl-Hennig C, Matz-Rensing K, Schafer F, Schneider T, ter Meulen V, Muller JG
Journal Blood 2003 Feb 15;101(4):1213-9

NHP.303 (12502833) **Control of viremia and prevention of simian-human immunodeficiency virus-induced disease in rhesus macaques immunized with recombinant vaccinia viruses plus inactivated simian immunodeficiency virus and human immunodeficiency virus type 1 particles**
Authors Willey RL, Byrum R, Piatak M, Kim YB, Cho MW, Rossio Jr JL Jr, Bess Jr J Jr, Igarashi T, Endo Y, Arthur LO, Lifson JD, Martin MA
Journal J Virol 2003 Jan;77(2):1163-74
Objectives Challenge, Immunogenicity To evaluate the protective efficacy of a vaccine regimen that uses recombinant vaccinia viruses expressing SIV and HIV-1 structural proteins in combination with intact inactivated SIV and HIV-1 particles.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rVV-SIVmacgag/pol *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal
Vaccine Name rVV-HIV-1.DH12env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intradermal
Vaccine Name AT-2 rx SIVmac239 *Type:* Live Attenuated Virus *Route:* Intramuscular
Vaccine Name AT-2 rx HIV-1.DH12 *Type:* Live Attenuated Virus *Route:* Intramuscular
Challenge SHIV.DH12R-PS1 *Route:* Intravenous
Main Findings

- Following virus challenge, control animals experienced a rapid and complete loss of CD4(+) T cells, sustained high viral loads, and developed clinical disease by 17 to 21 weeks.
- All the vaccinated monkeys became infected, displayed reduced post-peak viremia, had no significant loss of CD4(+) T cells, and have remained healthy for more than 15 mpc.
- CD8(+) T-cell and nab responses demonstrated in vaccinated animals following challenge.
- Immunologic control of infection was incomplete (no sterilizing protection) by 22 wpc.

NHP.304 (12556683) **Post-exposure prophylaxis with human monoclonal antibodies prevented SHIV89.6P infection or disease in neonatal macaques**

Authors Ferrantelli F, Hofmann-Lehmann R, Rasmussen RA, Wang T, Xu W, Li PL, Montefiori DC, Cavacini LA, Katinger H, Stiegler G, Anderson DC, McClure HM, Ruprecht RM.

Journal AIDS 2003 Feb 14;17(3):301-309

Objectives Challenge, Immunotherapy, Passive Immunization To develop passive immunization with human neutralizing monoclonal antibodies against mother-to-child transmission of HIV during delivery and through breastfeeding.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Monoclonal antibody 2G12 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Monoclonal antibody 2F5 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name Monoclonal antibody 4E10 *Type:* Passive Antibody *Route:* Intravenous

Vaccine Name IgG1 b12 *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV89.6P *Route:* Oral

Main Findings

- 2/4 macaque infants treated with neutralizing mAbs showed no evidence of infection; the other 2 maintained normal CD4 T cell counts.
- In contrast, all control animals became highly viremic and had profound CD4 T cell losses; 3/4 died from AIDS within 1.5-6 weeks of the challenge
- Conclusions: Passive immunization with this quadruple neutralizing mAbs combination may represent a promising approach to prevent peri- and postnatal HIV transmission

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NHP.305 (12545074) **Live attenuated, nef-deleted SIV is pathogenic in most adult macaques after prolonged observation**

Authors Hofmann-Lehmann R, Vlasak J, Williams AL, Chenine AL, McClure HM, Anderson DC, O'Neil S, Ruprecht RM

Journal AIDS 2003 Jan 24;17(2):157-66

Objectives Immunogenicity, Pathogenicity To demonstrate the pathogenicity of a live attenuated SIV (SIVmac239Δ3).

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVmac239Δ3 (cell-infected) *Type:* Cell/Tissue *Route:* Intravenous

Vaccine Name SIVmac239Δ3 *Type:* Live Attenuated Virus *Routes:* Intravenous, Oral, Intra-amniotic

Main Findings

- 11/11 rhesus macaques vaccinated with SIVmac239δ3 developed signs of immune disfunction.
- 11/11 vaccinated animals had inverted CD4:CD8 ratio.
- 7/11 (64%) had persistent recurrent viremia.
- Other signs of immune disfunction included decreased CD4, low CD4CD29 lymphocyte subsets, low anti-gag antibodies, etc
- 2/11 (18%) vaccinees developed AIDS.
- Conclusion: Live attenuated virus can cause immune disfunction in vaccinees and similar live attenuated HIV seems contraindicated for mass vaccination of humans

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NHP.306.1 (11797011) **Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity**

Authors Shiver JW, Fu TM, Chen L, Casimiro DR, Davies ME, Evans RK, Zhang ZQ, Simon AJ, Trigona WL, Dubey SA, Huang L, Harris VA, Long RS, Liang X, Handt L, Schleif WA, Zhu L, Freed DC, Persaud NV, Guan L, Punt KS, Tang A, Chen M, Wilson KA, Collins KB, Heidecker GJ, Fernandez VR, Perry HC, Joyce JG, Grimm KM, Cook JC, Keller PM, Kresock DS, Mach H etc

Journal Nature 2002 Jan 17;415(6869):331-5

Objectives Challenge, Immunogenicity To compare vaccine vector delivery systems: 3 formulations of a plasmid DNA vector (MVA) and a replication incompetent adenovirus type 5 vector expressing SIV gag protein.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pV1R-SIVmac239-gag *Type:* DNA *Route:* Intramuscular
Vaccine Name MVA-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name Ad5-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Challenge SHIV89.6P *Route:* Intravenous
Main Findings

- A replication-incompetent Ad5 vector, used either alone or as a booster inoculation after priming with a DNA vector elicited the most effective response.
- After challenge with a pathogenic SHIV, the animals immunized with Ad5 vector exhibited the most pronounced attenuation of the virus infection.
- The replication-defective adenovirus is a promising vaccine vector for development of an HIV-1 vaccine.

NHP.306.2 (11797011) **Replication-incompetent adenoviral vaccine vector elicits effective anti-immunodeficiency-virus immunity**

Authors Shiver JW, Fu TM, Chen L, Casimiro DR, Davies ME, Evans RK, Zhang ZQ, Simon AJ, Trigona WL, Dubey SA, Huang L, Harris VA, Long RS, Liang X, Handt L, Schleif WA, Zhu L, Freed DC, Persaud NV, Guan L, Punt KS, Tang A, Chen M, Wilson KA, Collins KB, Heidecker GJ, Fernandez VR, Perry HC, Joyce JG, Grimm KM, Cook JC, Keller PM, Kresock DS, Mach H etc
Journal Nature 2002 Jan 17;415(6869):331-5
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pV1R-SIVmac239-gag *Type:* DNA *Route:* Intramuscular
Vaccine Name MVA-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name Ad5-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Challenge SHIV89.6P *Route:* Intravenous

NHP.308 (12551977) **Mucosal priming of simian immunodeficiency virus-specific cytotoxic T-lymphocyte responses in rhesus macaques by the Salmonella type III secretion antigen delivery system**

Authors Evans DT, Chen LM, Gillis J, Lin KC, Harty B, Mazzara GP, Donis RO, Mansfield KG, Lifson JD, Desrosiers RC, Galan JE, Johnson RP
Journal J Virol 2003 Feb;77(4):2400-9
Objectives Challenge, Immunogenicity To test attenuated strains of Salmonella expressing fragments of the SIV Gag protein fused to the type III-secreted SopE protein for the ability to prime virus-specific CTL responses in rhesus macaques.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name rSalmonella typhimurium-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intragastric
Vaccine Name rSalmonella typhi-SIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intragastric
Vaccine Name MVA-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intragastric
Challenge SIVmac239 *Route:* Intrarectal
Main Findings

- Strong Gag-specific CTL responses were consistently detected, and tetramer staining revealed the expansion of Gag181-189-specific CD8+ T-cell responses in peripheral blood also in lymphocytes isolated from the colon.
- A significant percentage of the Gag181-189-specific T-cell population in each animal also expressed the intestinal homing receptor $\alpha 4ß7$.
- Salmonella-primed/MVA-boosted animals did not exhibit improved control of virus replication following a rectal challenge with SIVmac239.

NHP.309 (12573592) **Replication, immunogenicity, and protective properties of live-attenuated simian immunodeficiency viruses expressing interleukin-4 or interferon-gamma**

Authors Stahl-Hennig C, Gundlach BR, Dittmer U, ten Haaft P, Heeney J, Zou W, Emilie D, Sopper S, Uberla K
Journal Virology 2003 Jan 20;305(2):473-85
Objectives Challenge, Immunogenicity, Pathogenicity To study the effect of interferon-γ and interleukin-4 on viral load, immunogenicity, and protective properties of Nef-lacking mutants of SIV-expressing SIV-IL4 or SIV-IFN.
Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIV-IL4 *Type:* Live Attenuated Virus *Route:* Intravenous
Vaccine Name SIV-IFN *Type:* Live Attenuated Virus *Route:* Intravenous
Challenge SIVmac239/nef-open *Route:* Intravenous
Main Findings

- During the acute phase of infection, the cell-associated viral load, but not the plasma viral RNA load, was approximately 10-fold lower in SIV-IFN-infected macaques than in SIV-IL4-infected animals.
- The viral load declined to hardly detectable levels 4 months postinfection in all animals.
- The titers and affinity of SIV antibodies were higher in SIV-IL4-infected macaques than in SIV-IFN-infected animals.
- Subsequent challenge with SHIV revealed protection in the absence of neutralizing antibodies.

NHP.310 (12477812) **Increased virus replication and virulence after serial passage of human immunodeficiency virus type 2 in baboons**
Authors Locher CP, Witt SA, Herndier BG, Abbey NW, Tenner-Racz K, Racz P, Kiviat NB, Murthy KK, Brasky K, Leland M, Levy JA
Journal J Virol 2003 Jan;77(1):77-83
Objectives Pathogenicity To enhance the pathogenicity of HIV-2 in order to shorten the amount of time to the development of disease in baboons.
Species/Subspecies Papio cynocephalus (Baboon)
Challenge HIV-2 (UC2-12741), HIV-2 (UC2-11999), HIV-2 (UC2-10568), HIV-2 (UC2-11966), HIV-2 (UC2-12281), HIV-2 (UC2-9429) *Route:* Intravenous
Main Findings

- After these serial passages, virus levels in plasma, peripheral blood mononuclear cells (PBMC) and lymphatic tissues in the acutely infected baboons were increased.
- Within 1 year of the HIV-2 infection, all of the inoculated baboons showed specific signs of AIDS-related disease progression within the lymphatic tissues, such as vascular proliferation and lymphoid depletion.
- HIV-2(UC2) isolate recovered after several serial passages in baboons will be useful in future studies of AIDS pathogenesis and vaccine development by using this animal model.

NHP.312 (12502815) **Increased mucosal transmission but not enhanced pathogenicity of the CCR5-tropic, simian AIDS-inducing simian/human immunodeficiency virus SHIV(SF162P3) maps to envelope gp120**
Authors Hsu M, Harouse JM, Gettie A, Buckner C, Blanchard J, Cheng-Mayer C
Journal J Virol 2003 Jan;77(2):989-98
Species/Subspecies Macaca mulatta (Rhesus macaque)
Challenge $SHIV_{SF162\text{-}PC}$ *Route:* Intravenous, Vaginal or perivaginal
Main Findings

- $SHIV_{SF162\text{-}PC}$ was as infectious as $SHIV_{SF162}$, and intermediate in pathogenicity between $SHIV_{SF162}$ and $SHIV_{SF162\text{-}P3}$.
- Fusogenic capacity and inhibition by T-20 fusion inhibitor were also assayed.
- Compared to wild-type SHIV(SF162) gp120, P3 gp120 conferred in vitro neutralization resistance and increased entry efficiency of the virus, but was compromised in its fusion-inducing capacity.
- In vivo, SHIV(SF162PC) infected 2/2 and 2/3 rhesus macaques by the intravenous and intravaginal routes, respectively.
- Although peak viremia reached 10^6 to 10^7 RNA copies per ml of plasma in some infected animals and was associated with depletion of gut-associated CD4(+) lymphocytes, none of the animals maintained a viral set point that would be predictive of progression to disease.

NHP.313.1 (12663776) **Global Dysfunction of CD4 T-Lymphocyte Cytokine Expression in Simian-Human Immunodeficiency Virus/SIV-Infected Monkeys Is Prevented by Vaccination**
Authors McKay PF, Barouch DH, Schmitz JE, Veazey RS, Gorgone DA, Lifton MA, Williams KC, Letvin NL
Journal J Virol 2003 Apr 15;77(8):4695-4702
Objectives Challenge, Immunogenicity To assess the functional capacity of CD4+ T lymphocytes in rhesus monkeys both prospectively during the course of a simian immunodeficiency virus (SIV) infection and in a cohort of SIV/SHIV-infected animals with nonprogressive disease.

Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Loss of the capacity of peripheral blood CD4+ T lymphocytes to express cytokines was first detected in SIV-infected monkeys during the peak of viral replication during primary infection and persisted thereafter.
- Infected monkeys with progressive disease had peripheral blood CD4+ T lymphocytes that expressed significantly less cytokine than infected monkeys that had undetectable viral loads and intact CD4+ T-lymphocyte counts.
- CD4+ T lymphocytes from vaccinated monkeys that effectively controlled the replication of a highly pathogenic immunodeficiency virus isolate following a challenge had a preserved functional capacity.

NHP.313.2 (12663776) **Global Dysfunction of CD4 T-Lymphocyte Cytokine Expression in Simian-Human Immunodeficiency Virus/SIV-Infected Monkeys Is Prevented by Vaccination**
Authors McKay PF, Barouch DH, Schmitz JE, Veazey RS, Gorgone DA, Lifton MA, Williams KC, Letvin NL
Journal J Virol 2003 Apr 15;77(8):4695-4702
Objectives Pathogenicity To compare the CD+ T cell profile in progressor and nonprogressor rhesus monkeys infected with SIV/SHIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Small difference between the cytokine expression profiles of the peripheral blood CD4+ T lymphocytes from normal monkeys and those from SIV/SHIV-infected clinical nonprogressor monkeys.

NHP.318 (10803879) **Multi-envelope HIV vaccine safety and immunogenicity in small animals and chimpanzees**
Authors Lockey TD, Slobod KS, Caver TE, D'Costa S, Owens RJ, McClure HM, Compans RW, Hurwitz JL
Journal Immunol Res 2000;21(1):7-21
Objectives Immunogenicity To compare the multi envelope vaccine vs. those containing a single component, inoculated by cutaenous or subcutaenous route.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Main Findings

- Cutaenous lesions were not required to elicit HIV-1 envelope or vaccinia virus-humoral immune response.
- Antibody responses could be substantially enhanced with envelope booster immunization.
- Immune response to envelope protein persisted to >1 year.
- Multi-envelope vaccines are more immunogenic than those containing a single envelope component.

NHP.319 (12706101) **Evidence for immune-mediated reduction of viral replication in Macaca nemestrina mucosally immunized with inactivated SHIV(89.6)**
Authors Ambrose Z, Thompson J, Larsen K, Kuller L, Panicali DL, Clements JD, Agy M, Montefiori DC, Hu SL, Bosch ML
Journal Virology 2003 Mar 30;308(1):178-90
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name vT107 *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification
Vaccine Name vAbT394 *Type:* Recombinant Vector (virus/bacteria) *Route:* Scarification
Vaccine Name AT-2-Inactivated SHIV89.6 *Type:* Whole (killed) Inactivated Virus *Routes:* Intragastric, Intranasal
Challenge SHIV89.6 *Route:* Vaginal or perivaginal
Main Findings

- Anti-SHIV T-cell responses were significant only in primed and boosted animals (group 2). Primed and boosted animals also showed significantly decreased viral loads compared to boosted only

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NHP.320 (9371609) **Identification of the V1 region as a linear neutralizing epitope of the simian immunodeficiency virus SIVmac envelope glycoprotein**
Authors Jurkiewicz E, Hunsmann G, Schaffner J, Nisslein T, Luke W, Petry H
Journal J Virol 1997 Dec;71(12):9475-81

Objectives Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIV-Mac-32H *Type:* Live Virus
Vaccine Name SIV-Mac-MPBMC *Type:* Live Virus
Vaccine Name oligomeric gp130 *Type:* Synthetic Protein/Peptide
Main Findings

- Rhesus macaques infected with clone Mac32H or immunized with Mac gp130 developed neutralizing antibodies directed at an epitope in the V1 region of Env

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NHP.321 (12719603) **Induction of broad and potent anti-human immunodeficiency virus immune responses in rhesus macaques by priming with a DNA vaccine and boosting with protein-adsorbed polylactide coglycolide microparticles**
Authors Otten G, Schaefer M, Greer C, Calderon-Cacia M, Coit D, Kazzaz J, Medina-Selby A, Selby M, Singh M, Ugozzoli M, Zur Megede J, Barnett SW, O'Hagan D, Donnelly J, Ulmer J
Journal J Virol 2003 May 15;77(10):6087-92
Objectives Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pCMV-gag-mod *Type:* DNA *Route:* Intramuscular
Vaccine Name HIV-IIIB-p55gag-VLP *Type:* Virus-like Particle *Route:* Intramuscular
Vaccine Name p55Gag *Type:* Purified Viral Products *Route:* Intramuscular
Main Findings

- Priming with Gag DNA and boosting with Gag protein adsorbed to polylactide coglycolide microparticles produced a stronger and broader immune response than either vaccine alone

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NHP.322 (12867656) **DNA vaccination of macaques by a full-genome simian/human immunodeficiency virus type 1 plasmid chimera that produces non-infectious virus particles**
Authors Akahata W, Ido E, Akiyama H, Uesaka H, Enose Y, Horiuchi R, Kuwata T, Goto T, Takahashi H, Hayami M
Journal J Gen Virol 2003 Aug;84(Pt 8):2237-2244
Objectives Challenge, Immunogenicity To evaluate the immunogenicity and protection from chanllenge of a full-genome SHIV plasmid in rhesus monkeys.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pSHIV-NM-3rn ZF1* *Type:* DNA *Route:* Intramuscular
Challenge SHIV-NM-3rN *Route:* Intravenous
Main Findings

- High CTL activity in vaccinees.
- In all macaques vaccinated, peak plasma virus loads after homologous challenge with SHIV were 2 to 3 orders of magnitude lower than those of the naive controls, and virus loads fell below the level of detection at 6 weeks post-challenge suggesting that the vaccination regime in this study was partially effective.

NHP.323 (12919751) **Convergent evolution of SIV env after independent inoculation of rhesus macaques with infectious proviral DNA**
Authors Buckley KA, Li PL, Khimani AH, Hofmann-Lehmann R, Liska V, Anderson DC, McClure HM, Ruprecht RM
Journal Virology 2003 Aug 1;312(2):470-80
Objectives Pathogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac239Δ3 *Type:* Live Attenuated Virus *Route:* Intramuscular
Vaccine Name SIVmac239Δ3+ *Type:* Live Attenuated Virus *Route:* Intramuscular
Vaccine Name pSIVNef-TPA *Type:* DNA *Route:* Intramuscular

Main Findings

- Rhesus macaques innoculated with SIV-MAC239, MAC239-delta3 or Mac239-delta3+ pathogenic revertant of delta3, each developed similar mutations, indicative of convergent evolution, in env

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NHP.324.1 (12922139) **Boosting of SIV-specific immune responses in rhesus macaques by repeated administration of Ad5hr-SIVenv/rev and Ad5hr-SIVgag recombinants**

Authors Zhao J, Lou Y, Pinczewski J, Malkevitch N, Aldrich K, Kalyanaraman VS, Venzon D, Peng B, Patterson LJ, Edghill-Smith Y, Woodward R, Pavlakis GN, Robert-Guroff M

Journal Vaccine 2003 Sep 8;21(25-26):4022-35

Objectives Challenge To evaluate ELISPOT reactivity to Gag, Env and Rev proteins after each of 2 innoculations with Adenovirus-Env-Rev and Adenovirus-Gag vectors.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intranasal

Vaccine Name Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Oral, Intranasal

Challenge SIVmac251 *Route:* Intrarectal

Main Findings

- Vaccination with 2 Ad4hr vectors containing SIV-smH4 Env-Rev and SIV-Mac239 Gag was followed by ELISPOT cellular immune response detection, and antibody titre of humoral responses.
- The second innuculation significantly boosted both responses.
- Second paper described intrarectal challenge with SIV-Mac251 at week 42.
- All animals developed persistent infection, but viral burden at peak viremia was reduced (14 fold; $P < 0.0001$) in vaccinated animals as compared to controls.
- Viremia at set point was not significanlty reduced in vaccinated animals compared to controls

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NHP.324.1 (12857905) **Improved protection of rhesus macaques against intrarectal simian immunodeficiency virus SIV(mac251) challenge by a replication-competent Ad5hr-SIVenv/rev and Ad5hr-SIVgag recombinant priming/gp120 boosting regimen**

Authors Zhao J, Pinczewski J, Gomez-Roman VR, Venzon D, Kalyanaraman VS, Markham PD, Aldrich K, Moake M, Montefiori DC, Lou Y, Pavlakis GN, Robert-Guroff M

Journal J Virol 2003 Aug;77(15):8354-65

NHP.325 (12097576) **Different patterns of immune responses but similar control of a simian-human immunodeficiency virus 89.6P mucosal challenge by modified vaccinia virus Ankara (MVA) and DNA/MVA vaccines**

Authors Amara RR, Villinger F, Staprans SI, Altman JD, Montefiori DC, Kozyr NL, Xu Y, Wyatt LS, Earl PL, Herndon JG, McClure HM, Moss B, Robinson HL

Journal J Virol 2002 Aug;76(15):7625-31

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIV-HIV89.6 DNA vaccine *Type:* DNA *Route:* Intradermal

Vaccine Name rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Challenge SHIV89.6P *Route:* Intrarectal

Main Findings

- Although individual animals in DNA/MVA and MVA/MVA groups had varying levels of antibody and CD8 T-cell response, all controlled challenge virus, as measured by viral load and decline in CD4 T-cells, equally well post challenge

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NHP.326 (12915583) **Protective Efficacy of an AIDS Vaccine, a Single DNA Priming Followed by a Single Booster with a Recombinant Replication-Defective Sendai Virus Vector, in a Macaque AIDS Model**

Authors Takeda A, Igarashi H, Nakamura H, Kano M, Iida A, Hirata T, Hasegawa M, Nagai Y, Matano T
Journal J Virol 2003 Sep 1;77(17):9710-9715
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name SeV-gag *Type:* DNA *Route:* Intranasal
Vaccine Name CMV SHIV dEN *Type:* DNA *Route:* Intramuscular
Challenge SHIV89.6PD *Route:* Intravenous

NHP.327.1 (14970317) **Early protection against pathogenic virus infection at a mucosal challenge site after vaccination with attenuated simian immunodeficiency virus**

Authors Tenner-Racz K, Hennig CS, Uberla K, Stoiber H, Ignatius R, Heeney J, Steinman RM, Racz P
Journal Proc Natl Acad Sci U S A 2004 Feb 17;
Objectives Challenge, Immunogenicity Exp 1: To investigate long-term protection induced by live attenuated delta deleted SIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVDeltaNU *Type:* Live Attenuated Virus *Routes:* Intravenous, Other
Challenge SIVmac251 *Route:* Other
Main Findings

- Experiment 1 and experiment 2: A traumatic application of attenuated SIVmac239Deltanef vaccine to the tonsils of rhesus macaques provided protection against challenge 26 weeks later with infectious SIVmac251 applied through this route.
- 10/10 vaccinnes did not show significantly raised RNA levels in the plasma or increase in infected cells in lymphoid tissue after challenge (exp. 2).
- Vaccine virus was found in the tonsils of all vaccinees, but challenge virus was only detected at this portal of entry in 4/10 monkeys.
- During tonsillar SIVDeltanef vaccination, infection is blocked early at the entry portal.

NHP.327.2 (14970317) **Early protection against pathogenic virus infection at a mucosal challenge site after vaccination with attenuated simian immunodeficiency virus**

Authors Tenner-Racz K, Hennig CS, Uberla K, Stoiber H, Ignatius R, Heeney J, Steinman RM, Racz P
Journal Proc Natl Acad Sci U S A 2004 Feb 17;
Objectives Challenge, Immunogenicity To investigate short-term protection induced by live attenuated delta deleted SIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVDeltaNU *Type:* Live Attenuated Virus
Challenge SIVmac251 *Route:*

NHP.328 (12885879) **Potent, persistent induction and modulation of cellular immune responses in rhesus macaques primed with Ad5hr-simian immunodeficiency virus (SIV) env/rev, gag, and/or nef vaccines and boosted with SIV gp120**

Authors Patterson LJ, Malkevitch N, Pinczewski J, Venzon D, Lou Y, Peng B, Munch C, Leonard M, Richardson E, Aldrich K, Kalyanaraman VS, Pavlakis GN, Robert-Guroff M
Journal J Virol 2003 Aug;77(16):8607-20
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Ad5hr-SIVenv *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name Recombinant HIV-1 gag core (p24,p15) antigen *Type:* Recombinant Subunit Protein *Route:* Intratracheal
Vaccine Name Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name Ad5hr-SIVnefδ1-13 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name SIVmac251-gp120 *Type:* Purified Viral Products *Route:* Intramuscular

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NHP.330 (12804847) **Specificity and effect on apoptosis of Tat antibodies from vaccinated and SHIV-infected rhesus macaques and HIV-infected individuals**

Authors Belliard G, Romieu A, Zagury JF, Dali H, Chaloin O, Le Grand R, Loret E, Briand JP, Roques B, Desgranges C, Muller S

Journal Vaccine 2003 Jul 4;21(23):3186-99
Objectives Immunogenicity, Immunotherapy To study the the recognition of several Tat mutants as well as various synthetic Tat fragments by anti-Tat monoclonal antibodies and by IgG antibodies in SHIV)-infected macaques (also human long-term survivals infected with HIV).
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Tat8-53 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal
Vaccine Name Tat1-20 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal
Vaccine Name Tat 19-53 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal
Vaccine Name Tat 19-53m *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal
Vaccine Name Tat 1-61 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal
Vaccine Name Tat 44-61 *Type:* Synthetic Protein/Peptide *Routes:* Intramuscular, Intranasal
Main Findings

- Tat peptides innoculated into Rhesus macaques produced antibody responses capable of inhibiting functions of extracellular Tat protein.

NHP.332 (9223407) **Protection of SIVmac-infected macaque monkeys against superinfection by a simian immunodeficiency virus expressing envelope glycoproteins of HIV type 1**
Authors Dunn CS, Hurtrel B, Beyer C, Gloeckler L, Ledger TN, Moog C, Kieny MP, Mehtali M, Schmitt D, Gut JP, Kirn A, Aubertin AM
Journal AIDS Res Hum Retroviruses 1997 Jul 20;13(11):913-22
Objectives Challenge, Immunogenicity To determine whether host immune responses to envelope glycoprotein are an essential component of the immunity to primate lentiviruses.
Main Findings

- Superinfection of SIVmac-infected macaque monkeys with a large dose of SHIVsbg resulted in isolation of the chimeric SHIVsbg by coculture of PBMCs from 4/5 SIV-infected monkeys, but 3 animals were protected from extracellular SHIV viremia and did not seroconvert to HIV-1 glycoproteins.
- In the 2 SIV-infected monkeys that did develop SHIV viremia, cell-associated viral load was reduced at least 100-fold.

NHP.334 (12970419) **Cellular immunity elicited by human immunodeficiency virus type 1/ simian immunodeficiency virus DNA vaccination does not augment the sterile protection afforded by passive infusion of neutralizing antibodies**
Authors Mascola JR, Lewis MG, VanCott TC, Stiegler G, Katinger H, Seaman M, Beaudry K, Barouch DH, Korioth-Schmitz B, Krivulka G, Sambor A, Welcher B, Douek DC, Montefiori DC, Shiver JW, Poignard P, Burton DR, Letvin NL
Journal J Virol 2003 Oct;77(19):10348-56

NHP.335 (12850342) **Mucosal administration of three recombinant Mycobacterium bovis BCG-SIVmac251 strains to cynomolgus macaques induces rectal IgAs and boosts systemic cellular immune responses that are primed by intradermal vaccination**
Authors Ruprecht RM, Ferrantelli F, Kitabwalla M, Xu W, McClure HM
Journal Vaccine 2003 Jul 28;21(24):3370-3

NHP.336 (12719580) **Molecular features of the broadly neutralizing immunoglobulin G1 b12 required for recognition of human immunodeficiency virus type 1 gp120**
Authors Zwick MB, Parren PW, Saphire EO, Church S, Wang M, Scott JK, Dawson PE, Wilson IA, Burton DR
Journal J Virol 2003 May;77(10):5863-76

NHP.339 (12359458) **Chimeric human papilloma virus-simian/human immunodeficiency virus virus-like-particle vaccines: immunogenicity and protective efficacy in macaques**
Authors Dale CJ, Liu XS, De Rose R, Purcell DF, Anderson J, Xu Y, Leggatt GR, Frazer IH, Kent SJ
Journal Virology 2002 Sep 15;301(1):176-87
Objectives Challenge, Immunogenicity To evaluate HPV-HIV VLPs for immunogenicity and protective immunity using a mucosal SHIV challenge model in macaques and to evaluate a DNA vaccine prime and HPV-HIV VLP boost approach to induce T cell mediated immunity in macaques.
Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Pooled SIVgag/HIVtat.rev DNA vaccine *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular
Vaccine Name HPV/SHIV-VLP *Type:* Virus-like Particle *Routes:* Intrarectal, Intramuscular
Challenge SHIV.229(mn) *Route:* Intrarectal
Main Findings

- HPV L1 antibodies were induced in all immunized macaques.
- Weak antibody or T cell responses to the chimeric SHIV antigens were detected only in animals receiving the DNA prime/HPV-SHIV VLP boost vaccine regimen.
- Significant but partial protection from a virulent mucosal SHIV challenge was detected only in the prime/boosted macaques and not in animals receiving the HPV-SHIV VLP vaccines alone, with 3/5 prime/boosted animals retaining some CD4 T cells following challenge.

NHP.340 (14498982) **Multigene DNA prime-boost vaccines for SHIV89.6P**
Authors Doria-Rose NA, Pierce CC, Hensel MT, Sutton WF, Sheikh N, Polacino P, Kuller L, Zhu YD, Hu SL, Anderson D, Haigwood NL
Journal J Med Primatol 2003 Aug;32(4-5):218-28

NHP.341 (14627745) **Transfer of neutralizing IgG to macaques 6 h but not 24 h after SHIV infection confers sterilizing protection: Implications for HIV-1 vaccine development**
Authors Nishimura Y, Igarashi T, Haigwood NL, Sadjadpour R, Donau OK, Buckler C, Plishka RJ, Buckler-White A, Martin MA
Journal Proc Natl Acad Sci U S A 2003 Dec 9;100(25):15131-6
Objectives Challenge, Passive Immunization .
Species/Subspecies Macaca nemestrina (pigtailed macaque)

NHP.344 (12519210) **Immune responses in baboons vaccinated with HIV-2 genetic expression libraries**
Authors Locher CP, Sykes KF, Blackbourn DJ, Johnston SA
Journal J Med Primatol 2002 Dec;31(6):323-9
Objectives Challenge, Immunogenicity To evaluate the effectiveness of an HIV-2 vaccine made from a genomic expression library in baboons.
Main Findings

- HIV-2 expression library immunization induced HIV-2-specific memory responses but low levels of CD8+ cell anti-viral responses and neutralizing antibodies.
- Immunization with HIV-2 expression library did not sigificantly alter the viral load in vaccinated animals compared to control group.
- The approach does not provide protection in baboons against intravenous challenge with HIV-2.

NHP.345 (14741150) **Avipox-based simian immunodeficiency virus (SIV) vaccines elicit a high frequency of SIV-specific CD4+ and CD8+ T-cell responses in vaccinia-experienced SIVmac251-infected macaques**
Authors Nacsa J, Radaelli A, Edghill-Smith Y, Venzon D, Tsai WP, Morghen Cde G, Panicali D, Tartaglia J, Franchini G
Journal Vaccine 2004 Jan 26;22(5-6):598-607
Objectives Immunogenicity, Immunotherapy, Chemotherapy To test the ability of ALVAC- or fowlpox-based SIV vaccines to boost SIV-specific CD4+ and CD8+ T-cell responses in 10 vaccinia-experienced macaques infected with SIVmac251.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVmac251 *Type:* Live Virus *Route:* Intrarectal
Vaccine Name FP-SIV-gp (FP74) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Vaccine Name ALVAC-SIV-gp *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular
Main Findings

- The 2 vaccine modalities effectively boosted both CD4+ and CD8+ SIV-specific T-cell response despite prior exposure to the vaccinia-derivative NYVAC vector, suggesting that sequential boosting with either avipox-based vector vaccine candidate is a realistic approach in immune therapy of HIV-1-infected individuals.

NHP.346 (14645590) **Multispecific vaccine-induced mucosal cytotoxic T lymphocytes reduce acute-phase viral replication but fail in long-term control of simian immunodeficiency virus SIVmac239**

Authors Vogel TU, Reynolds MR, Fuller DH, Vielhuber K, Shipley T, Fuller JT, Kunstman KJ, Sutter G, Marthas ML, Erfle V, Wolinsky SM, Wang C, Allison DB, Rud EW, Wilson N, Montefiori D, Altman JD, Watkins DI

Journal J Virol 2003 Dec;77(24):13348-60

Objectives Challenge, Immunogenicity To ascertain the effect of vaccine-induced multispecific mucosal CTL.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- The vaccination induced virus-specific CTL and CD4+ helper T lymphocytes with CTL frequencies as high as 20,000/million peripheral blood mononuclear cells.
- The final rMVA vaccination, delivered intravenously, engendered long-lived mucosal CTL.
- Massive early anamnestic cellular immune responses controlled acute-phase viral replication; however, the 3 vaccinees were unable to control virus replication in the chronic phase.
- Multispecific mucosal CTL, in the absence of neutralizing antibodies, can achieve a modicum of control over early viral replication but unable to control chronic-phase viral replication after a high-dose mucosal challenge with a pathogenic simian immunodeficiency virus.

NHP.348.1 (14585346) **Immunogenicity in pig-tailed macaques of poliovirus replicons expressing HIV-1 and SIV antigens and protection against SHIV-89.6P disease**

Authors Fultz PN, Stallworth J, Porter D, Novak M, Anderson MJ, Morrow CD

Journal Virology 2003 Oct 25;315(2):425-37

Objectives Immunogenicity To determine whether poliovirus replicons expressing various HIV-1 Env and SIVmac239 Gag antigens would be immunogenic in macaques.

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Polio (Sabin 1) -HIV-1.gag/env (1) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intranasal

Vaccine Name Polio (Sabin 1) - HIV-1.gag/env (2) *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Intranasal

Vaccine Name Polio (Sabin 2) - HIV-1.gag/env (3) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name Polio (Sabin 2) - HIV-1.gag/env (4) *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name rgp140-env (HIV-1.89.6) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

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NHP.348.2 (14585346) **Immunogenicity in pig-tailed macaques of poliovirus replicons expressing HIV-1 and SIV antigens and protection against SHIV-89.6P disease**

Authors Fultz PN, Stallworth J, Porter D, Novak M, Anderson MJ, Morrow CD

Journal Virology 2003 Oct 25;315(2):425-37

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name rgp140-env (HIV-1.89.6) *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name Polio-LAI/IIIB-Env *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Vaccine Name Polio- SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Challenge SHIV89.6P *Route:* Intravenous

NHP.349 (14585221) **Gp120-alum boosting of a Gag-Pol-Env DNA/MVA AIDS vaccine: poorer control of a pathogenic viral challenge**

Authors Buge SL, Ma HL, Amara RR, Wyatt LS, Earl PL, Villinger F, Montefiori DC, Staprans SI, Xu Y, Carter E, O'Neil SP, Herndon JG, Hill E, Moss B, Robinson HL, McNicholl JM

Journal AIDS Res Hum Retroviruses 2003 Oct;19(10):891-900

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name Soluble 89.6 gp120 protein *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Vaccine Name SIV-HIV89.6 DNA vaccine *Type:* DNA *Route:* Intradermal
Vaccine Name rMVA 89.6 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular
Challenge SHIV89.6P *Route:* Intrarectal

NHP.350 (14583643) **Evaluation of simian immunodeficiency virus-specific immune responses induced by a defective proviral DNA vaccine in macaques**
Authors Takeda A, Nakamura H, Matano T
Journal Jpn J Infect Dis 2003 Aug;56(4):172-3
Objectives Immunogenicity To examine if macaques vaccinated with FMSIV DNA and an mCAT1-expression plasmid DNA (pCMVmCAT1) had SIV-specific T-cell levels significantly higher than control macaques vaccinated with replication-negative FMSIV DNA vaccine.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pCMVmCAT1 *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular
Vaccine Name FMSIV *Type:* DNA *Routes:* Intradermal (Gene Gun DNA-coated gold beads), Intramuscular
Main Findings

- SIV-specific CD4+ T cells and SIV-specific CD8+ T cells were efficiently induced in macaques vaccinated with FMSIV plus mCAT1 DNAs and levels of SIV-specific CD4+ T cells and SIV-specific CD8+ T cells in the group II macaques were significantly higher than those in the control group.
- Macaques immunized with FMSIV plus pCMVmCAT1 had significantly higher levels of plasma anti-p27 antibodies than those in the control both at week 3 and week 8 after the initial vaccination.

NHP.351 (14557642) **Multigene DNA priming-boosting vaccines protect macaques from acute CD4+-T-cell depletion after simian-human immunodeficiency virus SHIV89.6P mucosal challenge**
Authors Doria-Rose NA, Ohlen C, Polacino P, Pierce CC, Hensel MT, Kuller L, Mulvania T, Anderson D, Greenberg PD, Hu SL, Haigwood NL
Journal J Virol 2003 Nov;77(21):11563-77
Species/Subspecies Macaca nemestrina (pigtailed macaque)

NHP.352 (14512560) **Microarray profiling of antibody responses against simian-human immunodeficiency virus: postchallenge convergence of reactivities independent of host histocompatibility type and vaccine regimen**
Authors Neuman de Vegvar HE, Amara RR, Steinman L, Utz PJ, Robinson HL, Robinson WH
Journal J Virol 2003 Oct;77(20):11125-38

NHP.353 (14505895) **Mucosal administration of three recombinant Mycobacterium bovis BCG-SIVmac251 strains to cynomolgus macaques induces rectal IgAs and boosts systemic cellular immune responses that are primed by intradermal vaccination**
Authors Mederle I, Le Grand R, Vaslin B, Badell E, Vingert B, Dormont D, Gicquel B, Winter N
Journal Vaccine 2003 Oct 1;21(27-30):4153-66
Objectives Challenge, Immunogenicity To investigate anti-SIV immune responses induced by intradermal vaccination of cynomolgus macaques with rBCG-SIV strains followed by a late mucosal booster dose.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name rBCG-SIV^3 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intrarectal, Oral, Intradermal
Challenge SIVmac251 *Route:* Intrarectal
Main Findings

- Intradermal immunization of cynomolgus macaques with a multi-component rBCG vaccine induces CTL responses targeted against 3 SIVmac251 antigens.
- PBLs from rBCG-SIV3-immunized monkeys produce interferon-gamma in response to SIV antigens and production increases after the mucosal booster.
- Anti-Gag IgAs are detected in rectal lavages of rBCG-SIV3-immunized monkeys only after the mucosal booster.
- rBCG-SIV3 does not protect against a highly pathogenic SIVmac251 challenge despite induction of anamnestic immune responses.

NHP.354 (15096801) **Immunogenicity of HIV-1 Env and Gag in baboons using a DNA prime/boost regimen**

Authors Leung L, Srivastava IK, Kan E, Legg H, Sun Y, Greer C, Montefiori DC, zur Megede J, Barnett SW
Journal AIDS 2004 Apr 30;18(7):991-1001
Objectives Immunogenicity To evaluate the immunogenicity of sequence-modified HIV env and gag in baboons using DNA prime and protein boost strategy.
Species/Subspecies Papio cynocephalus (Baboon)
Vaccine Name pCMV-gag-mod *Type:* DNA *Route:* Intramuscular
Vaccine Name pCMVKm2-gp140mut *Type:* DNA *Route:* Intramuscular
Vaccine Name CMVKm2-gp140TM *Type:* DNA *Route:* Intramuscular
Vaccine Name o-gp140-US4 *Type:* Synthetic Protein/Peptide *Route:* Intramuscular
Vaccine Name p55gagSF2 *Type:* DNA *Route:* Intramuscular
Vaccine Name Chimp-anti-HIV-IgG *Type:* Passive Antibody
Main Findings

- Modest antibody responses and low or no lymphoproliferative responses were observed following multiple DNA immunizations.
- Strong antibodies and substantial antigen-specific lymphoproliferative responses were seen following booster immunizations with oligomeric Env protein (o-gp140US4) in MF59.
- Neutralizing antibody responses were scored against T cell line adapted HIV-1 strains after the protein boosters, but neutralizing responses were low or absent against homologous and heterologous primary isolate strains.

NHP.361 (3413127) **Failure of a human immunodeficiency virus (HIV) immune globulin to protect chimpanzees against experimental challenge with HIV**
Authors Prince AM, Horowitz B, Baker L, Shulman RW, Ralph H, Valinsky J, Cundell A, Brotman B, Boehle W, Rey F, et al.
Journal Proc Natl Acad Sci U S A 1988 Sep;85(18):6944-8
Objectives Challenge, Passive Immunization To assess the possible efficacy of passive immunization against HIV using plasma from HIV seropositive donors.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Vaccine Name HIVIG *Type:* Passive Antibody *Route:* Intravenous
Challenge HIV-1 IIIB *Route:*

NHP.362 (1714748) **Immunization of chimpanzees with the HIV-1 glycoprotein gp160 induces long-lasting T-cell memory**
Authors Mannhalter JW, Pum M, Wolf HM, Kupcu Z, Barrett N, Dorner F, Eder G, Eibl MM
Journal AIDS Res Hum Retroviruses 1991 May;7(5):485-93
Objectives Immunogenicity To investigate the antigen-specific T-cell response to the recombinant HIV env gp160 and to test the effect of various adjuvant formulations on the efficiency of T-cell priming as well as on magnitude and longevity of the gp160-specific T-cell response.
Species/Subspecies Pan Troglodytes (Chimpanzee)
Vaccine Name rgp160 *Type:* Recombinant Subunit Protein *Route:* Intramuscular
Main Findings

- In combination with an appropriate adjuvant (lipid-based adjuvant or mineral carrier complex), immunization with recombinant gp160 led to the appearance of gp160-primed T cells.
- The memory T-cell response toward the immunogen gp160 was substantial and long-lasting.

NHP.363 (14963117) **Protection against mucosal simian immunodeficiency virus SIV(mac251) challenge by using replicating adenovirus-SIV multigene vaccine priming and subunit boosting**
Authors Patterson LJ, Malkevitch N, Venzon D, Pinczewski J, Gomez-Roman VR, Wang L, Kalyanaraman VS, Markham PD, Robey FA, Robert-Guroff M
Journal J Virol 2004 Mar;78(5):2212-21
Objectives Challenge, Immunogenicity To investigate a prime-boost strategy in macaques using priming with replicating adenovirus recombinants encoding SIV env/rev, gag, and/or nef genes, followed by boosting with SIV gp120 or an SIV polypeptide.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIVIG-2 *Type:* Passive Antibody *Route:* Intramuscular

Vaccine Name Ad5hr-SIVmac239gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name Ad5hr-SIVnefδ1-13 *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name Ad5hr-SIVsmH4 env/rev *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name Mono-gp120H (89.6) *Type:* Recombinant Subunit Protein *Routes:* Intratracheal, Oral, Intranasal
Vaccine Name HIV env_{MN}/rev(pCEnv) *Type:* DNA *Route:* Intramuscular
Vaccine Name SIVmac251-gp120 *Type:* Purified Viral Products *Route:* Intramuscular
Challenge SIVmac251 *Route:* Intrarectal
Main Findings

- Priming with replicating adenovirus recombinants encoding SIV env/rev, gag, and/or nef genes, followed by boosting with SIV gp120 or an SIV polypeptide mimicking the CD4 binding region of the envelope, protects rhesus macaques from intrarectal infection with the highly pathogenic SIV(mac251).
- Within immunization groups exhibiting significant protection, a subset (39%) of macaques have exhibited either no viremia, cleared viremia, or controlled viremia at the threshold of detection, now more than 40 weeks postchallenge.
- Protection in macaques did not correlate with the Mamu A*01 allele.

NHP.365 (14645581) **Intravenous inoculation of replication-deficient recombinant vaccinia virus DIs expressing simian immunodeficiency virus gag controls highly pathogenic simian-human immunodeficiency virus in monkeys**

Authors Izumi Y, Ami Y, Matsuo K, Someya K, Sata T, Yamamoto N, Honda M
Journal J Virol 2003 Dec;77(24):13248-56
Objectives Challenge, Immunogenicity To assess the immunogenicity and protection induced by immunization with rDIsSIVgag.
Species/Subspecies Macaca fascicularis (cynomolgus macaque)
Vaccine Name Vaccinia-rDIsSIVgag *Type:* Recombinant Vector (virus/bacteria) *Route:* Intravenous
Challenge SHIV-C2/1 *Route:* Intravenous
Main Findings

- Intravenous inoculation of 10^6 PFU of rDIsSIVGag in cynomologus macaques induced significant levels of gamma interferon (IFN-gamma) spot-forming cells (SFC) specific for SIV Gag.
- Antigen-specific lymphocyte proliferative responses were also induced and were temporally associated with the peak of IFN-gamma SFC activity in each macaque.
- CD4(+) T lymphocytes were maintained in the peripheral blood and lymphoid tissues of the immunized macaques after challenge with pathogenic SHIV.

NHP.366 (15004179) **Control of Simian/Human Immunodeficiency Virus Viremia and Disease Progression after IL-2-Augmented DNA-Modified Vaccinia Virus Ankara Nasal Vaccination in Nonhuman Primates**

Authors Bertley FM, Kozlowski PA, Wang SW, Chappelle J, Patel J, Sonuyi O, Mazzara G, Montefiori D, Carville A, Mansfield KG, Aldovini A
Journal J Immunol 2004 Mar 15;172(6):3745-3757
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name pVacc4 DNA *Type:* DNA *Route:* Intranasal
Vaccine Name rMVA.SIVmac239gagpolHIVenv *Type:* Recombinant Vector (virus/bacteria) *Route:* Intranasal
Challenge SHIV89.6P *Route:* Intranasal
Main Findings

- The vaccine and challenge induced humoral responses, by the detection of both binding and neutralizing SHIV-specific IgG in plasma, and SHIV-specific IgA in rectal secretions.
- After rectal challenge of vaccinated and naive animals with SHIV89.6P, all animals became infected. However a subset of animals was protected from CD4+ T cell loss and AIDS development.
- SHIV DNA/MVA vaccine administered nasally can stimulate rectal antiviral IgA but was not effective at inducing antiviral systemic IgG.

- IL-2/Ig or IL-12 DNA and the rMVA added to the vaccination did not result in significant differences in these humoral immune responses.

NHP.367 (15003872) **Priming B cell-mediated anti-HIV envelope responses by vaccination allows for the long-term control of infection in macaques exposed to a R5-tropic SHIV**

Authors Buckner C, Gines LG, Saunders CJ, Vojtech L, Srivastava I, Gettie A, Bohm R, Blanchard J, Barnett SW, Safrit JT, Stamatatos L
Journal Virology 2004 Mar 1;320(1):167-80
Objectives Challenge, Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Antibodies elicited by the SF162gp140 immunogen recognize elements of the V1, V2, and V3 loops, the CD4-binding site, and the C1 and C2 regions on the homologous SF162 gp120.
- Deletion of the V2 has a two-fold effect: 1) it alters the immunogenicity of the V3 and V1 loops, and 2) it renders the C5 region immunogenic.
- Sterilizing immunity was not achieved.
- All vaccinated animals effectively controlled and remained free of disease over 3 years of observation.

NHP.368 (14980480) **Functional simian immunodeficiency virus Gag-specific CD8+ intraepithelial lymphocytes in the mucosae of SIVmac251- or simian-human immunodeficiency virus KU2-infected macaques**

Authors Stevceva L, Moniuszko M, Alvarez X, Lackner AA, Franchini G
Journal Virology 2004 Feb 20;319(2):190-200
Objectives Immunogenicity .

NHP.369 (14610180) **Simian-human immunodeficiency virus escape from cytotoxic T-lymphocyte recognition at a structurally constrained epitope**

Authors Peyerl FW, Barouch DH, Yeh WW, Bazick HS, Kunstman J, Kunstman KJ, Wolinsky SM, Letvin NL
Journal J Virol 2003 Dec;77(23):12572-8

NHP.370 (14550583) **Enhanced immunogenicity of SIV Gag DNA vaccines encoding chimeric proteins containing a C-terminal segment of Listeriolysin O**

Authors Ye L, Bu Z, Skeen MJ, Ziegler HK, Compans RW, Yang C
Journal Virus Res 2003 Nov;97(1):7-16
Objectives Immunogenicity Investigation of the potential of the C-terminal 59-amino acid segment of Listeriolysin O (LLO) in enhancing immune responses against the SIV Gag antigen in the context of DNA immunization.

NHP.371 (15018712) **Evaluation of combination DNA/replication-competent Ad-SIV recombinant immunization regimens in rhesus macaques**

Authors Malkevitch N, Rohne D, Pinczewski J, Aldrich K, Kalyanaraman VS, Letvin NL, Robert-Guroff M
Journal AIDS Res Hum Retroviruses 2004 Feb;20(2):235-44
Objectives Immunogenicity .
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name Ad5hr-SIVsmH4 env/rev *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intratracheal, Intranasal
Vaccine Name pCMV/SIVsmH4/rev-gp160 *Type:* DNA *Route:* Intradermal
Vaccine Name HIV-1 IIIB gp120 *Type:* Purified Viral Products *Route:* Intramuscular

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NHP.372 (14722263) **Simian immunodeficiency virus promoter exchange results in a highly attenuated strain that protects against uncloned challenge virus**

Authors Blancou P, Chenciner N, Ho Tsong Fang R, Monceaux V, Cumont MC, Guetard D, Hurtrel B, Wain-Hobson S
Journal J Virol 2004 Feb;78(3):1080-92
Species/Subspecies Macaca mulatta (Rhesus macaque)

NHP.373 (14593121) **High attenuation and immunogenicity of a simian immunodeficiency virus expressing a proteolysis-resistant inhibitor of NF-kappaB**

Authors Quinto I, Puca A, Greenhouse J, Silvera P, Yalley-Ogunro J, Lewis MG, Palmieri C, Trimboli F, Byrum R, Adelsberger J, Venzon D, Chen X, Scala G

Journal J Biol Chem 2004 Jan 16;279(3):1720-8. Epub 2003 Oct 30

NHP.374 (15016855) **Qualitative T-helper responses to multiple viral antigens correlate with vaccine-induced immunity to simian/human immunodeficiency virus infection**

Authors Mooij P, Nieuwenhuis IG, Knoop CJ, Doms RW, Bogers WM, Ten Haaft PJ, Niphuis H, Koornstra W, Bieler K, Kostler J, Morein B, Cafaro A, Ensoli B, Wagner R, Heeney JL

Journal J Virol 2004 Apr;78(7):3333-42

Objectives Challenge, Immunogenicity To determine whether immunization with multiple antigens can influence individual Th responses and increase protection relative to a single antigen.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pc-synTat (HIV-1IIIB) *Type:* DNA *Route:* Intramuscular

Vaccine Name pc-syngp120 (SHIV-189.6p) *Type:* DNA *Route:* Intramuscular

Vaccine Name pc-synGag (SIVmac239) *Type:* DNA *Route:* Intramuscular

Vaccine Name HIV-189.6 Env gp140-ISCOM *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name SIVmac239 Gag-Pol-ISCOM *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Vaccine Name tat protein *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge SHIV89.6P *Route:* Intravenous

NHP.375 (15047809) **Highly effective control of an AIDS virus challenge in macaques by using vesicular stomatitis virus and modified vaccinia virus Ankara vaccine vectors in a single-boost protocol**

Authors Ramsburg E, Rose NF, Marx PA, Mefford M, Nixon DF, Moretto WJ, Montefiori D, Earl P, Moss B, Rose JK

Journal J Virol 2004 Apr;78(8):3930-40

Objectives Challenge, Immunogenicity To compare the effectiveness of single prime-boost protocol consisting of VSV vectors expressing SHIV Env, Gag, and Pol proteins to that of VSV vector prime followed with a single boost with MVA expressing the same SHIV proteins.

Species/Subspecies Macaca mulatta (Rhesus macaque)

NHP.376 (15047820) **Induction of autoantibodies to CCR5 in macaques and subsequent effects upon challenge with an R5-tropic simian/human immunodeficiency virus**

Authors Chackerian B, Briglio L, Albert PS, Lowy DR, Schiller JT

Journal J Virol 2004 Apr;78(8):4037-47

Objectives Challenge, Immunogenicity To generate autoantibodies against CCR5 in macaques and to assess their role in protection from challenge with R5-tropic SHIV.

Main Findings

- 5 rhesus macaques injected with VLP-SA-EC1 developed antibodies against CCR5. IV challenge with SHIV resulted in infection, but some ability to control viremia

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NHP.377 (15140996) **Passive immunotherapy in simian immunodeficiency virus-infected macaques accelerates the development of neutralizing antibodies**

Authors Haigwood NL, Montefiori DC, Sutton WF, McClure J, Watson AJ, Voss G, Hirsch VM, Richardson BA, Letvin NL, Hu SL, Johnson PR

Journal J Virol 2004 Jun;78(11):5983-95

Objectives Challenge, Passive immunotherapy .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name SIVIG *Type:* Passive Antibody *Route:* Intravenous

Challenge SIVsmE660 *Route:* Intravenous

Main Findings

- SIVIG treatment significantly delayed disease.

- Virus levels in PBMC and plasma predict disease outcome.
- Gag-specific CTLs were detected in macaques surviving beyond 1 year.
- Infused IgG delayed binding antibody and accelerated NAb production.

NHP.378 (15149785) **Human immunodeficiency virus type 2 DNA vaccine provides partial protection from acute baboon infection**

Authors Locher CP, Witt SA, Ashlock BM, Polacino P, Hu SL, Shiboski S, Schmidt AM, Agy MB, Anderson DM, Staprans SI, Megede Jz J, Levy JA

Journal Vaccine 2004 Jun 2;22(17-18):2261-72

Objectives Challenge, Immunogenicity To determine if GM-CSF and B7-2 could boost immune responses to an HIV-2 DNA vaccine and help protect baboons against HIV-2 challenge by the intravaginal route.

Species/Subspecies Papio cynocephalus (Baboon)

Vaccine Name HIV-2UC2.tat.nef.gag *Type:* DNA *Routes:* Intradermal, Intramuscular, Intranasal

Challenge HIV-2 (UC2-9429) *Route:* Vaginal or perivaginal

Main Findings

- Baboons immunized with HIV-2 DNA vaccine with or without the genetic adjuvants had significant reductions in the viral loads in the peripheral blood mononuclear cells (PBMC) following challenge (P=0.028) while the reductions in their plasma viremia were suggestive of a protective effect (P=0.1).
- Partial protection against HIV-2 vaginal challenge, as measured by reduced viral load, can be achieved using only a DNA vaccine formulation.

NHP.379 (15193413) **Enhancement of DNA vaccine potency in rhesus macaques by electroporation**

Authors Otten G, Schaefer M, Doe B, Liu H, Srivastava I, Megede Jz J, O'Hagan D, Donnelly J, Widera G, Rabussay D, Lewis MG, Barnett S, Ulmer JB

Journal Vaccine 2004 Jun 23;22(19):2489-93

NHP.380 (12551968) **Changes in the immunogenic properties of soluble gp140 human immunodeficiency virus envelope constructs upon partial deletion of the second hypervariable region**

Authors Srivastava IK, VanDorsten K, Vojtech L, Barnett SW, Stamatatos L

Journal J Virol 2003 Feb;77(4):2310-20

Objectives Immunogenicity To identify the envelope regions whose immunogenicity is altered following V2 loop deletion.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Antibodies elicited by the SF162gp140 immunogen recognize elements of the V1, V2, and V3 loops, the CD4-binding site, and the C1 and C2 regions on the homologous SF162 gp120.
- Deletion of the V2 has a two-fold effect: 1) it alters the immunogenicity of the V3 and V1 loops, and 2) it renders the C5 region immunogenic.

NHP.381 (15220422) **Heterologous envelope immunogens contribute to AIDS vaccine protection in rhesus monkeys**

Authors Letvin NL, Huang Y, Chakrabarti BK, Xu L, Seaman MS, Beaudry K, Korioth-Schmitz B, Yu F, Rohne D, Martin KL, Miura A, Kong WP, Yang ZY, Gelman RS, Golubeva OG, Montefiori DC, Mascola JR, Nabel GJ

Journal J Virol 2004 Jul;78(14):7490-7

Objectives Challenge, Immunogenicity To evaluate a plasmid DNA prime-recombinant replication-defective adenovirus (ADV) boost immunization strategy for an HIV vaccine.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- Vaccine regimens Gag-Pol-Nef immunogens that included the matched or mismatched Env immunogens conferred better protection against CD4+ T-lymphocyte loss than that seen with comparable regimens that did not include Env immunogens.
- T-lymphocyte immunity to Env can broaden the protective cellular immune response to HIV despite significant sequence diversity of the strains of the Env immunogens and can contribute to immune protection in this AIDS vaccine model.

- The control group had significantly higher peak viral loads than the vaccinated monkeys. However, the 3 groups of experimentally vaccinated monkeys did not differ significantly in their peak viral loads (P = 0.28, Kruskal-Wallis test).

NHP.382 (15210746) **Cytotoxic T Lymphocyte-based Control of Simian Immunodeficiency Virus Replication in a Preclinical AIDS Vaccine Trial**

Authors Matano T, Kobayashi M, Igarashi H, Takeda A, Nakamura H, Kano M, Sugimoto C, Mori K, Iida A, Hirata T, Hasegawa M, Yuasa T, Miyazawa M, Takahashi Y, Yasunami M, Kimura A, O'Connor DH, Watkins DI, Nagai Y

Journal J Exp Med 2004 Jun 21;199(12):1709-18

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca mulatta (Rhesus macaque)

Main Findings

- 5/8 vaccinees controlled viral replication and had undetectable plasma viremia after 5 weeks of infection.
- 5/8 macaques rapidly selected for CTL escape mutations in Gag, indicating that vaccine-induced CTLs successfully contained replication of the challenge virus.
- Vaccine induction of highly effective CTLs can result in the containment of replication of a highly pathogenic immunodeficiency virus.

NHP.384 (15242543) **Multiprotein HIV type 1 clade B DNA/MVA vaccine: construction, safety, and immunogenicity in Macaques**

Authors Smith JM, Amara RR, McClure HM, Patel M, Sharma S, Yi H, Chennareddi L, Herndon JG, Butera ST, Heneine W, Ellenberger DL, Parekh B, Earl PL, Wyatt LS, Moss B, Robinson HL

Journal AIDS Res Hum Retroviruses 2004 Jun;20(6):654-65

Objectives Immunogenicity To construct and test a Gag-Pol-Env DNA/MVA vaccine.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name pGA2/JS2-HIV-1.gag.pol.env *Type:* DNA *Route:* Intramuscular

Vaccine Name MVA/HIV 48 *Type:* Recombinant Vector (virus/bacteria) *Route:* Intramuscular

Main Findings

- The vaccine constructs contain the gag region derived from HIV-1 HXB2 and do not include the zinc finger mutations found in pGA2/JS2; pol was from pGA2/JS2 including the RT mutations.
- Safety: by abrogating reverse transcription, inactivating RNase H activity and strand transfer activity, Env gene was expression-deffective.
- Safety: No adverse effects of the inoculations on the vaccinated monkeys.
- Vaccine-elicited cellular as well as humoral immunity.
- Vaccine-elicited T cells were at, or below, the level of detection following the DNA primes, rapidly expanded after the rMVA booster and then contracted into memory.
- CD4 and CD8 epitopes are found throughout Gag and Env inserts of the vaccine.
- The immunizations elicited only low levels of raised antibody.

NHP.385 (9557706) **Recombinant vaccine-induced protection against the highly pathogenic simian immunodeficiency virus SIV(mac251): dependence on route of challenge exposure**

Authors Benson J, Chougnet C, Robert-Guroff M, Montefiori D, Markham P, Shearer G, Gallo RC, Cranage M, Paoletti E, Limbach K, Venzon D, Tartaglia J, Franchini G

Journal J Virol 1998 May;72(5):4170-82

Objectives Challenge .

Main Findings

- Vaccination with NYVAC-SIV-gpe carrying SIV-Mac-251 gag pol and env protected against intrarectal, but not intravenous infection with SIV-Mac-251, as determined by culture of virus. Viral loads were lower in vaccinated-infected than in non-vaccinated controls

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NHP.386 (15113931) **Induction of disease by a molecularly cloned highly pathogenic simian immunodeficiency virus/human immunodeficiency virus chimera is multigenic**

Authors Sadjadpour R, Theodore TS, Igarashi T, Donau OK, Plishka RJ, Buckler-White A, Martin MA
Journal J Virol 2004 May;78(10):5513-9
Species/Subspecies Macaca mulatta (Rhesus macaque)
Challenge SHIV-DH12clone7, SHIV-DH12clone8 *Route:* Intravenous
Main Findings

- $SHIV_{DH12R\text{-}CLone7}$ induces rapid CD4 decline in rhesus macaques whereas the $SHIV_{DH12R}$ parental clone does not. Subtitution of the clone 7 env into the nonpathogenic parental background did not confer pathogenicity. Amino acid changes in multiple genes were required for pathogenic effect

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NHP.387 (10570196) **Emergence of a highly pathogenic simian/human immunodeficiency virus in a rhesus macaque treated with anti-CD8 mAb during a primary infection with a nonpathogenic virus**

Authors Igarashi T, Endo Y, Englund G, Sadjadpour R, Matano T, Buckler C, Buckler-White A, Plishka R, Theodore T, Shibata R, Martin M
Journal Proc Natl Acad Sci U S A 1999 Nov 23;96(24):14049-54
Species/Subspecies Macaca mulatta (Rhesus macaque)
Challenge SHIV-MD14YE (DH12) *Route:* Intravenous
Main Findings

- Mutations in many genes resulted in increased pathogenicity of the SHIV-DH12R clone

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NHP.388 (11861859) **Evolution of a human immunodeficiency virus type 1 variant with enhanced replication in pig-tailed macaque cells by DNA shuffling**

Authors Pekrun K, Shibata R, Igarashi T, Reed M, Sheppard L, Patten PA, Stemmer WP, Martin MA, Soong NW
Journal J Virol 2002 Mar;76(6):2924-35
Objectives Pathogenicity .
Main Findings

- A SHIV composed primarily of HIV-1 sequences with a SIV-Mac239 YE version of Nef was created and passaged to achieve a molecular clone that replicates in pig-tailed macaque PBMCs and can infect macaques. SIVMD17 accession number AF465242

NHP.389 (9237701) **Infection and pathogenicity of chimeric simian-human immunodeficiency viruses in macaques: determinants of high virus loads and CD4 cell killing**

Authors Shibata R, Maldarelli F, Siemon C, Matano T, Parta M, Miller G, Fredrickson T, Martin MA
Journal J Infect Dis 1997 Aug;176(2):362-73
Species/Subspecies Macaca fascicularis (cynomolgus macaque), Macaca nemestrina (pigtailed macaque)
Challenge SHIV-MD14YE (DH12), SHIV.MD1 *Route:* Intravenous
Main Findings

- $SHIV_{MD1}$ carrying HIV-1 subtype B sequences from clones pNL43 (vpr) and DH12 (tat-nef) in a SIV_{Mac239} background, produced slower CD4+ T-cell decline in pig-tailed macaques than $SHIV_{MD14YE}$ in which the HIV-1 nef in $SHIV_{MD1}$ was replaced by SIV_{Mac239} nef with R17Y plus Q18E mutations
- The nef with R17Y plus Q18E mutations had previously been shown to be determinants of pathogenicity in the SIV_{SMM9} to SIV_{PBJ14} series of viruses

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NHP.390 (8648760) **Requirements for lymphocyte activation by unusual strains of simian immunodeficiency virus**

Authors Du Z, Ilyinskii PO, Sasseville VG, Newstein M, Lackner AA, Desrosiers RC
Journal J Virol 1996 Jun;70(6):4157-61
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- A single amino acid change in Nef R17Y was shown to be sufficient to confer pathogenicity to non-activated macaque T-cells in SIV_{Mac239} and that conversely, Y17R reversion in SIV_{PBJ14} eliminated the lymphocyteactivation phenotype of that highly pathogenic clone

- YXXLXXXXXXXYXXL SH2-binding ITAM motif is created by R17Y mutation and abolished by Y28F mutation

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NHP.391 (10888632) **Short- and long-term clinical outcomes in rhesus monkeys inoculated with a highly pathogenic chimeric simian/human immunodeficiency virus**

Authors Endo Y, Igarashi T, Nishimura Y, Buckler C, Buckler-White A, Plishka R, Dimitrov DS, Martin MA

Journal J Virol 2000 Aug;74(15):6935-45

Species/Subspecies Macaca mulatta (Rhesus macaque)

Challenge SHIV.DH12R-PS1 *Route:* Intrarectal, Intravenous, Vaginal or perivaginal

Main Findings

- $SHIV_{DH12R}$, derived from $SHIV_{MD14YE}$ by passage in rhesus macaque, induces CD4+ T-cell loss in rhesus macaques in a dose-dependent manner. The DH12R innoculum was uncloned, and higher doses apparently allow more antibody neutralization escape variants to survive

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NHP.392 (7769705) **Isolation and characterization of a syncytium-inducing, macrophage/T-cell line-tropic human immunodeficiency virus type 1 isolate that readily infects chimpanzee cells in vitro and in vivo**

Authors Shibata R, Hoggan MD, Broscius C, Englund G, Theodore TS, Buckler-White A, Arthur LO, Israel Z, Schultz A, Lane HC, et al.

Journal J Virol 1995 Jul;69(7):4453-62

Species/Subspecies Pan Troglodytes (Chimpanzee)

Challenge HIV-1.DH12 *Route:* Intravenous

Main Findings

- Of 23 different HIV-1 isolates tested, only one (DH12) was able to initiate infections in all chimpanzee PBMC cultures tested. The DH12 isolate was innoculated into three chimpanzees and was able to establish a robust infection with symptoms including lymphadenopathy and rashes
- All DH12 clones sequenced had defective vpu genes, although the GenBank entry for the complete genome AF069140 was submitted with the ATA defective start codon corrected to ATG

NHP.393 (7769705) **Isolation and characterization of a syncytium-inducing, macrophage/T-cell line-tropic human immunodeficiency virus type 1 isolate that readily infects chimpanzee cells in vitro and in vivo**

Authors Shibata R, Hoggan MD, Broscius C, Englund G, Theodore TS, Buckler-White A, Arthur LO, Israel Z, Schultz A, Lane HC, et al.

Journal J Virol 1995 Jul;69(7):4453-62

NHP.394 (11836389) **Determination of a statistically valid neutralization titer in plasma that confers protection against simian-human immunodeficiency virus challenge following passive transfer of high-titered neutralizing antibodies**

Authors Nishimura Y, Igarashi T, Haigwood N, Sadjadpour R, Plishka RJ, Buckler-White A, Shibata R, Martin MA

Journal J Virol 2002 Mar;76(5):2123-30

Species/Subspecies Macaca nemestrina (pigtailed macaque)

Vaccine Name Chimp-anti-HIV-IgG *Type:* Passive Antibody *Route:* Intravenous

Challenge SHIV.MD1 *Route:* Intravenous

Main Findings

- Neutralizing antibodies from a chimpanzee infected with HIV-1 isolate DH12 can protect macaques from a SHIV containing the DH12 envelope gene. The recipient serum titre needed to protect 99% of macaques from 75 TCID50 IV innoculation was calculated to be 1:38

NHP.395 (15356916) **CCR5 targeted SIV vaccination strategy preventing or inhibiting SIV infection**

Authors Bogers WM, Bergmeier LA, Oostermeijer H, ten Haaft P, Wang Y, Kelly CG, Singh M, Heeney JL, Lehner T

Journal Vaccine 2004 Aug 13;22(23-24):2974-84

Objectives Challenge, Immunogenicity To attempt to prevent SIV infection by (a) upregulating the three CC chemokines, (b) eliciting antibodies to CCR5 and (c) downmodulating the cell-surface expression of CCR5.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name HSP70-Baculovirus-infected cells.gp120-pGEX-3X.p27 *Type:* Recombinant Subunit Protein *Route:* Intramuscular

Challenge SIVmac8980 *Route:* Intramuscular
Main Findings
- Immunization with protein (HSP70) covalently linked to the CCR5 peptides, SIV gp120 and p27 protected rhesus monkeys from infection after challenge with SIVmac8980

NHP.396 (15452269) **Heterologous human immunodeficiency virus type 1 priming-boosting immunization strategies involving replication-defective adenovirus and poxvirus vaccine vectors**
Authors Casimiro DR, Bett AJ, Fu TM, Davies ME, Tang A, Wilson KA, Chen M, Long R, McKelvey T, Chastain M, Gurunathan S, Tartaglia J, Emini EA, Shiver J
Journal J Virol 2004 Oct;78(20):11434-8
Objectives Immunogenicity To assesse the ability of poxvirus vectors to boost Ad5-primed responses as a means of enhancing the levels of vaccine-elicited responses.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings
- Heterologous Ad5 priming-poxvirus boosting regimen induced a significantly greater immune response in rhesus monkeys than immunization elicited by homologous prime-boost regimens with the individual vectors or by a heterologous poxvirus priming-Ad5 boosting regimen.

NHP.397 (15302953) **Macaques infected long-term with attenuated simian immunodeficiency virus (SIVmac) remain resistant to wild-type challenge, despite declining cytotoxic T lymphocyte responses to an immunodominant epitope**
Authors Sharpe SA, Cope A, Dowall S, Berry N, Ham C, Heeney JL, Hopkins D, Easterbrook L, Dennis M, Almond N, Cranage M
Journal J Gen Virol 2004 Sep;85(Pt 9):2591-602
Objectives Challenge, Immunogenicity To investigate mechanisms of protective immunity induced by live, attenuated SIV.
Species/Subspecies Macaca mulatta (Rhesus macaque)
Vaccine Name SIV.GX2 *Type:* Live Attenuated Virus
Challenge SIVmac220 *Route:* Intravenous
Main Findings
- 3 macaques immunized with live attenuated SIVmacGX2 were resistant to challenge with an uncloned pool of wild-type SIVmac220, whereas four naive controls became infected.
- Both attenuated (vaccine) and wild-type (challenge) viruses induced a disseminated CD8+ T-cell response, which was of a higher magnitude in lymphoid tissues than in the periphery

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NHP.398 (9732063) **Rhesus macaques that become systemically infected with pathogenic SHIV 89.6-PD after intravenous, rectal, or vaginal inoculation and fail to make an antiviral antibody response rapidly develop AIDS**
Authors Lu Y, Pauza CD, Lu X, Montefiori DC, Miller CJ
Journal J Acquir Immune Defic Syndr Hum Retrovirol 1998 Sep 1;19(1):6-18
Species/Subspecies Macaca mulatta (Rhesus macaque)
Challenge SHIV89.6PD *Route:* Intrarectal, Intravenous, Vaginal or perivaginal
Main Findings
- The pathogenicity of an uncloned stock of SHIV-89.6P was tested in 12 rhesus macaques. Two were injected IV, 6 were innoculated intravaginally, and 4 were innoculated intrarectally. Intraveinous innoculation resulted in peak viremia in 7 days vs 14 daysfor mucosal innoculation

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NHP.399 (12163269) **A novel chimeric Rev, Tat, and Nef (Retanef) antigen as a component of an SIV/HIV vaccine**
Authors Hel Z, Johnson JM, Tryniszewska E, Tsai WP, Harrod R, Fullen J, Tartaglia J, Franchini G
Journal Vaccine 2002 Aug 19;20(25-26):3171-86
Species/Subspecies Macaca mulatta (Rhesus macaque)
Main Findings

- Retanef is a synthetic open reading frame encoding epitopes from Rev, Tat and Nef proteins. Inserted into the NYVAC vaccinia virus vector, and injected into naive macaques, it induced CTL responses. It also boosted responses 2 to 7-fold in previously infected macaques undergoing HAART

NHP.400 (15258286) **Recombinant poxvirus boosting of DNA-primed rhesus monkeys augments peak but not memory T lymphocyte responses**

Authors Santra S, Barouch DH, Korioth-Schmitz B, Lord CI, Krivulka GR, Yu F, Beddall MH, Gorgone DA, Lifton MA, Miura A, Philippon V, Manson K, Markham PD, Parrish J, Kuroda MJ, Schmitz JE, Gelman RS, Shiver JW, Montefiori DC, Panicali D, Letvin NL

Journal Proc Natl Acad Sci U S A 2004 Jul 27;101(30):11088-93. Epub 2004 Jul 16

Objectives Challenge, Immunogenicity To assess the relative immunogenicity including a CTL response of vaccine regimens that included a cytokine-augmented plasmid DNA prime and a boost with DNA or recombinant pox vectors.

Species/Subspecies Macaca mulatta (Rhesus macaque)

Vaccine Name HIV-1 89.6P Env gp140 (KB9) DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name SIV mac239 Gag DNA *Type:* DNA *Route:* Intramuscular

Vaccine Name Recombinant fowlpox (rFPV).SHIV89.6P env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name Recombinant fowlpox (rFPV) SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name Recombinant MVA-SHIV89.6P env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name Recombinant MVA-SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name Recombinant vaccinia viruse (rVac).SHIV89.6P Env *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Vaccine Name Recombinant vaccinia viruse (rVac).SIVmac239 gag *Type:* Recombinant Vector (virus/bacteria) *Routes:* Intradermal, Intramuscular

Challenge SHIV89.6P *Route:* Intravenous

Main Findings

- Recombinant vaccinia virus, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity.
- Whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge.
- The memory T cell responses for the three vaccines were comparable.
- Protection from clinical disease in all groups of experimentally vaccinated monkeys was similar.
- The steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine

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NHP.401 (15269383) **Enhanced cellular immunity and systemic control of SHIV infection by combined parenteral and mucosal administration of a DNA prime MVA boost vaccine regimen**

Authors Makitalo B, Lundholm P, Hinkula J, Nilsson C, Karlen K, Morner A, Sutter G, Erfle V, Heeney JL, Wahren B, Biberfeld G, Thorstensson R

Journal J Gen Virol 2004 Aug;85(Pt 8):2407-19

Objectives Challenge, Immunogenicity .

Species/Subspecies Macaca fascicularis (cynomolgus macaque)

NHP.402 (15308348) **Long-term protection against SHIV89.6P replication in HIV-1 Tat vaccinated cynomolgus monkeys**

Authors Maggiorella MT, Baroncelli S, Michelini Z, Fanales-Belasio E, Moretti S, Sernicola L, Cara A, Negri DR, Butto S, Fiorelli V, Tripiciano A, Scoglio A, Caputo A, Borsetti A, Ridolfi B, Bona R, ten Haaft P, Macchia I, Leone P, Pavone-Cossut MR, Nappi F, Ciccozzi M, Heeney J, Titti F, Cafaro A, Ensoli B

Journal Vaccine 2004 Sep 3;22(25-26):3258-69

NHP.403 (15105535) **Protective efficacy of a multicomponent vector vaccine in cynomolgus monkeys after intrarectal simian immunodeficiency virus challenge**

Authors Negri DR, Baroncelli S, Catone S, Comini A, Michelini Z, Maggiorella MT, Sernicola L, Crostarosa F, Belli R, Mancini MG, Farcomeni S, Fagrouch Z, Ciccozzi M, Boros S, Liljestrom P, Norley S, Heeney J, Titti F

Journal J Gen Virol 2004 May;85(Pt 5):1191-201

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Akahata W, Ido E, Akiyama H, Uesaka H, Enose Y, Horiuchi R, Kuwata T, Goto T, Takahashi H, Hayami., DNA vaccination of macaques by a full-genome simian/human immunodeficiency virus type 1 plasmid chimera that produces non-infectious virus particles. J Gen Virol 2003;84(Pt 8):2237-2244. Trial: NHP.322

Allen TM, Jing P, Calore B, Horton H, O Connor DH, Hanke T, Piekarczyk M, Ruddersdorf R, Mothe BR, Emerson C, Wilson N, Lifson JD, Belyakov IM, Berzofsky JA, Wang C, Allison DB, Montefiori DC, Desrosiers RC, Wolinsky S, Kunstman KJ, Altman JD, Sette A, McMichael AJ, Watkins D., Effects of cytotoxic T lymphocytes (CTL) directed against a single simian immunodeficiency virus (SIV) Gag CTL epitope on the course of SIVmac239 infection. J Virol 2002;76(20):10507-11. Trial: NHP.288

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