The Identification of Optimal HIV-Derived CTL Epitopes in Diverse Populations Using HIV Clade-Specific Consensus

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Introduction

Primarily due to the use of high throughput approaches such as Elispot and intracellular cytokine staining (ICS), which allow for the rapid and comprehensive assessment of CTL activity *ex vivo* and after *in vitro* stimulation of PBMC, more than 25 new optimally defined HIV epitopes have been reported over the last year. Using overlapping peptide sets spanning the entire HIV protein sequences, many laboratories are now able to assess anti-HIV specific CTL responses more comprehensively than was possible in the past. Not surprisingly, this and more extensive focus of studies on individuals from ethnicities that have traditionally been understudied, have allowed the identification of epitopes in all HIV proteins presented by HLA alleles different from the ones that dominate in Caucasian populations. These findings are of highest interest for the design of HIV vaccine candidates to be effective in populations hardest hit by the HIV epidemic.

Use of autologous and consensus HIV sequences

An increasing number of reports have highlighted the limitations that are posed by using a defined source of antigen representing a single viral isolate, be it recombinant vaccinia virus expressing isolate specific HIV proteins or peptide sequences based on well characterized viral isolates such as HXB2 or SF2. It is now widely recognized that minor epitope sequence variation can profoundly alter the recognition of CTL targets, and thus the need for more suitable sources for viral antigen (and viral sequences) has become evident. The efforts of researchers involved with the HIV Molecular Immunology Database (http://hiv-web.lanl.gov/immunology/index.html) have provided new consensus sequences that are designed to be more reflective of currently circulating HIV sequences and that serve as the best available, albeit not ideal, reference sequence for synthesizing overlapping peptide sets. These new consensus sequences established for HIV clade B and C are generally closer to autologous HIV sequences in a given population than are the autologous sequences to a specific viral isolate. Thus, these updated consensus sequences, which are accessible at the HIV sequence database (http://hiv-web.lanl.gov/seq-db.html), represent a good compromise between using an isolate specific reference sequence and synthesizing the impossibly large number of peptides required to test all individuals in a specific study with their autologous sequence. However, despite the apparent usefulness of these consensus sequences as the basis for synthetic peptide sets, this sequence does not necessarily represent a replication competent viral sequence and may in certain instances be further removed from the autologous sequences than a selected viral isolate's sequence. Work currently in progress (Altfeld *et al*., Draenert *et al*., unpublished) addresses these issues to establish the overall advantage of these consensus sequences for the purposes of T cell epitope definition, and of using autologous sequence derived peptides. In our hands, these consensus sequences have proven very useful (Frahm *et al*., unpublished) as even after studying 40 patients only, more than 60% of the peptides in our 410 peptide set are targeted by at least one HIV clade B infected individual.

All HIV proteins induce CTL responses

Rapid and relatively inexpensive assays such as the ubiquitous Elispot have largely facilitated comprehensive analyses for CTL and T-helper cell responses against all HIV proteins. These analyses show that all HIV proteins (including HIV Vpu, M. Addo *et al*., in press and N. Frahm *et al*., unpublished) can be targeted by CD8+ CTL and thus may contribute to control of HIV replication in infected individuals. Comprehensive analyses covering the entire genome will undoubtedly add to our appreciation of HIV specific T cell immunity, both CD4 and CD8 T cell mediated, and identify new candidates for vaccine development. In addition, identification of these additional responses may prove instructive for understanding the kinetics of CTL response induction, antigen processing and immunodominance. However, as described above, responses may generally be underestimated since non-autologous viral sequences are being used for peptide synthesis. Proteins, such as Tat, that have the greatest variability and therefore divergence from the consensus sequence, may be

particularly underrepresented. Thus, although very expensive and labor intensive, at least in some instances responses need to be assessed using autologous sequences to estimate the degree of potential underestimation resulting from use of consensus sequence. These studies are currently underway (Altfeld *et al*., unpublished). Sharing resources as well as exchanging immunological and virological data on a platform such as the present HIV Molecular Immunology database will help to provide this required information.

Inclusion of Non-Caucasian ethnicities

Many investigators have started to shift their focus from European and US Caucasians populations to those worst afflicted by the HIV epidemic and to sites where a vaccine could have the most impact in fighting the further spread of HIV. Also, significant funding has been made available by national and international agencies and foundations that foster investigations in HIV infected individuals of non-Caucasian descent. These efforts, including virological and host genetic analyses, will lead to an extensive number of newly defined CTL epitopes in the next few years as traditionally understudied ethnicities are included in or dominate these studies. Thereby, the identification of epitopes presented by HLA class I alleles dominant in non-Caucasian populations will provide important information on epitope clustering, HLA class I allele specific binding motifs, and sequence variation in the targeted region. Along with more detailed HLA subtype information, this will hopefully lead to the identification of potential vaccine candidates that are tailored more to the needs of the ethnicities most affected by the HIV epidemic.

Viral evolution as a result of immune pressure

Recent studies in animal models of HIV infection and in human mother-child transmission of HIV have highlighted the possible consequences of strong immune pressure exerted on the virus. For instance, very early in acute SIV infection of macaques, a strongly targeted SIV Tat epitope shows rapid escape from these CTL by sequence variability in the encoding region of Tat [Allen et al, Nature 2000]. Escape at a single Gag epitope in chronic infection heralded loss of control of viremia and progression to AIDS as had been shown earlier in HIV infection [Barouch et al, Nature 2002, Goulder et al, Nat Med 1997]. Not only do these studies underline the existence of qualitative differences between CTL of different specificities, but raise questions regarding the actual relevance of a broad CTL response. The breadth of the CTL response has been hypothesized to play a critical role in control of viremia [Carrington et al, Science 1999], but the more recent studies emphasise the importance of the quality of the response as opposed to the number of epitopes targeted.

CTL escape may similarly play an important role at the time of transmission and in evolution of the virus over the course of the epidemic, For HIV transmission from mother to child, transmission of CTL escape variants to the infant has been demonstrated [Goulder et al, Nature, 2001]. Importantly, since children share at least 50% of the HLA genes with their mothers, a viral escape variant may deprive the infant of the possibility of developing this response, potentially contributing to the faster progression HIV infection seen in infants compared to adults. If taken to a population level, the accumulation of CTL escape variants in a genetically homogeneous population may gradually lead to the loss of CTL epitopes in the HIV sequence. Such a phenomenon might not be observed in a genetically heterogeneous population, as the virus would have a chance to intermittently passage through different genetic backgrounds, assuming that escape variants were to revert back in the absence of the evolutionary pressure that originally drove their selection. Whether such broad reversion in fact occurs remains to be determined. Similarly, escape variants may or may not possess reduced viral fitness. It could be hypothesised that the gradual accumulation of CTL escape mutants over time may reduce the pathogeneity of the virus, since such viruses would be replicatively less fit. Equally, it could be hypothesised that loss of the critical epitopes associated with effective control of viremia may prove to be of sufficient advantage to the virus to increase viral fitness *in vivo*. Where the balance between immunogenicity and pathogenicity will lie is a subject for speculation but remains an important issue of relevance to vaccine design. Ongoing studies comparing current and historic HIV sequences from genetically dissimilar populations will enable this question to be addressed. The definition of CTL responses in these populations and the accompanying sequencing and HLA typing data will provide the first step towards finding an answer to this potentially devastating scenario.

Acknowledgments

As every year, we would like to express our gratitude to the large number of researchers in the field who continuously contribute to this database. 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.

The mostly unpublished data added to this years update stemming from the AIDS Research Center at Mass. General Hospital have been largely funded by an NIH contract (#NO1 A1 15442) supporting HLA typing and HIV CTL epitope definition in non Caucasian populations and non clade B HIV infection.

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Table 1 Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*0201 (A2)			2 6 C	[Falk (1991), Barouch (1995)]
		1° anchor	**L** **L**	
			M **V**	
		2° anchor	V	
A*0201 (A2)	p17	77–85	SLYNTVATL	[Johnson (1991), Parker (1992), Parker (1994)]
A*0201 (A2)	p1	1–10	FLGKIWPSYK	[Xu (2002)]
A*0201 (A2)	Protease	76–84	LVGPTPVNI	[Altfeld (2001b)]
A*0201 (A2)	RT	33–41	ALVEICTEM	[Haas (1998), Haas(1999)]
A*0201 (A2)	RT	127–135	YTAFTIPSI	[Altfeld (2001b)]
A*0201 (A2)	RT	179–187	VIYQYMDDL	[Harrer (1996a)]
A*0201 (A2)	RT	309–317	ILKEPVHGV	[Walker (1989), Tsomides (1991)]
A*0201 (A2)	Vpr	59–67	AIIRILQQL	[Altfeld (2001a), Altfeld (2001b)]
A*0201 (A2)	Vpr	62–70	RILQQLLFI	[Altfeld (2001b)]
A*0201 (A2)	gp160	121–129	KLTPLCVTL	[Altfeld (2001b)]
A*0201 (A2)	gp160	311–320	RGPGRAFVTI	[Alexander-Miller (1996)]
A*0201 (A2)	gp160	813–822	SLLNATDIAV	[Dupuis (1995)]
A*0201 (A2)	Nef	136–145	PLTFGWCYKL	[Haas (1996), Maier & Autran(1999)]
A*0201 (A2)	Nef	137–146	LTFGWCFKLV	[Altfeld (2001b)]
A*0201 (A2)	Nef	180–189	VLEWRFDSRL	[Haas (1996), Maier & Autran(1999)]
A*0201 (A2)	p24/p2	230–7	VLAEAMSQV	[Altfeld (2001b)]
A*0202 (A2)			2 C	[Barouch (1995)]
			L **L**	
			V	
A*0202 (A2)	p17	77–85	SLYNTVATL	[Goulder (2000)]
A*0205 (A2)	p17	77–85	SLYNTVATL	[Goulder (2000)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*0301 (A3)			2 C **L K** **V Y** **M F**	[DiBrino (1993), Rammensee (1995)]
A*0301 (A3)	p17	18–26	KIRLRPGGK	[Harrer (1996b)]
A*0301 (A3)	p17	20–28	RLRPGGKKK	[Goulder (1997a), Culmann(1999), Lewinsohn (1999), Wilkes & Ruhl(1999)]
A*0301 (A3)	p17	20–29	RLRPGGKKKY	[Goulder (2000)]
A*0301 (A3)	RT	33–43	ALVEICTEMEK	[Haas (1998), Haas(1999)]
A*0301 (A3)	RT	93–101	GIPHPAGLK	[Altfeld (2000)]
A*0301 (A3)	RT	158–166	AIFQSSMTK	[Threlkeld (1997)]
A*0301 (A3)	RT	269–277	QIYPGIKVR	[Altfeld (2000)]
A*0301 (A3)	VIF	17–26	RIRTWKSLVK	[Altfeld (2000)]
A*0301 (A3)	Vif	17–26	RIRTWKSLVK	[Altfeld (2001a)]
A*0301 (A3)	gp160	37–46	TVYYGVPVWK	[Johnson (1994)]
A*0301 (A3)	gp160	770–780	RLRDLLLIVTR	[Takahashi (1991)]
A*0301 (A3)	Nef	73–82	QVPLRPMTYK	[Koenig (1990), Culmann (1991)]
A3 (A3)	RT	73–82	KLVDFRELNK	[Xu & Altfeld(2002)]
A3 (A3)	RT	356–366	RMRGAHTNDVK	[Xu & Altfeld(2002)]
A3 (A3)	Integrase	179–188	AVFIHNFKRK	[Xu & Altfeld(2002)]
A3 (A3)	Vif	28–36	HMYISKKAK	[Xu & Altfeld(2002)]
A3 (A3)	Vif	158–168	KTKPPLPSVKK	[Xu & Altfeld(2002)]
A3 (A3)	Rev	57–66	ERILSTYLGR	[M. Addo(2002)]
A3 (A3)	Nef	84–92	AVDLSHFLK	[Xu & Altfeld(2002)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*1101 (A11)			2 C **K** V I F Y	[Zhang (1993), Rammensee (1995)]
A*1101 (A11)	p17	84–92	TLYCVHQRI	[Harrer (1998)]
A*1101 (A11)	p24	217–227	ACQGVGGPGHK	[Sipsas (1997)]
A*1101 (A11)	RT	158–166	AIFQSSMTK	[Johnson & Walker(1994), Zhang (1993), Threlkeld (1997)]
A*1101 (A11)	RT	341–350	IYQEPFKNLK	[Culmann(1999)]
A*1101 (A11)	RNase	80–88	QIIEQLIKK	[Fukada (1999)]
A*1101 (A11)	Integrase	179–188	AVFIHNFKRK	[Fukada (1999)]
A*1101 (A11)	gp160	199–207	SVITQACPK	[Fukada (1999)]
A*1101 (A11)	Nef	73–82	QVPLRPMTYK	[Buseyne(1999)]
A*1101 (A11)	Nef	75–82	PLRPMTYK	[Culmann (1991)]
A*1101 (A11)	Nef	84–92	AVDLSHFLK	[Culmann (1991)]
A*2402 (A24)			2 C **Y** **I** **L** **F**	[Maier (1994)]
A*2402 (A24)	p17	28–36	KYKLKHIVW	[Ikeda-Moore (1998), Lewinsohn(1999)]
A*2402 (A24)	p24	162–172	RDYVDRFFKTL	[Dorrell (1999), Rowland-Jones(1999)]
A*2402 (A24)	gp160	52–61	LFCASDAKAY	[Lieberman (1992), Shankar (1996)]
A*2402 (A24)	gp160	585–593	RYLKDQQLL	[Dai (1992)]
A*2402 (A24)	Nef	134–141	RYPLTFGW	[Goulder (1997b), Ikeda-Moore (1998)]
A*2501 (A25)	p24	13–23	QAISPRTLNAW	[Kurane & West(1999)]
A*2501 (A25)	p24	71–80	ETINEEAAEW	[Klenerman (1996), van Baalen (1996)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A*2601 (A26)			12 6 C **V** **Y** **T** **F** **I** **L** **F** D I E L V	[Dumrese (1998)]
A*2601 (A26)	p24	35–43	EVIPMFSAL	[Goulder (1996a)]
A*2902 (A29)	gp160	209–217	SFEPIPIHY	[Altfeld (2000)]
A*3002 (A30)			12 C **Y** **Y** **F** **L** **V** R	[Rammensee (1999)]
A*3002 (A30)	p17	76–86	RSLYNTVATLY	[Goulder (2001a)]
A*3002 (A30)	RT	173–181	KQNPDIVIY	[Goulder (2001a)]
A*3002 (A30)	RT	263–271	KLNWASQIY	[Goulder (2001a)]
A*3002 (A30)	gp160	704–712	IVNRNRQGY	[Goulder (2001a)]
A*3002 (A30)	gp41	794–802	KYCWNLLQY	[Goulder (2001a)]
A*3101 (A31)			2 C **R** L V Y F	[Falk (1994), Rammensee (1999)]
A*3101 (A31)	gp160	770–780	RLRDLLLIVTR	[Safrit (1994a), Safrit (1994b)]
A*3201 (A32)	RT	392–401	PIQKETWETW	[Harrer (1996b)]
A*3201 (A32)	gp160	419–427	RIKQIINMW	[Harrer (1996b)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
A33 (A33)	Vpu	29–37	EYRKILRQR	[M. Addo(2002)]
A*6802 (A68)	Protease	3–11	ITLWQRPLV	[Rowland-Jones(1999)]
A*6802 (A68)	Protease	30–38	DTVLEEWNL	[Rowland-Jones(1999)]
A*6802 (A68)	gp160	777–785	IVTRIVELL	[Wilkes(1999)]
A*7401 (A19)	Protease	3–11	ITLWQRPLV	[Rowland-Jones(1999)]
B*0702 (B7)			123 C **P L** A R R K	[Englehard (1993), Rammensee (1999)]
B*0702 (B7)	p24	16–24	SPRTLNAWV	[Lewinsohn(1999)]
B*0702 (B7)	p24	48–56	TPQDLNTML	[Wilson (1999), Wilkes (1999), Jin (2000), Wilson (1997)]
B*0702 (B7)	p24	223–231	GPGHKARVL	[Goulder (2000)]
B*0702 (B7)	Vpr	34–42	FPRIWLHGL	[Altfeld (2001a)]
B*0702 (B7)	Vif	48–57	HPRVSSEVHI	[Altfeld (2001a)]
B*0702 (B7)	gp160	298–307	RPNNNTRKSI	[Safrit (1994b)]
B*0702 (B7)	gp160	843–851	IPRRIRQGL	[Wilkes & Ruhl(1999)]
B*0702 (B7)	Nef	68–77	FPVTPQVPLR	[Haas (1996), Maier & Autran(1999)]
B*0702 (B7)	Nef	71–79	TPQVPLRPM	[Goulder(1999)]
B*0702 (B7)	Nef	77–85	RPMTYKAAL	[Bauer (1997)]
B*0702 (B7)	Nef	128–137	TPGPGVRYPL	[Culmann-Penciolelli (1994), Haas (1996)]
?B*0702 (B7)	p24	84–92	HPVHAGPIA	[Xu & Altfeld(2002)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*0801 (B8)			23 5 C **K K L** **R** PR L	[Hill (1992), Sutton (1993), DiBrino (1994a)]
B*0801 (B8)	p17	24–32	GGKKKYKLK	[Rowland-Jones (1993), Goulder (1997d)]
B*0801 (B8)	p17	74–82	ELRSLYNTV	[Goulder (1997d)]
B*0801 (B8)	p24	128–135	EIYKRWII	[Sutton (1993), Goulder (1997d)]
B*0801 (B8)	p24	197–205	DCKTILKAL	[Sutton (1993)]
B*0801 (B8)	RT	18–26	GPKVKQWPL	[Walker (1989), Sutton (1993)]
B*0801 (B8)	gp160	2–10	RVKEKYQHL	[Sipsas (1997)]
B*0801 (B8)	gp160	586–593	YLKDQQLL	[Johnson (1992), Shankar (1996)]
B*0801 (B8)	Nef	13–20	WPTVRERM	[Goulder (1997d)]
B*0801 (B8)	Nef	90–97	FLKEKGGL	[Culmann-Penciolelli (1994), Price (1997)]
B*1402 (B14)			23 5 C **R R L** **K H** L Y F	[DiBrino (1994b)]
B*1402 (B14)	p24	166–174	DRFYKTLRA	[Harrer (1996b)]
B*1402 (B14)	gp160	584–592	ERYLKDQQL	[Johnson (1992)]
B*1501 (B62)			2 C **Q Y** **L F** **M**	[Barber (1997)] [Barber (1997)] [Barber (1997)]
B*1501 (B62)	p24	137–145	GLNKIVRMY	[Johnson (1991), Goulder(1999)]
B*1501 (B62)	RT	260–271	LVGKLNWASQIY	[Johnson(1999)]
B*1501 (B62)	RT	309–318	ILKEPVHGVY	[Johnson (1991), Johnson(1999)]
B*1501 (B62)	Nef	117–127	TQGYFPDWQNY	[Culmann(1999)]
B*1503 (B72)	Tat	38–47	FQTKGLGISY	[Novitsky (2001)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*1516 (B63)			2 9 **T Y** **S I** **V** **F**	[Barber (1997), Seeger (1998)]
B*1516 (B63)	gp160	375–383	SFNCGGEFF	[Wilson (1997), Wilson(1999)]
B*1801 (B18)	p24	161–170	FRDYVDRFYK	[Ogg (1998)]
B*1801 (B18)	Vif	102–111	LADQLIHLHY	[Altfeld (2001a)]
B*1801 (B18)	Nef	135–143	YPLTFGWCY	[Culmann (1991), Culmann-Penciolelli (1994)]
B*2705 (B27)			12 C **R L** **F** K K R R G I A	[Jardetzky (1991), Rammensee (1995)]
B*2705 (B27)	p17	19–27	IRLRPGGKK	[McKinney (1999), Lewinsohn(1999)]
B*2705 (B27)	p24	131–140	KRWIILGLNK	[Nixon (1988), Buseyne (1993), Goulder (1997c)]
B*2705 (B27)	gp160	786–795	GRRGWEALKY	[Lieberman (1992), Lieberman(1999)]
B*2705 (B27)	Nef	105–114	RRQDILDLWI	[Goulder (1997a)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*3501 (B35)			2 C **P Y** A F V M S L I	[Hill (1992), Rammensee (1999)]
B*3501 (B35)	p17	36–44	WASRELERF	[Goulder (1997b)]
B*3501 (B35)	p17	124–132	NSSKVSQNY	[Rowland-Jones (1995)]
B*3501 (B35)	p24	122–130	PPIPVGDIY	[Rowland-Jones (1995)]
B*3501 (B35)	RT	107–115	TVLDVGDAY	[Wilkes & Ruhl(1999), Wilson (1999)]
B*3501 (B35)	RT	118–127	VPLDEDFRKY	[Sipsas (1997), Shiga (1996)]
B*3501 (B35)	RT	175–183	NPDIVIYQY	[Sipsas (1997), Shiga (1996)]
B*3501 (B35)	gp160	42–52	VPVWKEATTTL	[Wilkes & Ruhl(1999)]
B*3501 (B35)	gp160	78–86	DPNPQEVVL	[Shiga (1996)]
B*3501 (B35)	gp160	606–614	TAVPWNASW	[Johnson (1994)]
B*3501 (B35)	Nef	74–81	VPLRPMTY	[Culmann (1991), Culmann-Penciolelli (1994)]
B*3701 (B37)			2 C **D F** **E M** **L** **I**	[Falk (1993)]
B*3701 (B37)	Nef	120–128	YFPDWQNYT	[Culmann (1991), Culmann(1999)]
B*3901 (B39)			2 C **R L** **H**	[Falk (1995a)]
B*3901 (B39)	p24	61–69	GHQAAMQML	[Kurane & West(1999)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*4001 (B60)			2 C **E L**	[Falk (1995b)]
B*4001 (B60)	p17	92–101	IEIKDTKEAL	[Altfeld (2000)]
B*4001 (B60)	p24	44–52	SEGATPQDL	[Altfeld (2000)]
B*4001 (B60)	p6	33–41	KELYPLTSL	[Yu & Altfeld(2001)]
B*4001 (B60)	RT	202–210	IEELRQHLL	[Altfeld (2000)]
B*4001 (B60)	gp160	805–814	QELKNSAVSL	[Altfeld (2000)]
B*4001 (B60)	Nef	92–100	KEKGGLEGL	[Altfeld (2000)]
B*4201 (B42)	p24	48–56	TPQDLNTML	[Goulder (2000)]
B*4201 (B42)	RT	271–279	YPGIKVRQL	[Wilkes & Ruhl(1999)]
B*4201 (B42)	Nef	128–137	TPGPGVRYPL	[Goulder(1999)]
B*4402 (B44)			2 C **E F** **Y**	[Rammensee (1999)]
B*4402 (B44)	p24	162–172	RDYVDRFYKTL	[Ogg (1998)]
B*4402 (B44)	p24	174–184	AEQASQDVKNW	[Lewinsohn(1999)]
B*4402 (B44)	gp160	31–40	AENLWVTVYY	[Borrow (1997)]
B*5101 (B51)			2 C **A F** **P I** **G**	[Falk (1995a)]
B*5101 (B51)	RT	42–50	EKEGKISKI	[Haas (1998), Haas(1999)]
B*5101 (B51)	RT	128–135	TAFTIPSI	[Sipsas (1997)]
B*5101 (B51)	gp160	416–424	LPCRIKQII	[Tomiyama (1999)]
B*5101 (B51)	gp160	557–565	RAIEAQQHL	[Sipsas (1997)]
B*5201 (B52)			2 C **I** **V** Q	[Rammensee (1999)]
B*5201 (B52)	p24	143–150	RMYSPTSI	[Wilkes & Ruhl(1999), Wilson (1997)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*5301 (B53)			2 C **P L**	[Hill (1992)]
B*5301 (B53)	p24	176–184	QASQEVKNW	[Buseyne (1996), Buseyne (1997), Buseyne(1999)]
B*5301 (B53)	Tat	2–11	EPVDPRLEPW	[Addo (2001)]
B*5501 (B55)			2 C **P** A	[Barber (1995)]
B*5501 (B55)	gp160	42–51	VPVWKEATTT	[Shankar (1996), Lieberman(1999)]
B*5701 (B57)			12 C **A F** **T W** **S** K Y	[Barber (1997)]
B*5701 (B57)	p24	15–23	ISPRTLNAW	[Johnson (1991), Goulder (1996b)]
B*5701 (B57)	p24	30–40	KAFSPEVIPMF	[Goulder (1996b)]
B*5701 (B57)	p24	108–118	TSTLQEQIGWF	[Goulder (1996b)]
B*5701 (B57)	p24	176–184	QASQEVKNW	[Goulder (1996b)]
B*5701 (B57)	RT	244–252	IVLPEKDSW	[van der Burg (1997), Hay(1999)]
B*5701 (B57)	Integrase	173–181	KTAVQMAVF	[Goulder (1996b), Hay(1999)]
B*5701 (B57)	Vpr	30–38	AVRHFPRIW	[Altfeld (2001a)]
B*5701 (B57)	Vif	31–39	ISKKAKGWF	[Altfeld (2001a)]
B*5701 (B57)	Rev	14–23	KAVRLIKFLY	[Addo(2001)]
B*5701 (B57)	Nef	116–124	HTQGYFPDW	[Culmann (1991), Draenert(2002)]
B*5701 (B57)	Nef	120–127	YFPDWQNY	[Culmann (1991), Draenert(2002)]
B57 (B57)	Nef	116–124	HTQGYFPDW	[Draenert(2002)]
B*5703 (B57)	p24	30–37	KAFSPEVI	[Goulder (2000)]
B*5703 (B57)	p24	30–40	KAFSPEVIPMF	[Goulder (2000)]

Table 1 (cont.) Best Defined HIV CTL Epitopes

HLA	Protein	AA	Sequence	Reference
B*5801 (B58)			12 C **A F** **T W** **S** K V I	[Barber (1997), Falk (1995b)]
B*5801 (B58)	p24	108–117	TSTLQEQIGW	[Goulder (1996b)]
B*5801 (B58)	Rev	14–23	KAVRLIKFLY	[Addo (2001)]
B*8101 (B81)	p24	48–56	TPQDLNTML	[Goulder (2000)]
B*8101 (B81)	Vpr	34–42	FPRIWLHGL	[Altfeld (2001a)]
Cw*0102 (Cw1)			23 C **A L** **L** P	[Barber (1997)]
Cw*0102 (Cw1)	p24	36–43	VIPMFSAL	[Goulder (1997b)]
Cw*0401 (Cw4)			2 6 C **Y L** **P F** **F M** V I L	[Falk (1994)]
Cw*0401 (Cw4)	gp160	375–383	SFNCGGEFF	[Wilson (1997), Johnson (1993)]
Cw*0702	Nef	105–115	RRQDILDLWIY	[Xu (2002)]
Cw*0802 (Cw8)	p24	48–56	TPQDLNTML	[Goulder (2000)]
Cw*0802 (Cw8)	Nef	82–91	KAAVDLSHFL	[Nixon (1999)]
B14 or Cw8	Rev	67–75	SAEPVPLQL	[van Baalen & Gruters(2000)]
Cw*0501 (Cw5)	Rev	67–75	SAEPVPLQL	[Addo (2001)]

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