Total Assessment of HIV-Specific CTL Responses: Epitope Clustering, Processing Preferences, and the Impact of HIV Sequence Heterogeneity

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The HIV Immunology database at the Los Alamos National Laboratory has collected data on HIV-specific cellular immune responses for over 8 years now and the list of targeted regions within the HIV protein sequences has been growing steadily. These compiled data and our own studies using comprehensive sets of overlapping peptides indicate that almost all parts of the viral protein sequence can be targeted by virus-specific T cells, especially CTL [Addo2003, Frahm2003]. HIV is the pathogen that has been characterized most extensively in terms of T-cell epitope distribution and the well-defined epitope landscape of HIV has allowed for a number of studies beyond assessing CTL activity in relation to HIV disease progression [Brander2002].

TARGETS OF HIV-SPECIFIC CTL

Whilst in the early years of HIV CTL epitope mapping, attention was focused on structural proteins, more recent studies have included regulatory and accessory proteins as well [Tomiyama1999a, Altfeld2001a, van Baalen1997, Addo2001, Addo2002b]. High-throughput assays such as intracellular cytokine staining (ICS), and the Elispot assay are now routinely used to assess genome wide immune responses to HIV [Edwards2002, Frahm2003, Betts01, Addo2003, Novitsky2001, Novitsky2002]. This is especially true for the characterization of CD8+ CTL responses, but newer data also include the identification of Th cell activity. Studies from several labs, including ours, using overlapping peptide sets spanning the entire HIV protein sequence have now shown that at least 90% of these peptides can be targeted by HIV-specific CTL, indicating that all viral proteins undergo appropriate antigen processing *in vivo* and that epitopes from all HIV proteins can be effectively presented to CD8 T cells [Addo2003, Frahm2003]. However, there are specific patterns among these responses which will impact HIV vaccine design and which can potentially help to address more fundamental aspects of antigen processing, antigen presentation and T-cell repertoire development [Yusim2002].

Of special interest for these extended studies, but also for questions of CTL escape and (sub-unit)-vaccine development, is the identification of optimally defined CTL epitopes. Since 1995, largely through the voluntary contributions of unpublished data from many laboratories, regularly updated lists of "optimal CTL epitopes" have been made accessible through the Los Alamos National Laboratory's HIV database [Brander1995]. This year's update again adds a number of new epitopes whilst some others were removed as they were erroneously included before (mainly some HLA-A*0201 restricted epitopes from our own lab which were based on epitope prediction only and which were not defined with the same stringency as the other epitopes in this list). While the earliest reports clearly focused on alleles common in individuals infected early in the US epidemic, more attention is now given to individuals of non-Caucasian descent [Frahm2003, Sabbaj2003]. In addition, epitopes from non-clade B infections are increasingly identified [Novitsky2002, Novitsky2003, Bond2001, Fukada2002, Lynch1998, Sriwanthana2001, Goulder2001]. The identification of these epitopes provides valuable information for vaccine development in non-Caucasians and non-clade B infection.

In addition, these new epitopes, when characterized in full detail, can provide important insights into HLA binding motifs for these less well characterized alleles; again facilitating the design of a potential HIV vaccine. To support this work, the HIV database offers additional tools such as

EPILIGN:
http://hiv-web.lanl.gov/content/hiv-db/EPILIGN/EPI.html,
PeptGen:
http://hiv-web.lanl.gov/content/hiv-db/PEPTGEN/
PeptGenSubmitForm.html
MotifScan:
http://hiv-web.lanl.gov/content/hiv-db/MOTIFSCAN/MotifScanner.html
as well as valuable links to other sites, including the
SYFPEITHI HLA binding motifs database:
http://www.syfpeithi.de/
and others:
http://hiv.basic.nwu.edu/HLA,
http://bimas.dcrt.nih.gov/cgi-bin/molbio/ken_parker_comboform,

http://www.jenner.ac.uk/JenPep/

Clearly, these databases and prediction softwares can profit from each other and facilitate the future identification of T-cell targets in HIV and other infections.

IMMUNODOMINANT REGIONS IN HIV PROTEIN SEQUENCES

As mentioned above, the described optimal CTL epitopes are not evenly distributed over the entire viral genome. Rather, there are regions where many epitopes overlap. This phenomenon has been described as early as 1993 and various explanations have been put forward [Goulder2000a, Buseyne1993]. Two factors that seem to significantly contribute to this epitope clustering appear to be viral sequence heterogeneity and processing preferences [Yusim2002].

Sequence heterogeneity affects all HIV proteins, albeit to variable degrees. Relatively conserved regions in Gag and Nef have been identified as immunodominant regions in a study of more than 150 individuals of different ethnicities [Frahm2003]. Independently of the HLA background, these clade B infected individuals made strong responses to the peptides spanning these regions. When comparing the sequence heterogeneity in published clade B sequences, these data also show that peptides with low sequence entropy (more conserved) are targeted more frequently than epitopes with higher entropy. It is likely that these differences are due to the fact that the average phylogenetic distance of the test reagent (consensus B sequence) to an individual‘s autologous viral sequence is larger in higher variable regions than in more conserved ones and thus, responses against the less conserved peptides are not detected due to differences between test reagent and inoculum sequence [Yusim2002, Gaschen2002].

In addition to sequence incompatibility between test reagent and autologous virus, certain regions of the HIV protein sequence may not be processed and presented very effectively. Although 86% of our overlapping peptide sets used in the study above were targeted by at least one individual in the cohort of 150 people, there are still some relatively conserved peptides that do not seem to induce a detectable CTL response in natural HIV infection [Frahm2003]. These peptides may lie within stretches of viral proteins that are relatively resistant to proteasomal digestions or may lack adequate “Transporter associated with Antigen Processing” (TAP) binding motifs [Brander2002, Yusim2002]. The HIV Immunology database provides valuable web links to software where sequences of choice can be analyzed for proteasomal processing preferences (NetChop by C. Kesmir *et al*., http://www.cbs.dtu.dk/services/NetChop/). Recent work by Yusim *et al*., demonstrates the accuracy and predictive potential of this algorithm and its usefulness in identifying CTL epitopes [Yusim2002].

Together, these studies indicate that CTL epitope clustering may reflect the biased detection of these responses in rather conserved regions and that processing preferences may play an important role in providing processed antigen. In addition, sequence variability may not only affect CTL recognition but could also have an effect on processing of viral proteins [Yellen-Shaw1997]. Although we have been unable to show such an effect for the flanking regions of the immunodominant, HLA-A*0201 restricted CTL epitope SL9 (SLYNTVATL) in HIV Gag p17, other studies outside the HIV field suggest that escape from processing may be an effective means of immune evasion [Yellen-Shaw1997, Kuckelkorn2002, Gileadi1999, Brander1999]. These studies also highlight the importance of defining T-cell targets in maximal detail, so that prediction algorithm such as NetChop and binding motif algorithms can be optimized by a precisely characterized training set of defined epitopes. In addition, in order to discriminate between processing escape and escape from T-cell receptor recognition or HLA binding, the boundaries of targeted epitopes need to be optimally determined. The present listing is designed to provide these data specifically for HIV derived epitopes and we therefore still separate CTL epitopes in a list of optimally and suboptimally defined epitopes. We hope that this discrimination continues to provide support for the HIV immunologists and laboratories involved in antigen processing and presentation, who want to take advantage of the exceptionally well defined epitope landscape of HIV.

As every year, we would like to express our gratitude to the large number of researchers in the field who continuously contribute to this database. We very much welcome any criticism, comments and additions to this list since we are sure that some epitopes will unintentionally escape our attention, despite close monitoring of the literature. Also, pertinent information, such as resources for single HLA allele expressing cell lines, HLA subtype information and new technologies for CTL epitope mapping could be listed or referenced in this list, providing additional help to problems encountered by investigators.

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Table 1 Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*0101 (A1)	gp160	787–795	RRGWEVLKY	[Cao2002]
A*0201 (A2)			2 6 C	[Falk1991, Barouch1995]
		1° anchor	**L** **L**	
			M **V**	
		2° anchor	V	
A*0201 (A2)	p17	77–85	SLYNTVATL	[Johnson1991, Parker1992, Parker1994]
A*0201 (A2)	p1	1–10	FLGKIWPSYK	[Yu2002b]
A*0201 (A2)	RT	33–41	ALVEICTEM	[Haas1998, Haas1999]
A*0201 (A2)	RT	179–187	VIYQYMDDL	[Harrer1996a]
A*0201 (A2)	RT	309–317	ILKEPVHGV	[Walker1989, Tsomides1991]
A*0201 (A2)	Vpr	59–67	AIIRILQQL	[Altfeld2001a, Altfeld2001b]
A*0201 (A2)	gp160	311–320	RGPGRAFVTI	[Alexander-Miller1996]
A*0201 (A2)	gp160	813–822	SLLNATDIAV	[Dupuis1995]
A*0201 (A2)	Nef	136–145	PLTFGWCYKL	[Haas1996, Maier1999]
A*0201 (A2)	Nef	180–189	VLEWRFDSRL	[Haas1996, Maier1999]
A*0202 (A2)			2 C	[Barouch1995]
			L **L**	
			V	
A*0202 (A2)	p17	77–85	SLYNTVATL	[Goulder1999]
A*0205 (A2)	p17	77–85	SLYNTVATL	[Goulder1999]
A*0205 (A2)	gp41	335–343	RIRQGLERA	[Sabbaj2003]
A*0207 (A2)	p24	164–172	YVDRFYKTL	[Currier2002]
A*03 (A3)	RT	73–82	KLVDFRELNK	[Yu2002a]
A*03 (A3)	RT	356–366	RMRGAHTNDVK	[Yu2002a]
A*03 (A3)	Integrase	179–188	AVFIHNFKRK	[Yu2002a]
A*03 (A3)	Vif	28–36	HMYISKKAK	[Yu2002a]
A*03 (A3)	Vif	158–168	KTKPPLPSVKK	[Yu2002a]
A*03 (A3)	Rev	57–66	ERILSTYLGR	[Addo2002a, Yu2002a]
A*03 (A3)	Nef	84–92	AVDLSHFLK	[Yu2002a]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*0301 (A3)			2 C **L K** **V Y** **M F**	[DiBrino1993, Rammensee1995]
A*0301 (A3)	p17	18–26	KIRLRPGGK	[Harrer1996b]
A*0301 (A3)	p17	20–28	RLRPGGKKK	[Goulder1997a, Culmann1999, Lewinsohn1999b, Wilkes1999b]
A*0301 (A3)	p17	20–29	RLRPGGKKKY	[Goulder2000b]
A*0301 (A3)	RT	33–43	ALVEICTEMEK	[Haas1998, Haas1999]
A*0301 (A3)	RT	93–101	GIPHPAGLK	[Yu2002a]
A*0301 (A3)	RT	158–166	AIFQSSMTK	[Threlkeld1997]
A*0301 (A3)	RT	269–277	QIYPGIKVR	[Yu2002a]
A*0301 (A3)	Vif	17–26	RIRTWKSLVK	[Altfeld2001a, Yu2002a]
A*0301 (A3)	gp160	37–46	TVYYGVPVWK	[Johnson1994a]
A*0301 (A3)	gp160	770–780	RLRDLLLIVTR	[Takahashi1991]
A*0301 (A3)	Nef	73–82	QVPLRPMTYK	[Koenig1990, Culmann1991]
A*1101 (A11)			2 C **K** V I F Y	[Zhang1993, Rammensee1995]
A*1101 (A11)	p17	84–92	TLYCVHQRI	[Harrer1998]
A*1101 (A11)	p24	217–227	ACQGVGGPGHK	[Sipsas1997]
A*1101 (A11)	RT	158–166	AIFQSSMTK	[Johnson1994b, Zhang1993, Threlkeld1997]
A*1101 (A11)	RT	341–350	IYQEPFKNLK	[Culmann1999]
A*1101 (A11)	RNase	80–88	QIIEQLIKK	[Fukada1999]
A*1101 (A11)	Integrase	179–188	AVFIHNFKRK	[Fukada1999]
A*1101 (A11)	gp160	199–207	SVITQACPK	[Fukada1999]
A*1101 (A11)	Nef	73–82	QVPLRPMTYK	[Buseyne1999]
A*1101 (A11)	Nef	75–82	PLRPMTYK	[Culmann1991]
A*1101 (A11)	Nef	84–92	AVDLSHFLK	[Culmann1991]
A*23 (A23)	gp41	74–82	RYLKDQQLL	[Cao2003]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*2402 (A24)			2 C **Y** **I** **L** **F**	[Maier1994]
A*2402 (A24)	p17	28–36	KYKLKHIVW	[Ikeda-Moore1998, Lewinsohn1999a]
A*2402 (A24)	p24	162–172	RDYVDRFFKTL	[Dorrell1999, Rowland-Jones1999]
A*2402 (A24)	gp160	52–61	LFCASDAKAY	[Lieberman1992, Shankar1996]
A*2402 (A24)	gp160	585–593	RYLKDQQLL	[Dai1992]
A*2402 (A24)	Nef	134–141	RYPLTFGW	[Goulder1997b, Ikeda-Moore1998]
A*2501 (A25)	p24	13–23	QAISPRTLNAW	[Kurane1999]
A*2501 (A25)	p24	71–80	ETINEEAAEW	[Klenerman1996, van Baalen1996]
A*2601 (A26)			12 6 C **V** **Y** **T** **F** **I** **L** **F** D I E L V	[Dumrese1998]
A*2601 (A26)	p24	35–43	EVIPMFSAL	[Goulder1996a]
A*2601 (A26)	Pol	604–612	ETKLGKAGY	[Sabbaj2003]
A*2902 (A29)	gp160	209–217	SFEPIPIHY	[Altfeld2000a]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*3002 (A30)			12 C **Y** **Y** **F** **L** **V** R	[Rammensee1999]
A*3002 (A30)	p17	76–86	RSLYNTVATLY	[Goulder2001]
A*3002 (A30)	RT	173–181	KQNPDIVIY	[Goulder2001]
A*3002 (A30)	RT	263–271	KLNWASQIY	[Goulder2001]
A*3002 (A30)	RT	356–365	RMRGAHTNDV	[Sabbaj2003]
A*3002 (A30)	Integrase	219–227	KIQNFRVYY	[Sabbaj2003, Addo2002c]
A*3002 (A30)	gp160	704–712	IVNRNRQGY	[Goulder2001]
A*3002 (A30)	gp120	310–318	HIGPGRAFY	[Sabbaj2003]
A*3002 (A30)	gp41	283–291	KYCWNLLQY	[Goulder2001]
A*3101 (A31)			2 C **R** L V Y F	[Falk1994, Rammensee1999]
A*3101 (A31)	gp160	770–780	RLRDLLLIVTR	[Safrit1994a, Safrit1994b]
A*3201 (A32)	RT	392–401	PIQKETWETW	[Harrer1996b]
A*3201 (A32)	gp160	419–427	RIKQIINMW	[Harrer1996b]
A*3303 (A33)	gp41	187–196	VFAVLSIVNR	[Hossain2001]
A*3303 (A33)	gp41	320–327	EVAQRAYR	[Hossain2001]
A*3303 (A33)	Vpu	29–37	EYRKILRQR	[Addo2002b]
A*3303 (A33)	Nef	133–141	TRYPLTFGW	[Cao2002]
A*6801 (A68)	Tat	39–49	ITKGLGISYGR	[Oxenius2002]
A*6802 (A68)	Protease	3–11	ITLWQRPLV	[Rowland-Jones1999]
A*6802 (A68)	Protease	30–38	DTVLEEWNL	[Rowland-Jones1999]
A*6802 (A68)	gp160	777–785	IVTRIVELL	[Wilkes1999a]
A*7401 (A19)	Protease	3–11	ITLWQRPLV	[Rowland-Jones1999]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*07 (B7)	p24	84–92	HPVHAGPIA	[Yu2002a]
B*0702 (B7)			123 C **P** **L** A R R K	[Englehard1993, Rammensee1999]
B*0702 (B7)	p24	16–24	SPRTLNAWV	[Lewinsohn1999a]
B*0702 (B7)	p24	48–56	TPQDLNTML	[Wilson1999a, Wilkes1999c, Jin2000, Wilson1997]
B*0702 (B7)	p24	223–231	GPGHKARVL	[Goulder1999]
B*0702 (B7)	Vpr	34–42	FPRIWLHGL	[Altfeld2001a]
B*0702 (B7)	Vif	48–57	HPRVSSEVHI	[Altfeld2001a]
B*0702 (B7)	gp160	298–307	RPNNNTRKSI	[Safrit1994b]
B*0702 (B7)	gp160	843–851	IPRRIRQGL	[Wilkes1999b]
B*0702 (B7)	Nef	68–77	FPVTPQVPLR	[Haas1996, Maier1999]
B*0702 (B7)	Nef	68–76	FPVTPQVPL	[Bauer1997, Frahm2002]
B*0702 (B7)	Nef	71–79	TPQVPLRPM	[Goulder1999]
B*0702 (B7)	Nef	77–85	RPMTYKAAL	[Bauer1997]
B*0702 (B7)	Nef	106–115	RQDILDLWIY	[Goulder1999]
B*0702 (B7)	Nef	128–137	TPGPGVRYPL	[Culmann-Penciolelli1994, Haas1996]
B*0801 (B8)			23 5 C **K** **K** **L** **R** PR L	[Hill1992, Sutton1993, DiBrino1994a]
B*0801 (B8)	p17	24–32	GGKKKYKLK	[Rowland-Jones1993, Goulder1997d]
B*0801 (B8)	p17	74–82	ELRSLYNTV	[Goulder1997d]
B*0801 (B8)	p24	128–135	EIYKRWII	[Sutton1993, Goulder1997d]
B*0801 (B8)	p24	197–205	DCKTILKAL	[Sutton1993]
B*0801 (B8)	RT	18–26	GPKVKQWPL	[Walker1989, Sutton1993]
B*0801 (B8)	gp160	2–10	RVKEKYQHL	[Sipsas1997]
B*0801 (B8)	gp160	586–593	YLKDQQLL	[Johnson1992, Shankar1996]
B*0801 (B8)	Nef	13–20	WPTVRERM	[Goulder1997d]
B*0801 (B8)	Nef	90–97	FLKEKGGL	[Culmann-Penciolelli1994, Price1997]
B*14 (B14)	p15	42–50	CRAPRKKGC	[Yu2002b]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*1402 (B14)			23 5 C **R R L** **K H** L Y F	[DiBrino1994b]
B*1402 (B14)	p24	166–174	DRFYKTLRA	[Harrer1996b]
B*1402 (B14)	gp160	584–592	ERYLKDQQL	[Johnson1992]
B*1501 (B62)			2 C **Q Y** **L F** **M**	[Barber1997] [Barber1997] [Barber1997]
B*1501 (B62)	p24	137–145	GLNKIVRMY	[Johnson1991, Goulder1999]
B*1501 (B62)	RT	260–271	LVGKLNWASQIY	[Johnson1999]
B*1501 (B62)	RT	309–318	ILKEPVHGVY	[Johnson1991, Johnson1999]
B*1501 (B62)	Nef	19–27	RMRRAEPAA	[Cao2002]
B*1501 (B62)	Nef	117–127	TQGYFPDWQNY	[Culmann1999]
B*1503 (B72)	Integrase	263–271	RKAKIIRDY	[Cao2003]
B*1503 (B72)	Tat	38–47	FQTKGLGISY	[Novitsky2001]
B*1503 (B72)	Pol	651–660	VTDSQYALGI	[Sabbaj2003]
B*1503 (B72)	Nef	183–191	WRFDSRLAF	[Cao2002]
B*1516 (B63)			2 9 **T Y** **S I** **V** **F**	[Barber1997, Seeger1998]
B*1516 (B63)	gp160	375–383	SFNCGGEFF	[Wilson1997, Wilson1999a]
B*1801 (B18)	p24	161–170	FRDYVDRFYK	[Ogg1998]
B*1801 (B18)	Vif	102–111	LADQLIHLHY	[Altfeld2001a]
B*1801 (B18)	Nef	135–143	YPLTFGWCY	[Culmann1991, Culmann-Penciolelli1994]
B*2703 (B27)	p24	131–140	RRWIQLGLQK	[Rowland-Jones1998, Rowland-Jones1999]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*2705 (B27)			12 C **R** **L** **F** K K R R G I A	[Jardetzky1991, Rammensee1995]
B*2705 (B27)	p17	19–27	IRLRPGGKK	[McKinney1999, Lewinsohn1999a]
B*2705 (B27)	p24	131–140	KRWIILGLNK	[Nixon1988, Buseyne1993, Goulder1997c]
B*2705 (B27)	gp160	786–795	GRRGWEALKY	[Lieberman1992, Lieberman1999]
B*2705 (B27)	Nef	105–114	RRQDILDLWI	[Goulder1997a]
B*3501 (B35)			2 C **P** **Y** A F V M S L I	[Hill1992, Rammensee1999]
B*3501 (B35)	p17	36–44	WASRELERF	[Goulder1997b]
B*3501 (B35)	p17	124–132	NSSKVSQNY	[Rowland-Jones1995]
B*3501 (B35)	p24	122–130	PPIPVGDIY	[Rowland-Jones1995]
B*3501 (B35)	p24	122–130	NPVPVGNIY	[Rowland-Jones1995]
B*3501 (B35)	RT	107–115	TVLDVGDAY	[Wilkes1999b, Wilson1999b]
B*3501 (B35)	RT	118–127	VPLDEDFRKY	[Sipsas1997, Shiga1996]
B*3501 (B35)	RT	175–183	NPDIVIYQY	[Sipsas1997, Shiga1996]
B*3501 (B35)	RT	175–183	HPDIVIYQY	[Rowland-Jones1995]
B*3501 (B35)	gp160	42–52	VPVWKEATTTL	[Wilkes1999b]
B*3501 (B35)	gp160	78–86	DPNPQEVVL	[Shiga1996]
B*3501 (B35)	gp160	606–614	TAVPWNASW	[Johnson1994a]
B*3501 (B35)	Nef	74–81	VPLRPMTY	[Culmann1991, Culmann-Penciolelli1994]
B*3701 (B37)			2 C **D** **F** **E** **M** **L** **I**	[Falk1993]
B*3701 (B37)	Nef	120–128	YFPDWQNYT	[Culmann1991, Culmann1999]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*3801 (B38)	gp160	104–112	MHEDIISLW	[Cao2002]
B*3901 (B39)			2 C **R L** **H**	[Falk1995a]
B*3901 (B39)	p24	61–69	GHQAAMQML	[Kurane1999]
B*4001 (B60)			2 C **E L**	[Falk1995b]
B*4001 (B60)	p17	92–101	IEIKDTKEAL	[Altfeld2000b]
B*4001 (B60)	p24	44–52	SEGATPQDL	[Altfeld2000b]
B*4001 (B60)	p6	33–41	KELYPLTSL	[Yu2002b]
B*4001 (B60)	RT	202–210	IEELRQHLL	[Altfeld2000b]
B*4001 (B60)	gp160	805–814	QELKNSAVSL	[Altfeld2000b]
B*4001 (B60)	Nef	92–100	KEKGGLEGL	[Altfeld2000b]
B*4002 (B61)	p17	11–19	GELDRWEKI	[Sabbaj2003]
B*4002 (B61)	p24	70–78	KETINEEAA	[Sabbaj2003]
B*4002 (B61)	p24	78–86	AEWDRVHPV	[Sabbaj2003]
B*4002 (B61)	Nef	92–100	KEKGGLEGL	[Sabbaj2003, Altfeld2000b]
B*4002 (B61)	p15	64–71	TERQANFL	[Sabbaj2003]
B*42 (B42)	Integrase	260–268	VPRRKAKII	[Kiepiela2002]
B*4201 (B42)	p24	48–56	TPQDLNTML	[Goulder2000a]
B*4201 (B42)	RT	271–279	YPGIKVRQL	[Wilkes1999b]
B*4201 (B42)	Nef	128–137	TPGPGVRYPL	[Goulder1999]
B*4402 (B44)			2 C **E F** **Y**	[Rammensee1999]
B*4402 (B44)	p24	162–172	RDYVDRFYKTL	[Ogg1998]
B*4402 (B44)	p24	174–184	AEQASQDVKNW	[Lewinsohn1999a]
B*4402 (B44)	gp160	31–40	AENLWVTVYY	[Borrow1997]
B*4415 (B12)	p24	28–36	EEKAFSPEV	[Bird2002]
B*51 (B51)	Vpr	29–37	EAVRHFPRI	[Cao2003]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*5101 (B51)			2 C **A F** **P I** **G**	[Falk1995a]
B*5101 (B51)	RT	42–50	EKEGKISKI	[Haas1998, Haas1999]
B*5101 (B51)	RT	128–135	TAFTIPSI	[Sipsas1997]
B*5101 (B51)	gp160	416–424	LPCRIKQII	[Tomiyama1999b]
B*5201 (B52)			2 C **I** **V** Q	[Rammensee1999]
B*5201 (B52)	p24	143–150	RMYSPTSI	[Wilkes1999b, Wilson1997]
B*53 (B53)	Nef	135–143	YPLTFGWCF	[Kiepiela2002]
B*5301 (B53)			2 C **P L**	[Hill1992]
B*5301 (B53)	p24	48–56	TPYDINQML	[Gotch1993]
B*5301 (B53)	p24	176–184	QASQEVKNW	[Buseyne1996, Buseyne1997, Buseyne1999]
B*5301 (B53)	Tat	2–11	EPVDPRLEPW	[Addo2001]
B*5301 (B53)	Nef	135–143	YPLTFGWCY	[Sabbaj2003]
B*5501 (B55)			2 C **P** A	[Barber1995]
B*5501 (B55)	gp160	42–51	VPVWKEATTT	[Shankar1996, Lieberman1999]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*5701 (B57)			12 C **A F** **T W** **S** K Y	[Barber1997]
B*5701 (B57)	p24	15–23	ISPRTLNAW	[Johnson1991, Goulder1996b]
B*5701 (B57)	p24	30–40	KAFSPEVIPMF	[Goulder1996b]
B*5701 (B57)	p24	108–118	TSTLQEQIGWF	[Goulder1996b]
B*5701 (B57)	p24	176–184	QASQEVKNW	[Goulder1996b]
B*5701 (B57)	RT	244–252	IVLPEKDSW	[van der Burg1997, Hay1999]
B*5701 (B57)	Integrase	173–181	KTAVQMAVF	[Goulder1996b, Hay1999]
B*5701 (B57)	Vpr	30–38	AVRHFPRIW	[Altfeld2001a]
B*5701 (B57)	Vif	31–39	ISKKAKGWF	[Altfeld2001a]
B*5701 (B57)	Rev	14–23	KAVRLIKFLY	[Addo2001]
B*5701 (B57)	Nef	116–125	HTQGYFPDWQ	[Culmann1991]
B*5701 (B57)	Nef	120–128	YFPDWQNYT	[Culmann1991]
B57 (B57)	Nef	116–124	HTQGYFPDW	[Draenert2002]
B*5703 (B57)	p24	30–37	KAFSPEVI	[Goulder2000b]
B*5703 (B57)	p24	30–40	KAFSPEVIPMF	[Goulder2000b]
B*5801 (B58)			12 C **A F** **T W** **S** K V I	[Barber1997, Falk1995b]
B*5801 (B58)	p24	108–117	TSTVEEQQIW	[Bertoletti1998]
B*5801 (B58)	p24	108–117	TSTLQEQIGW	[Goulder1996b]
B*5801 (B58)	RT	375–383	IAMESIVIW	[Kiepiela2002]
B*5801 (B58)	Rev	14–23	KAVRLIKFLY	[Addo2001]
B*81 (B81)	Pol	715–723	LFLDGIDKA	[Addo2002a]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*8101 (B81)	p24	48–56	TPQDLNTML	[Goulder2000a]
B*8101 (B81)	Vpr	34–42	FPRIWLHGL	[Altfeld2001a]
Cw*0102 (Cw1)			23 C **A** **L** **L** P	[Barber1997]
Cw*0102 (Cw1)	p24	36–43	VIPMFSAL	[Goulder1997b]
Cw*0304 (Cw10)	gp41	46–54	RAIEAQQHL	[Currier2002, Trocha2002]
Cw*0401 (Cw4)			2 6 C **Y** **L** **P** **F** **F** **M** V I L	[Falk1994]
Cw*0401 (Cw4)	gp160	375–383	SFNCGGEFF	[Wilson1997, Johnson1993]
Cw*0501 (Cw5)	Rev	67–75	SAEPVPLQL	[Addo2001]
Cw*07 (Cw7)	Nef	105–115	KRQEILDLWVY	[Kiepiela2002]
Cw*07 (Cw7)	Nef	105–115	RRQDILDLWIY	[Yu2002a]
Cw*0802 (Cw8)	p24	48–56	TPQDLNTML	[Goulder2000a]
Cw*0802 (Cw8)	Nef	83–91	AAVDLSHFL	[Cao2003]
Cw*12 (Cw12)	Tat	30–37	CCFHCQVC	[Cao2003, Nixon1999]
Cw*15 (Cw15)	gp41	46–54	RAIEAQQHL	[Trocha2002]

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