Table 17: **gp160**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(2–10)	gp160(2–10 IIIB)	RVKEKYQHL	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
gp160(2–10)	gp160(2–10 IIIB)	RVKEKYQHL	HIV-1 infection	human(B8)	[Sipsas (1997)]
	• 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				
gp160(29–49)	gp120( )	AAEQLWVTVYYGVPV-WKEAT	HIV-infection	human(A11)	[Weekes (1999b)]
	• 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 β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ6				
gp160(31–40)	gp160(30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human(B*4402)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*4402 epitope				
gp160(31–40)	gp160(30–39 WEAU)	AENLWVTVYY	HIV-1 infection	human(B44)	[Borrow (1997), Goulder (1997a), Borrow & Shaw(1998)]
	• 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 • [Goulder (1997a)] and [Borrow & Shaw(1998)] are Reviews of immune escape that summarize this study in the context of CTL escape to fixation				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(31–55)	gp120(32–56 LAI)	TEKLWVTVYYGVPVW-KEATTTLFCA	gp160 vaccinia vaccine	human(B18)	[Johnson (1994a)]
• HLA restricted CTL response to epitope in HIV-1 vaccinia-Env vaccinees					
gp160(31–55)	gp120(32–56 LAI)	TEKLWVTVYYGVPVW-KEATTTLFCA	gp160 vaccinia vaccine	human(B18)	[Hammond (1995), Ferris (1999)]
• 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	MN rec gp160	human(A2)	[Dupuis (1995)]
• CTL from HLA-A2 positive subject react with this peptide					
gp160(33–42)	Env(32–41 Clade B)	KLWVTVYYGV	HIV-1 infection plus HIV-1 MN rgp160 stimulation	human(A2.1)	[Kundu (1998a)]
• 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(34–55)	gp120(25–46 BRU)	LWVTVYYGVPVWKEA-TTTLFCA	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through peptide blocking of CTL activity, and Env deletions					
gp160(36–46)	gp120( )	VTVYYGVPVWK	HIV-1 infection	human(A11 and A*6801)	[Threlkeld (1997)]
• 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	gp160 vaccinia vaccine	human(A*0301)	[Johnson (1994b)]
• Multiple CTL clones obtained from two vaccinees • C. Brander notes that this is an A*0301 epitope in the 1999 database					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	gp160 vaccinia vaccine	human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
gp160(37–46)	Env( )	TVYYGVPVWK	DNA multi-epitope vaccine	SJL/J HLA transgenic mice(A11)	[Ishioka (1999)]
	• 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				
gp160(37–46)	gp120(37–46)	TVYYGVPVWK	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)	human(A3)	[Carruth (1999)]
	• 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)	[Goulder (1997b), Goulder (1997a)]
	• 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 • [Goulder (1997a)] is a review of immune escape that summarizes this study				
gp160(37–46)	gp120(38–41 LAI)	TVYYGVPVWK	gp160 vaccinia vaccine	human(A3.1)	[Johnson (1994a)]
	• Highly conserved epitope recognized by multiple CTL clones from vaccinee				
gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	gp160 vaccinia vaccine	human(A3.1)	[Hammond (1995), Ferris (1999)]
	• This peptide can be processed for HLA-A3.1 presentation by TAP-1/2 independent and dependent pathways				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(37–46)	gp120(37–46 LAI)	TVYYGVPVWK	HIV-1 infection	human(B*0301)	[Wilson (2000)]
	• 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)	[Nehete (1998)]
	• 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)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5501 epitope				
gp160(42–51)	gp120(42–51 PV22)	VPVWKEATTT	HIV-1 infection	human(B55)	[Brander & Walker(1995)]
	• P. Johnson, unpublished				
gp160(42–52)	gp120(42–52)	VPVWKEATTTL	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
gp160(42–52)	gp120(42–52 PV22)	VPVWKEATTTL	HIV-1 infection	human(B35)	[Cao (1997)]
	• 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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(42–61)	gp120(49–68)	VPVWKEATTTLFCAS-DAKAY	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
gp160(42–61)	gp120(49–68 SF2)	VPVWKEATTTLFCAS-DAKAY	HIV infection	human( )	[Lieberman (1997a)]
	• 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)	VPVWKEATTTLFCAS-DAKAY	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
gp160(52–61)	gp120(59–68 HXB2)	LFCASDAKAY	HIV-1 infection	human(A*2402)	[Lieberman (1992)]
	• CTL epitope defined by T cell line and peptide mapping • C. Brander notes that this is an A*2402 epitope in the 1999 database				
gp160(52–61)	gp120(53–62 LAI)	LFCASDAKAY	HIV-1 infection	human(A*2402)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*2402 epitope				
gp160(52–61)	gp120(53–62 LAI)	LFCASCAKAY	HIV-1 infection	human(B38)	[Shankar (1996)]
	• Uncertain whether optimal, binds A24 as well				
gp160(52–71)	gp120(59–78)	LFCASDAKAYDTEVHI-NVWAT	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
gp160(52–71)	gp120(59–78 SF2)	LFCASDAKAYDTEVHI-NVWAT	HIV infection	human( )	[Lieberman (1997a)]
	• 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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(62–80)	gp120(69–88 SF2)	DTEVHNVWATHACVP-TDPN	HIV-1 infection	human( )	[Lieberman (1997a)]
	• 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(78–86)	Env(77–85)	DPNPQEVVL	HIV-1 infection	human(A*3501)	[Ogg (1999)]
	• 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)	gp120(77–85)	DPNPQEVVL	HIV-1 infection	human(B*3501)	[Ogg (1998b)]
	• 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)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
gp160(78–86)	gp120(77–85 SF2)	DPNPQEVVL	HIV-1 infection	human(B*3501)	[Tomiyama (1997)]
	• 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(B35)	[Dyer (1999)]
	• 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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(78–86)	( )	DPNPQEVVL	HIV-1 infection	human(B35)	[Wilson (2000)]
	• 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(78–86)	( )	DPNPQEVVL	HIV-1 infection	human(B35)	[Kawana (1999)]
	• 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, B51)	[Shiga (1996)]
	• Binds HLA-B*3501 and B*5101 – binds and kills gp120-vaccinia virus infected cells carrying B35 or B51				
gp160(104–119)	gp120(111–126 IIIB)	MQEDIISLWDQSLKPC	primary *in vitro* response to peptide	human( )	[Macatonia (1991)]
	• Primary CTL response with cells from non-infected donors stimulated by the peptide				
gp160(105–117)	gp120( )	HEDIISLWDQSLK	HIV-1 infection	chimpanzee( )	[Lubeck (1997)]
	• 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)				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV exposure	human( )	[Pinto (1995)]
• CTL and T helper cell reactivity in healthcare workers exposed to HIV					
gp160(105–117)	gp120(112–124 IIIB)	HEDIISLWDQSLK	HIV-1 infection	human(A2)	[Clerici (1991)]
• Helper and cytotoxic T cells can be stimulated by this peptide (T2)					
gp160(108–116)	Env(107–115 Clade B)	IISLWDQSL	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
• 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(112–130)	gp120(119–139 SF2)	WDQSLKPCVKLTPLC-VSLK	HIV-1 infection	human( )	[Lieberman (1997a)]
• 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(117–126)	Env(72–81)	KPCVKLTPLC	HIV-1 infection	human(B7)	[Jin (2000)]
• 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					
gp160(121–129)	gp120(120–128 LAI)	KLTPLCVTL	MN rec gp160	human(A2)	[Dupuis (1995)]
• CTL from HLA-A2 positive subject react with this peptide					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(121–129)	gp120(120–128)	KLTPLCVTL	HIV A2-Polyepitope (Polytope) DNA vaccine with vaccinia boost (rVV.HIV.pt)	human(A2)	[Woodberry (1999)]

- 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)	[Kundu (1998b)]

- 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)	[Kmieciak (1998)]

- Increased CTL response to cells expressing a VV construct Δv3 mutant compared with a full-length Env gene product

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(121–129)	gp120(121–129)	KLTPLCVSL	*in vitro* stimulation	human(A2)	[Zarling (1999)]
	• 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)	Env( )	KLTPLCVTL	DNA multi-epitope vaccine	SJL/J HLA trans-genic mice(A2.1)	[Ishioka (1999)]
	• 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 Clade B)	KLTPLCVTL	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
	• 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 Location	Sequence	Immunogen	Species(HLA)	References
gp160(156–165)	gp120(156–165)	NCSFNISTSI	HIV-1 infection	human(Cw*08)	[Ferris (1999)]
• 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					
gp160(156–165)	gp120(156–165 IIIB)	NCSFNISTSI	HIV-1 infection	human(Cw8)	[Sipsas (1997)]
• 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					
gp160(188–207)	gp120(193–212 BRU)	TTSYTLTSCNTSVITQA-CPK	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through blocking CTL activity, and Env deletions					
gp160(192–200)	gp120(192–199 HXB2R)	KLTSCNTSV	HIV-1 infection	human(A2)	[Brander (1995)]
• 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)	[Huang (2000)]
• 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-γ-production ELISPOT					
gp160(192–200)	gp120(197–205)	TLTSCNTSV	no CTL shown	human(A2)	[Garboczi (1992)]
• Crystallization of HLA-A2 molecules complexed with antigenic peptides – refers to Dadaglio *et al* 1991					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(192–200)	gp120(199–207)	TLTSCNTSV	peptide immunization and HIV-1 infection	human(A2.1)	[Brander (1996)]
	• 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)	SLTSCNTSVITQACPK-VSFE	HIV-1 infection	human( )	[Lieberman (1997a)]
	• 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, -B21				
gp160(201–225)	gp120(201–225 LAI)	ITQACPKVSFEPIPHYC-APAGFAI	gp160 vaccinia vaccine	human(CD4+ CTL)	[Johnson (1994b), Johnson (1994a)]
	• CD4+ CTL isolated from LAI IIIB gp160 vaccinees				
gp160(202–221)	gp120(209–228)	TQACPKVSFEPIPIHYC-APA	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
gp160(202–221)	gp120( )	TQACPKVSFEPIPIHYC-APA	HIV-infection	human( )	[Weekes (1999b)]
	• 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 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 β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.1				
gp160(202–221)	gp120( )	TQACPKVSFEPIPIHYC-APA	HIV-infection	human( )	[Weekes (1999a)]
	• Peptide 740.18: Memory CTL-specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(202–221)	gp120(209–228 SF2)	TQACPKVSFEPIPIHYC-APA	HIV infection	human( )	[Lieberman (1997a)]
	• 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)	TQACPKVSFEPIPIHYC-APA	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
gp160(208–217)	gp120( )	VSFEPIPIHY	HIV-1 exposed seronegative	human(A29)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-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+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
gp160(209–217)	( )	SFEPIPIHY		(A29)	[Brander & Goulder(2001), Altfeld(2000)]
gp160(212–231)	gp120( )	PIPIHYCAPAGFAILKC-NNK	HIV-infection	human( )	[Weekes (1999a)]
	• 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)	PIPIHYCAPAGFAILKC-NNK	HIV-1 infection	human( )	[Lieberman (1992)]
	• CTL epitope defined by T cell line and peptide mapping				
gp160(212–231)	gp120(219–238)	PIPIHYCAPAGFAILKC-NNK	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(212–231)	gp120( )	PIPIHYCAPAGFAILKC-NNK	HIV-infection	human(A2)	[Weekes (1999b)]
	• 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 β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ13.6			
gp160(239–247)	gp120(241–249 LAI)	CTNVSTVQC	HIV-1 infection	human(Cw8)	[Sipsas (1997)]
	• 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)	VSTVQCTHGIRPVVST-QLLL	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
gp160(242–261)	gp120(249–268 SF2)	VSTVQCTHGIRPVVST-QLLL	HIV infection	human( )	[Lieberman (1997a)]
	• 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)	VSTVQCTHGIRPVVST-QLLL	HIV-1 infection	human( )	[Lieberman (1997b)]
	• 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)	[Tomiyama (1997)]
	• 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)	[Shiga (1996)]
	• Binds HLA-B*3501				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(252–260)	( )	RPIVSTQLL	HIV-1 infection	human(B35)	[Kawana (1999)]
	• 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(252–271)	gp120(256–275 LAI)	RPVVSTQLLLNGSLAE-EEVV	HIV-1 infection	human(B7)	[Shankar (1996)]
gp160(291–307)	gp120(295–312 BRU)	SVEINCTRPNNNTRKSI	HIV-1 infection	human(A2)	[Dadaglio (1991)]
	• Defined through blocking CTL activity, and Env deletions				
gp160(297–322)	gp120(297–322 IIIB)	TRPNNNTRKRIRIQRG-PGRAFVTIGK	V3 loop HIV-1 peptide vaccine with liposomes as adjuvant	murine(H-2D^{d})	[Chang (1999)]
	• 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)	TRPNNNTRKSIHIGPG-RAFYATGEIIGDIRQAH	Lipopeptide vaccine	human( )	[Gahery-Segard (2000)]
	• 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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(298–307)	gp120(298–307)	RPNNNTRKSI	HIV-1 infection	human(B*07)	[Ferris (1999), Hammond (1995)]
	• 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 • 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)	RPNNNTRKSI	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Safrit (1994b)]
	• CTL from two acute seroconversion cases				
gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Hammond (1995)]
	• Peptide processed by a TAP-1/2-dependent pathway only • CTL from an acute seroconverter				
gp160(298–307)	gp120(302–312 HXB2)	RPNNNTRKSI	HIV infection	human(B7)	[Wolinsky (1996)]
	• Longitudinal study of epitope variation *in vivo*				
gp160(298–307)	gp120(303–312 IIIB)	RPNNNTRKSI	HIV-1 infection	human(B7?)	[Wilson (1996)]
	• 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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(298–307)	gp120(302–311 Clade B)	RPNNNTRKSI	HIV-1 infection	human(B7)	[Wilson (1998b)]
	• 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				
gp160(303–322)	gp120( )	TRKSIHIGPGRAFYTT-GE	Gag/Env VLP	murine BALB/c( )	[Luo (1998)]
	• 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	Chimeric Gag-Env VLPs	murine(H-2^d)	[Kang (1999)]
	• 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) • 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(308–322)	gp160( )	RIHIGPGRAFYTTKN	Immunization with HIV Env peptides in Montanide ISA 51	human( )	[Pinto (1999)]
	• Peptide P18: Eight HIV+ individuals were vaccinated with peptides containing specific T helper, CTL and Ab epitopes in a Phase I trial • Four displayed a 4-fold increase in PCLUS 3–18 MN-specific T helper responses • One patient developed a new, sustained P18MN-peptide-specific CTL response – the patients 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( )	RIHIGPGRAFYTTKN	HIV-1 infection	chimpanzee( )	[Lubeck (1997)]
	• 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 exposure	human( )	[Pinto (1995)]
	• CTL and T helper cell reactivity in healthcare workers exposed to HIV				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(308–322)	gp120(313–327 MN)	RIHIGPGRAFYTTKN	HIV exposure	human( )	[Pinto (1995)]
• CTL and T helper cell reactivity in healthcare workers exposed to HIV					
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	vaccinia IIIB gp160	human(A11)	[Achour (1994)]
• One of 3 HLA type restrictions associated with this peptide					
gp160(308–322)	gp120(315–329 BRU)	RIQRGPGRAFVTIGK	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through blocking CTL activity, and Env deletions					
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	HIV-1 infection	human(A2)	[Clerici (1991)]
• Helper and cytotoxic T cells can be stimulated by this peptide (P18)					
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	gp160 vaccinia	human(A2, A3)	[Achour (1993)]
• Two of 3 HLA type restrictions associated with this peptide					
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	IIIB peptide	murine(D^d)	[Takahashi (1989a)]
• R(8) F(10) MHC/peptide interaction					
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	IIIB peptide	murine(D^d)	[Sastry (1992)]
• Free peptide injected into the footpad of a mouse could stimulate specific CTL					
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	peptide immunization	murine(D^d)	[Ahlers (1997b)]
• 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	MN gp160 vaccinia	murine(D^d)	[Takahashi (1989b)]
• Y(11 MN) exchange with V(11 IIIB) interchanges specificities					
gp160(308–322)	gp120(313–327 IIIB MN RF)	SITKGPGRVIYATGQ	RF gp160 vaccinia	murine(D^d)	[Takahashi (1992)]
• Comparison of MN, IIIB, and RF specificities, position 11 is critical					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(308–322)	gp120( )	RIQRGPGRAFVTIGK	Pr55 Gag-Env VLPs	murine(H-2^d)	[Deml (1997)]
	• 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	DNA immunization	murine BALB/c(H-2^d)	[Fomsgaard (1998a)]
	• 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	peptide vaccine	murine BALB/c(H-2^d)	[Ahlers (1996), Ahlers (1997a)]
	• 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	V3:Ty-Virus-like particles	murine(H-2^d)	[Layton (1993)]
	• V3-Ty-Virus-like particles can induce type-specific CTL in mice in the absence of adjuvant				
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	vaccinia IIIB gp160	murine(H-$2^{d,p,u,q}$)	[Shirai (1992), Shirai (1993)]
	• 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( )	RIQRGPGRAFVTIGK	Gag-V3 fusion	murine(H-2^d)	[Griffiths (1993)]
	• Gag-V3 fusion protein immunization elicited V3 CTL response in mice				
gp160(308–322)	gp120( )	RIQRGPGRAFVTIGK	DNA vaccine pV1J-gp120	murine(H-2^d)	[Barouch (1998)]
	• This study showed that a response to an HIV-1 DNA vaccine could be either augmented or suppressed by plasmid Cytokine/Ig administration				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(308–322)	gp160( )	RIHIGPGRAFYTTKN	DNA vaccine, MN gp160	murine BALB/c and C57/BL6(H-2^d and H-2^b)	[Fomsgaard (1998b)]
	• 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)	gp160( )	GIHIGPGRAFYAARK	HIV-gp160, an Env CTL epitope (E7), and the mucosal adjuvant LT(R192G)	murine(H-2D^d)	[Morris (2000)]
	• 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	Intranasal peptide with cholera toxin as a mucosal adjuvant	murine(H-2D^d)	[Porgador (1997)]
	• 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	Rec vaccinia expressing HIV-1 P18 IIIB in an H1 influenza hemagglutinin (HA) gene cassette	(H-2D^d)	[Chiba (1999)]
	• 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( )	RIHIGPGRAFYTTKN	V3 loop peptides	murine(H-2D^d)	[Casement (1995)]
	• V3 peptides from MN and SC induce murine CTL that are cross-reactive with diverse strains				
gp160(308–322)	gp120(313–327 MN)	RIHIGPGRAFYTTKN	MN rgp120 with QS-21 adjuvant	murine(H-2D^d)	[Newman (1997)]
	• MN vaccine induced CTL reactive with MN, IIIB and RF vaccinia-expressed Env, but not this peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(308–322)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	IIIB rgp120 with QS-21 adjuvant	murine(H-2D^d)	[Newman (1997)]
• 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	vaccinia IIIB gp160	murine(H-2D^d)	[Takahashi (1988)]
• V3 loop CTL response in mice vaccinated with gp160					
gp160(308–322)	gp120(315–329)	RIQRGPGRAFVTIGK	18IIIB peptides coated with peptide	murine BALB/c(H-2D^d)	[Fukasawa (1998)]
• 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)	gp120(315–329 IIIB)	RIQRGPGRAFVTIGK	rec vaccinia gp160	murine(H-2D^{d,p,q}, H-2^u)	[Shirai (1996)]
• Multiple murine MHC can cross-present this epitope (P18) and HP53, DRVIEVVQGAYRAIR, to specific CTL					
gp160(309–317)	gp120(310–318 SF2)	IYIGPGRAF	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
• 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(310–323)	gp120(315–328 MN)	HIGPGRAFYTTKNI	vCP205, canarypox vector, MN gp120 + Gag/Pro IIIB, HIV-1 pseudovirion boost	murine(H-2D^d)	[Arp (1999)]
• Epitope p97: HIV-1 pseudovirion boost enhanced the CTL to this epitope in immunized BALB/ c mice as measured by CTL lysis and IFN-γ production					
gp160(311–319)	gp120(312–320 SF2)	IGPGRAFHT	DNA gp120-plasmid immunization	murine(D^d)	[Selby (1997)]
• 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					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(311–319)	gp120( )	IGPGRAFHT	gp120(SF2) DNA vaccine, rgp120 protein boost	murine(H-2D^d)	[Barnett (1997)]
	• 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	DNA gp160 plasmid + peptide boost	Macaca fuscata( )	[Okuda (1997)]
	• 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( )	[Kmieciak (1998)]
	• 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( )	RGPGRAFVTI	IIIB DNA vaccine with MIP-1α expression vector	murine BALB/c( )	[Lu (1999)]
	• A MIP-1α expression plasmid increased the CTL response to this DNA vaccine, as well as the T help response, presumably by the MIP-1α interacting with T lymphocytes and macrophages				
gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	CTL line from HIV- donor	human(A*0201)	[Alexander-Miller (1996)]
	• 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)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0201 epitope				
gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	vaccinia IIIB gp160	human(A2)	[Achour (1996)]
	• 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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(311–320)	gp160(318–327 SIMI)	MGPKRAFYAT	vaccinia SIMI gp160	human(A2)	[Achour (1996)]
	• 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)	gp160(318–327 IIIB)	RGPGRAFVTI	IIIB peptide	murine(D)	[Nehete (1995)]
	• RGPGRAFVTI was defined as the optimal peptide for vaccination, out of RIQRGPGRAFVTIGK • This peptide, in a carrier-free form in Freunds adjuvant, could stimulate Env specific CTL in BALB/c mice				
gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	IIIB peptide	murine(D^d)	[Takahashi (1993)]
	• Successful priming with vaccination of peptide pulsed splenic dendritic cells				
gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	IIIB peptide	murine(D^d)	[Takahashi (1996)]
	• 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)	Env(318–327)	RGPGRAFVTI		murine(H-2^d)	[Lopez (2000)]
	• 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 • 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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(311–320)	gp120( )	RGPGRAFVTI	Polyepitope encoding DNA in VVA	murine(H-2^d)	[Hanke (1998b), Hanke (1998a)]
• 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	Combination peptide vaccine	murine BALB/c(H-2^d)	[Hamajima (1997)]
• 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	HIV-1 DNA vaccine (gp160-CMV) with 8 Br-cAMP as adjuvant	murine(H-2^d)	[Arai (2000)]
• 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	rec vaccinia-gp160	murine(H-2^d)	[Goletz (1997)]
• 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)	gp120(318–327 IIIB)	RGPGRAFVTI	vaccinia IIIB gp160	murine(H-$2^{d,p,u}$)	[Shirai (1997)]
• 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	Polyepitope encoding DNA expressed in modified virus Ankara (MVA) DNA vectors	murine(H-2^{d17})	[Hanke (1998a)]
• 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 • γ IFN and CTL activity were induced after a single vaccination • An MVA boost enhanced the response					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(311–320)	gp160( )	RGPGRAFVTI	Env DNA prime/boost with IL-12	murine(H-2^d)	[Gherardi (2000)]
	• Induction of HIV-1 specific CD8 γ-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	DNA vaccine pCMV160IIIB/REV with IL-15 and IL-2 or IL-12 expression plasmids	murine(H-2^d)	[Xin (1999)]
	• 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	HIV-1 peptide p18 in vaccinia (vp18) or Sindbis (SINp18) vector	murine(H-2^d)	[Villacres & Bergmann(1999)]
	• 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 γ-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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(311–320)	Env( )	IGPGRARYAR	MVA gp160 89.6	murine BALB/c(H-2D)	[Belyakov (1998b)]
	• 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				
gp160(311–320)	Env( )	IGPGRARYAR	HIV peptide PCLUS3–18IIIB	murine BALB/c(H-2D)	[Belyakov (1998a)]
	• 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( )	IGPGRAFYTT	*B. abortus*-peptide conjugate	murine(H-2D^d)	[Lapham (1996)]
	• *B. abortus*-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice				
gp160(311–320)	gp160( )	RGPGRAFVTI	rec non-replicating adenoviruses (RAd501 (Env) and RAd46 (Rev) or RAd142 (Env+Rev))	murine(H-2D^d)	[Bruce (1999)]
	• 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( )	IGPGRAFYTT	*B. abortus*-peptide conjugate	murine(H-2D^d)	[Lapham (1996)]
	• *B. abortus*-peptide conjugate induced a virus-specific CTL response in CD4+ lymphocyte depleted mice				
gp160(311–320)	gp160(318–327 IIIB)	RGPGRAFVTI	peptide	murine(H-2D^d)	[Takeshita (1995)]
	• XGPXRXXXXI are critical for binding, consistent with H-2D^d motif XGPX(RKH)XXX(X)(LIF)				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(311–320)	Env( )	RGPGRAFTVTI	multi-epitope DNA vaccine	murine(H-2D^d)	[Hanke & McMichael(1999), Hanke (1999)]
	• 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 a MVA boost was as good as i. m. immunization followed by an 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)	gp160(318–327 IIIB)	RGPGRAFVTI	A rapidly degraded form of Env	murine(L^d)	[Tobery & Siliciano(1997)]
	• 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(314–322)	gp120(314–322)	GRAFVTIGK	no CTL shown	human(B27)	[Jardetzky (1991)]
	• Study of peptide binding to HLA-B27				
gp160(337–361)	gp120(337–368 LAI)	KWNNTLKQIDSKLRE-QFGNNKTIIF	gp160 vaccinia vaccine	human(CD4+ CTL)	[Johnson (1994a)]
	• CD4+ CTL clones were obtained from an HIV-1 vaccinia-Env vaccinee				
gp160(339–354)	gp120(339–361 LAI)	NNTLKQIDSKLREQFG	gp160 vaccinia	human(CD4+ CTL)	[Johnson (1994b)]
	• CD4+ CTL isolated from LAI IIIB gp160 vaccinees				
gp160(340–349)	gp120( )	NTLKQIVIKL	HIV-1 rgp120 vaccine	chimpanzee(Patr-B*14)	[Balla-Jhagjhoorsingh (1999a)]
	• 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)	[Dadaglio (1991)]
	• Defined through blocking CTL activity, and Env deletions				
gp160(375–383)	gp120(379–387 LAI)	SFNCGGEFF	HIV-1 infection	human(B*1516)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*1516 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(375–383)	gp120(375–383 IIIB)	SFTCGGEFF	HIV-1 infection	human(B15)	[Wilson (1999a)]
	• 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 IIIB)	SFNCGGEFF	HIV-1 infection	human(B63,B15)	[Wilson (1997)]
	• 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)	[Brander & Goulder(2001)]
	• C. Brander notes this is a C*0401 epitope				
gp160(375–383)	gp120(376–383 PV22)	SFNCGGEFF	HIV-1 infection	human(Cw4)	[Johnson (1993)]
	• Conserved epitope				
gp160(375–383)	gp120(376–383 PV22)	SFNCGGEFF	CTL not shown	human(Cw4)	[Wolinsky (1996)]
	• Longitudinal study of epitope variation *in vivo*				
gp160(376–383)	gp120( )	FNCGGEFF		human(Cw4)	[Rowland-Jones (1999)]
	• 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 [Johnson (1993)]				
gp160(376–384)	gp120(376–384 IIIB)	FNCGGEFFY	HIV-1 infection	human(A29)	[Wilson (1997)]
	• 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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(376–384)	gp120(376–384 IIIB)	PNCGGEFFY	HIV-1 infection	human(A29)	[Wilson (1999a)]
	• 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(376–387)	gp120(381–392 BRU)	KNCGGEFFYCNS	HIV-1 infection	human(A2)	[Dadaglio (1991)]
	• Defined through blocking CTL activity, and Env deletions				
gp160(377–387)	gp120(377–387)	NSGGEFFYSNS		human(A2)	[Hickling (1990)]
	• 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-Moore (1997)]
	• 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)	GSDTITLPCRIKQFINM-WQE	PBMC stimulation *in vitro* by gp120 pulsed autologous monocytes	human(CD4+DRA)	[Bouhdoud (2000)]
	• 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 • 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)	[Tomiyama (1999)]
	• 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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(416–424)	gp160(416–424 LAI)	LPCRIKQII		human(B*5101)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*5101 epitope					
gp160(416–429)	gp120(410–429 H3DCG)	LPCRIKQFINMWQE	HIV-1 infection	human(DR4 CD4+)	[Siliciano (1988)]
• CD4+ CTL restricted by class II HLA-DR4, targets primed by CD4 mediated uptake of gp120					
gp160(416–435)	gp120(421–440 LAI)	LPCRIKQFINMWQEV-GKAMY	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through blocking CTL activity, and Env deletions					
gp160(419–427)	gp120(424–432 HXB2)	RIKQIINMW		human(A*3201)	[Harrer (1996b)]
• 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)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*3201 epitope					
gp160(419–427)	gp120(419–427)	RIKQIINMW?	HIV-1 infection	human(A29,A32)	[Betts (2000)]
• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon 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)	[Ray (1998)]
• 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					
gp160(419–427)	gp120(420–428)	RIKQIINMW	HIV-1 infection	human(A32)	[Ferris (1999)]
• This epitope is processed by a TAP1/2 dependent mechanism					
gp160(421–435)	gp120(421–440 LAI)	KQFINMWQEVGKAMY	HIV-1 infection	human(A2)	[Dadaglio (1991)]
• Defined through blocking CTL activity, and Env deletions					
gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	HIV exposure	human( )	[Pinto (1995)]
• CTL and T helper cell reactivity in healthcare workers exposed to HIV					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(421–436)	gp120( )	KQIINMWQEVGKAMY-A	HIV-1 infection	chimpanzee( )	[Lubeck (1997)]
	• 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)	KQIINMWQEVGKAMY-A	HIV-1 infection	human(A2)	[Clerici (1991)]
	• Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	HIV-1 infection	human(A2)	[Cease (1987)]
	• Helper and cytotoxic T cells can be stimulated by this peptide (T1)				
gp160(421–436)	gp120(428–443 IIIB)	KQIINMWQEVGKAMY-A	vaccinia IIIB gp160	murine(H-$2^{a,b,f}$)	[Shirai (1992)]
	• In a murine system multiple class I molecules can present to CTL				
gp160(432–451)	gp120(439–458 IIIB)	KAMYAPPISGQIRCSS-NITG	HIV-1 Pr55Gag VLP with gp120 or V3+CD4 linear domains	*Macaca mulatta*( )	[Wagner (1998b)]
	• 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	synthetic peptide	murine(H-2K^d)	[Duarte (1996)]
	• Tolerization of CTL response with continued administration of soluble peptide				
gp160(435–443)	( )	YAPPISGQI	SHIV-infection	Rhesus macaques(Mamu A*01)	[Egan (1999)]
	• 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(489–508)	gp120(494–513 BRU)	VKIEPLGVAPTKAKRR-VVQR	HIV-1 infection	human(A2)	[Dadaglio (1991)]
	• Defined through blocking CTL activity, and Env deletions				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(519–543)	gp41(519–543)	FLGFLGAAGSTMGAA-SLTLTVQARC	HIV-1 infection	human(Cw7)	[Nehete (1998)]
	• 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(557–565)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human( )	[Wilson (1996)]
	• 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( )	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon 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(B*5101)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5101 epitope				
gp160(557–565)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human(B15)	[Wilson (1999a)]
	• 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)	gp41(557–565 IIIB)	RAIEAQQHL	HIV-1 infection	human(B51)	[Sipsas (1997)]
	• 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				
gp160(557–565)	gp41(557–565)	RAIEAQQHL	HIV-1 infection	human(B51)	[Ferris (1999)]
	• This epitope can be processed by a TAP1/2 dependent mechanism				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(570–589)	gp41(571–590 LAI)	VWGIKQLQARILAVER-YLKD	rec LAI gp160 vaccinia HIVAC-1e and rgp160	human(CD4+ CTL(DR-1))	[Kent (1997a)]
	• 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)	GIKQLQARILAVERYL-KDQ	rgp160 BRU vaccine	human(DPw4.2)	[Hammond (1991)]
	• CD4+ CTL				
gp160(575–599)	gp41(575–599 IIIB)	QLQARILAVERYLKDQ-QLLGIWGCS	HIV-1 infection	human(B14)	[Jassoy (1992)]
	• Epitope recognized by CTL clone derived from CSF				
gp160(583–592)	gp41(583–592 PV22)	VERYLKDQQL	HIV-1 infection	human(B14)	[Jassoy (1993)]
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human( )	[Price (1995)]
	• Study of cytokines released by HIV-1 specific activated CTL				
gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human( )	[Borrow (1994)]
	• 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				
gp160(584–592)	gp41(584–592 PV22)	ERYLKDQQL	HIV-1 infection	human(B*1402)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*1402 epitope				
gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 infection	human(B14)	[Wagner (1998a)]
	• 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-1α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Kalams (1999b)]
• 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					
gp160(584–592)	gp41(591–599 SF2)	ERYLKDQQL	HIV-1 infection	human(B14)	[Lieberman (1997a)]
• 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					
gp160(584–592)	gp41(591–599 SF2)	ERYLKDQQL	HIV-1 infection	human(B14)	[Cao (1997)]
• The consensus sequence for clades B, C, and D is ERYLKDQQL • The consensus sequence for clade A is ERYLRDQQL and it is equally reactive • The consensus sequence for clade E is ERYLKDQKF and it is not reactive					
gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 exposure	human(B14)	[Rowland-Jones (1998a)]
• 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)	[Sipsas (1997)]
• 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)	[Yang (1996)]
• 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 Location	Sequence	Immunogen	Species(HLA)	References
gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Yang (1997a)]
	• 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)	[Johnson (1992)]
	• 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)	[Jassoy (1993)]
	• 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)	[Kalams (1994), Kalams (1996)]
	• 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	no CTL shown	human(B14)	[DiBrino (1994a)]
	• Epitope studied in the context of HLA-B14 binding				
gp160(584–592)	gp41(584–592)	ERYLKDQQL	HIV-1 infection	human(B14)	[Hammond (1995)]
	• 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)	[Kalams (1996)]
	• 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 • 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)	[Ferris (1999), Hammond (1995)]
	• This epitope is processed by both TAP1/2 dependent and independent mechanisms				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(584–592)	gp41( )	ERYLKDQQL		human(B14)	[Rowland-Jones (1999)]
• 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 [Johnson (1992)]					
gp160(584–592)	gp41( )	ERYLKDQQL	HIV-1 exposure	human(B14, B*1402)	[Rowland-Jones (1998b)]
• 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(585–592)	gp41(584–591 SF2)	RYLRDQQL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
• 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)	[Shankar (1996)]
gp160(585–593)	gp41(584–591 SF2)	RYLRDQQLL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
• 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)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*2402 epitope					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(585–595)	gp41(584–591 SF2)	RYLRDQQLLGI	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
	• 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(586–593)	gp41(584–591 NL43)	YLKDQQLL	HIV-1 infection	human(A*2402)	[Dai (1992)]
	• 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(586–593)	YLKDQQLL	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
gp160(586–593)	gp41(586–593)	YLKDQQLL	HIV-1 infection	human(B8)	[Johnson (1992)]
	• Two overlapping CTL epitopes were mapped with different HLA restriction (also see ERYLKDQQL HLA-B14)				
gp160(586–593)	gp41(586–593)	YLKDQQLL	no CTL shown	human(B8)	[Sutton (1993)]
	• Predicted epitope based on B8-binding motifs, from larger peptide QLQARILAVERYLKDQQLLGIWGCS				
gp160(586–593)	gp41(76–83)	YLKDQQLL		human(B8)	[Goulder (1997g)]
	• Included in a study of the B8 binding motif				
gp160(586–593)	gp41( )	YLKDQQLL		human(B8)	[Rowland-Jones (1999)]
	• 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 [Johnson (1992)]				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(586–598)	gp41(586–598)	YLRDQQLLGIWGC	HIV-1 infection	human(Cw7)	[Nehete (1998)]
• 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(606–614)	gp41(605–615 LAI)	TAVPWNASW	gp160 vaccinia	human(B*3501)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*3501 epitope					
gp160(606–614)	gp41(606–614 HXB2)	TAVPWNASW	synthetic peptide	human(B*3501)	[Ferris (1996)]
• 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	gp160 vaccinia	human(B35)	[Johnson (1994b)]
• Epitope for vaccine induced CD8+ clone					
gp160(606–614)	gp41(606–614 LAI)	TAVPWNASW	gp160 vaccinia vaccine	human(B35)	[Johnson (1994a)]
• HLA restricted CTL response to epitope in HIV-1 vaccinia-Env vaccinees					
gp160(606–614)	gp41(606–614 LAI)	TAVPWNASW	gp160 vaccinia vaccine	human(B35)	[Hammond (1995)]
• Peptide only processed by a TAP-1/2-dependent pathway					
gp160(606–614)	gp41(606–614)	TAVPWNASW	HIV-1 infection	human(B35)	[Ferris (1999)]
• This epitope is processed by a TAP1/2 dependent mechanism					
gp160(606–614)	gp41( )	TAVPWNASW	HIV-1 exposure	human(B35)	[Rowland-Jones (1998b)]
• 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(634–648)	gp41(641–655 SF2)	EIDNYTNTIYTLLEE	HIV-1 infection	human( )	[Lieberman (1997a)]
	• 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 Clade B)	WLWYIKIFI	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
	• 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(680–689)	gp41(679–687 SF2)	WYIKIFIFMI	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
	• 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(685–693)	Env(686–694 Clade B)	FIMIVGGLV	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
	• 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 • ALTERNATIVE EPITOPE: IMIVGGLVGL – no CTL response was shown to the peptides FIMIVGGLV or IMIVGGLVGL				
gp160(700–708)	gp41(705–714)	AVLSVVNRV	HIV-1 infection	human(A2)	[Ferris (1999)]
	• This epitope is processed by a TAP1/2 dependent mechanism				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(701–720)	gp41(701–720 BH10)	VLSIVNRVRQGYSPLS-FQTH	HIV-1 infection	human(A32)	[Safrit (1994a)]
	• Recognized by CTL derived from acute seroconverter				
gp160(704–712)	gp160(704–712 LAI)	IVNRNRQGY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001)]
	• C. Brander notes this is an A*3002 epitope				
gp160(747–755)	gp41(747–755)	RLVNGSLAL	HIV-1 infection	human(A2)	[Parker (1992)]
	• Studied in the context of HLA-A2 peptide binding				
gp160(767–775)	gp41(766–774 SF2)	SYRRLRDLL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
	• 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)	[Hammond (1995)]
	• 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( )	[Safrit (1994a)]
	• Recognized by CTL derived from acute seroconverter				
gp160(770–780)	gp41(775–785)	RLRDLLLIVTR	HIV-1 infection	human( )	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 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)	RLRDLLLIVTR	HIV-1 infection	human(A*0301)	[Takahashi (1991)]
	• CD8+ T cell clone				
gp160(770–780)	gp41(775–785 LAI)	RLRDLLLIVTR	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(770–780)	gp41(770–780 BH10)	RLRDLLLIVTR	HIV-1 infection	human(A*3101)	[Safrit (1994a), Safrit (1994b)]
	• Recognized by CTL derived from acute seroconverter • C. Brander notes that this is an A*3101 epitope in the 1999 database				
gp160(770–780)	gp160(770–780 LAI)	RLRDLLLIVTR		human(A*3101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*3002 epitope				
gp160(770–780)	gp41(768–778 NL43)	RLRDLLLIVTR	HIV-1 infection	human(A3)	[Cao (1997)]
	• 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				
gp160(770–780)	gp41(770–780)	RLRDLLLIVTR	HIV-1 infection	human(A31)	[Ferris (1999), Hammond (1995)]
	• This epitope is processed by a TAP1/2 dependent mechanism				
gp160(777–785)	gp41(782–790 LAI)	IVTRIVELL	?	human(A*6802)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*6802 epitope				
gp160(781–802)	gp120(788–809)	IVELLGRRGWEALKY-WWNLLQY	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
gp160(781–802)	gp41(788–809 HXB2)	IVELLGRRGWEALKY-WWNLLQY	HIV-1 infection	human(B27)	[Lieberman (1992)]
	• CTL epitope defined by T cell line and peptide mapping				
gp160(786–794)	gp41(791–799 LAI)	GRRGWEALK	HIV-1 infection	human(B27)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • Also: J. Liebermann 1992 and pers. comm. J. Liebermann				
gp160(786–795)	gp41(791–800 LAI)	GRRGWEALKY	HIV infection	human(B*2705)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*2705 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(786–795)	gp41(791–800 LAI)	GRRGWEALKY	HIV infection	human(B27)	[Lieberman(1998)]
• Optimal peptide mapped by titration J. Lieberman, Pers. Comm.					
gp160(794–802)	gp160(794–802 LAI)	KYCWNLLQY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001)]
• C. Brander notes this is an A*3002 epitope					
gp160(795–816)	gp41(802–823 HXB2)	YWWNLLQYWSQELKN-SAVNLLN	HIV-1 infection	human( )	[Lieberman (1992)]
• CTL epitope defined by T cell line and peptide mapping					
gp160(799–807)	Env(800–808 Clade B)	LLQYWSQEL	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
• 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)	gp41(810–819 LAI)	QELKNSAVSL		human(B*4001)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*4001,B60 epitope					
gp160(813–822)	gp41(814–823 LAI)	SLLNATDIAV	MN rec gp160	human(A*0201)	[Dupuis (1995)]
• 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	MN rec gp160	human(A*0201)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*0201 epitope					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(813–822)	gp41(814–823)	SLLNATDIAV	HIV-1 infection	human(A2)	[Kundu (1998b)]
	• 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				
gp160(813–822)	gp41(818–827)	SLLNATDIAV	HIV-1 infection	human(A2)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes, including this epitope				
gp160(813–822)	Env(814–823 Clade B)	SLLNATDIAV	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
	• 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 • 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(814–822)	gp41(815–823 LAI)	LLNATDIAV	MN rec gp160	human(A2)	[Dupuis (1995)]
	• 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)	[Kmieciak (1998)]
	• Increased CTL response to cells expressing a VV construct ΔV3 mutant compared with a full-length Env gene product				
gp160(827–841)	gp41(834–848 IIIB)	DRVIEVVQGAYRAIR	HIV exposure	human( )	[Pinto (1995)]
	• 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)	[Clerici (1991)]
	• Helper and cytotoxic T cells can be stimulated by this peptide (Th4)				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(827–841)	gp41(834–848 IIIB)	DRVIEVVQGAYRAIR	vaccinia IIIB gp160	murine(H-$2^{d,p,u,q}$)	[Shirai (1992)]
• In a murine system multiple class I molecules can present to CTL					
gp160(827–841)	gp41(834–848 IIIB)	DRVIEVVQGAYRAIR	rec vaccinia gp160	murine(H-$2^{d,p,u,q}$)	[Shirai (1996)]
• Multiple murine MHC can cross-present this epitope (HP53), and P18 RIQRGPGRAFVTIGK, to specific CTL					
gp160(828–836)	gp41(829–837 LAI)	RVIEVLQRA	MN rec gp160	human(A2)	[Dupuis (1995)]
• CTL from HLA-A2 positive subject react with this peptide					
gp160(828–836)	Env(829–837 Clade B)	RVIEVLQRA	HIV-1 MN rgp160	human(A2.1)	[Kundu (1998a)]
• 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					
gp160(830–854)	gp41(831–853)	IEVVQGAYRAIIRHIPR-RIRQGLERI	HIV-1 infection	human( )	[Price (1995)]
• Study of cytokines released by HIV-1 specific activated CTL					
gp160(835–843)	Env(834–842 SF2)	RAYRAILHI	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]
• 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)	YRAIRHIPRRIRQGLER-ILL	HIV infection	human( )	[Lieberman (1995)]
• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(837–856)	gp120(844–863 SF2)	YRAIRHIPRRIRQGLER-ILL	HIV infection	human( )	[Lieberman (1997a)]
	• 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)	YRAIRHIPRRIRQGLER-ILL	HIV-1 infection	human(B35)	[Shankar (1996)]
gp160(837–856)	gp41(844–863 HXB2)	YRAIRHIPRRIRQGLER-ILL	HIV infection	human(B8)	[Lieberman (1992)]
	• CTL epitope defined by T cell line and peptide mapping				
gp160(843–851)	gp41(848–856 LAI)	IPRRIRQGL		human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
gp160(843–851)	gp41(848–856 LAI)	IPRRIRQGL		human(B7)	[Brander & Walker(1995)]
	• 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)	[Soudeyns (1999)]
	• 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: `--T------` and `--T-----F`, which abrogated the CT response *in vitro*, and also `----L---` and `-------D-` which gave diminished responses				
gp160(843–851)	gp41(848–856 LAI)	IPRRIRQGL	HIV-1 infection	human(B7)	[Cao (1997)]
	• 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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(843–851)	gp41(848–856 Clade B)	IPRRIRQGL	HIV-1 infection	human(B7)	[Wilson (1998b)]
	• 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)	[Hay (1999)]
	• 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: `----T----`; the other forms detected were `--------F, -----L--F, V-------F` and they could elicit a CTL response although the response to `-----L--F` was reduced • A second rapid progressor had a detectable CTL response exclusively to this epitope				
gp160(845–856)	gp41(852–863 HXB2)	RRIRQGLERILL	HIV-1 infection	human(A30, B8)	[Lieberman (1992)]
	• CTL epitope defined by T cell line and peptide mapping				
gp160(845–856)	gp41(852–863 LAI)	RRIRQGLERILL	HIV-1 infection	human(B7)	[Shankar (1996)]