I-A

Optimal CTL Epitope Identification in HIV Clade B and Non-Clade B Infection

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I-A-1 T cell immunity in HIV infection

HIV specific cytotoxic T lymphocytes (CTL) and T-helper cells (Th) remain one of the cornerstones of a potential HIV vaccine, and a number of vaccine trials and recent *in vitro* studies point towards the importance of the close interplay between these two arms of the cellular immune response in HIV infection. As more and more vaccine candidates find their way to clinical trials, not only the question of vaccine immunogen selection but also that of the appropriate *in vitro* monitoring of vaccine success become increasingly critical issues. The chosen approaches will need to balance the optimal sensitivity with the need of inter-trial comparability, and several efforts are under way to establish widely applicable *in vitro* antigen test sets to monitor several parallel vaccine trials in the future. The challenge for this undertaking is considerable, given that many vaccine trials are based on non-clade B immunogens, and thus require a comprehensive knowledge of immunogenic regions in various HIV clades, with the most pressing one likely being clade C. Part of this characterization will be the detailed delineation of the optimal CTL epitopes and their HLA restriction that are contained in these regions, so that reliable predictions can be made in terms of population coverage and how well local viral diversity is reflected by the vaccine sequence(s). Thus, although few laboratories nowadays follow through on identifying the precise nature of the targeted, optimal CTL epitopes in their various immunogens, we feel that epitope definition is not only desirable but actually urgently needed for an optimal vaccine design and appropriate analyses of induced responses. As in the past years, we here present an updated compilation of optimally defined CTL epitopes in all regions of HIV, which increasingly also includes epitopes defined in non-clade B infection. As argued above, especially non-clade B derived CTL epitopes will be most useful in refining vaccine approaches in the future and we thus include annotations to the epitopes indicating the test sequence used to identify the epitope. We feel that both of these additional pieces of information are important considerations as they can profoundly impact the detection rate of responses *in vivo* and obviously need to be included in vaccine immunogen design as well.

I-A-2 Escape from CTL recognition and antigen processing

Aside from sequence differences between various HIV clades, much focus has been given over the last few years to sequence variability within defined optimal epitopes as well as to regions in close proximity of such well-defined epitopes. Changes within the epitope are generally interpreted as CTL escape variants that either modulate binding to the HLA molecule or which reduce the binding affinity to the cognate T cell receptor [Brander *et al.*, 1998; Leslie *et al.*, 2004]. On the other hand, changes flanking the epitope, (as well as within) have been shown to interfere with efficient antigen processing, thereby also affording escape from CTL surveillance [Allen *et al.*, 2004; Draenert *et al.*, 2004b]. While CTL escape by changes within the targeted epitope has been well documented and used to link HIV evolution and host genetics [Moore *et al.*, 2002], the importance of processing escape is still unclear. However, processing may represent an effective escape route as no variant-specific CTL responses can be generated after escape has occurred. By inference from large-genome herpesviruses, which often have dedicated multiple genes towards interfering with antigen processing [Brander & Walker, 2000], this strategy seems to be a successful one and it is feasible that the highly variable HIV genome provides ample opportunities for this kind of immune evasion. This is different when escape occurs within the epitope and the epitope is still processed and presented. Except in cases of escape mutation in dominant anchor positions, these changes may mediate escape from TCR recognition but still bind to the restricting allele, thus allowing for the induction of a new population of CTL responses against the escaped variant [Allen *et al.*, 2005; Haas *et al.*, 1996]. Further work will need to be done to assess the frequency and relevance of processing escape, but existing and in

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some cases quite dramatic examples of TCR and/or HLA binding escape should not conceal this potential strategy. In addition, processing escape will or may already have influenced global viral evolution in different ways than CTL escape as other, likely more limited genetic polymorphisms (TAP for instance) may be imprinted on the viral sequences. These considerations can have profound implications for vaccine development and may complicate immunogen sequence design considerably, and the discrimination between processing and CTL escape depends on an accurate description of the actual presented epitopes.

I-A-3 Are "relic" epitopes on the rise?

Adaptation of (viral) pathogens to the human host has been well documented in the past and intensively studied for HIV. Work by a number of laboratories has pointed towards an important role of HLA class I polymorphism and viral evolution, presumably through viral adaptation to HLA class I restricted CTL responses [Altfeld *et al.*, 2005; Leslie *et al.*, 2005; Moore *et al.*, 2002]. A number of studies have in the meantime identified populations with particularly high frequencies of specific HLA class I alleles and associated specific local sequences with escape from CTL epitopes restricted by these common HLA alleles. Such studies include HLA-B57 positive individuals in South Africa, HLA-A24 expression subjects in the Japanese population and others that have been used to track potential CTL epitopes by reverse genetic approaches [Allen *et al.*, 2004; de Oliveira *et al.*, 2004; Furutsuki *et al.*, 2004; Leslie *et al.*, 2005]. Furthermore, in a recent work from our laboratory, population wide adaptation may even have rendered an HLA allele, in this case HLA-B*1503, from being associated with reduced viral load in a population with low allele frequency to a an allele associated with higher than average viral load in the population where it is overly frequent [Frahm *et al.*, 2005b]. However, the kinetics of such population wide adaptation and possible founder effects need to be seriously considered when interpreting these data as similar sequence patterns may emerge in population that do not share specific high frequency alleles [Korber *et al.*, 2005]. Regardless of whether founder effects may, at least partially, be responsible for the observed imprinting, high allele frequencies very likely facilitate the maintenance of escape variants and bear the question as to whether CTL responses restricted by common HLA alleles can be of significant importance for *in vivo* viral control [Lieberman, 2002]. As viral adaptation to any CTL pressure, including that restricted by common alleles, may result in reduced viral fitness and thus reduced *in vivo* viral burden, CTL responses restricted by common alleles may indeed contribute to viral control [Brander & Walker, 2003]. Despite frequent reversion of escaped CTL epitopes in hosts not expressing the restricting allele, especially CTL epitopes restricted by common alleles may be eliminated from the circulating viral population. Inclusion of such "relic" epitopes in vaccine design may for obvious reasons not provide much protection from infection by contemporary, circulating viral isolates and highlights again the need to have well defined epitope maps available for all clades of HIV.

As in the past years, we attempted to adhere for the present listing to a number of criteria that need to be fulfilled for inclusion [Brander & Walker, 1995; Hunziker *et al.*, 1998]. While these criteria should help to ensure proper identification of the minimal epitope targeted at the lowest peptide concentration and provide unequivocal identification of the restricting HLA class I allele, there may still be occasions where the data reported here conflict with data in other laboratories. We would like to encourage any investigator who observes discrepancies in his/her own data with what is reported here to bring this to our attention. Especially, we have reported earlier on cases of epitopes that appear to be presented on more than one allele; a phenomenon that may be more widespread than previously assumed and which may profoundly complicate data interpretation. Such information on additional presenting alleles can be highly useful for other investigators and we would welcome any contribution of this kind. Similarly, as newly identified epitopes may violate known HLA binding motifs or may be embedded in previously described epitope sequences, properly mapped epitopes may help to refine currently incompletely defined allele-specific binding motifs, thereby not only facilitating work in HIV but in other viral infections, cancer and autoimmunity as well.

I-A-4 Table of optimal HIV-1 CTL epitopes

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

HLA	Protein	AA	Sequence	Reference
A*0101 (A1)	gp160	787–795	RRGWEVLKY	Cao, 2002
A2	RT	127–135	YTAFTIPSV	Draenert, 2004
A*0201 (A2)			2 6 C	Falk *et al.*, 1991; Barouch *et al.*, 1995
		1° anchor	**L** **L**	
			M **V**	
		2° anchor	V	
A*0201 (A2)	p17	77–85	SLYNTVATL	Johnson *et al.*, 1991; Parker *et al.*, 1992, 1994
A*0201 (A2)	p1	1–10	FLGKIWPSYK	Yu *et al.*, 2002b
A*0201 (A2)	RT	33–41	ALVEICTEM	Haas *et al.*, 1998; Haas, 1999
A*0201 (A2)	RT	179–187	VIYQYMDDL	Harrer *et al.*, 1996a
A*0201 (A2)	RT	309–317	ILKEPVHGV	Walker *et al.*, 1989; Tsomides *et al.*, 1991
A*0201 (A2)	Vpr	59–67	AIIRILQQL	Altfeld *et al.*, 2001a,b
A*0201 (A2)	gp160	311–320	RGPGRAFVTI	Alexander-Miller *et al.*, 1996
A*0201 (A2)	gp160	813–822	SLLNATDIAV	Dupuis *et al.*, 1995
A*0201 (A2)	Nef	136–145	PLTFGWCYKL	Haas *et al.*, 1996; Maier & Autran, 1999
A*0201 (A2)	Nef	180–189	VLEWRFDSRL	Haas *et al.*, 1996; Maier & Autran, 1999
A*0202 (A2)			2 C	Barouch *et al.*, 1995
			L **L**	
			V	
A*0202 (A2)	p17	77–85	SLYNTVATL	Goulder, 1999
A*0205 (A2)	p17	77–85	SLYNTVATL	Goulder, 1999
A*0205 (A2)	gp160	846–854	RIRQGLERA	Sabbaj *et al.*, 2003
A*0207 (A2)	p24	164–172	YVDRFYKTL	Currier *et al.*, 2002
A*0301 (A3)	p17	18–26	KIRLRPGGK	Harrer *et al.*, 1996b
A*0301 (A3)	p17	20–28	RLRPGGKKK	Goulder *et al.*, 1997b; Culmann, 1999; Lewinsohn & Riddell, 1999; Wilkes & Ruhl, 1999
A*0301 (A3)	p17	20–29	RLRPGGKKKY	Goulder *et al.*, 2000b
A*0301 (A3)	RT	33–43	ALVEICTEMEK	Haas *et al.*, 1998; Haas, 1999
A*0301 (A3)	RT	73–82	KLVDFRELNK	Yu *et al.*, 2002a
A*0301 (A3)	RT	93–101	GIPHPAGLK	Yu *et al.*, 2002a
A*0301 (A3)	RT	158–166	AIFQSSMTK	Threlkeld *et al.*, 1997
A*0301 (A3)	RT	269–277	QIYPGIKVR	Yu *et al.*, 2002a
A*0301 (A3)	RT	356–366	RMRGAHTNDVK	Yu *et al.*, 2002a
A*0301 (A3)	Integrase	179–188	AVFIHNFKRK	Yu *et al.*, 2002a
A*0301 (A3)	Vif	17–26	RIRTWKSLVK	Altfeld *et al.*, 2001a; Yu *et al.*, 2002a
A*0301 (A3)	Vif	28–36	HMYISKKAK	Yu *et al.*, 2002a
A*0301 (A3)	Vif	158–168	KTKPPLPSVKK	Yu *et al.*, 2002a
A*0301 (A3)	Rev	57–66	ERILSTYLGR	Addo, 2002; Yu *et al.*, 2002a
A*0301 (A3)	gp160	37–46	TVYYGVPVWK	Johnson *et al.*, 1994
A*0301 (A3)	gp160	770–780	RLRDLLLIVTR	Takahashi *et al.*, 1991
A*0301 (A3)	Nef	73–82	QVPLRPMTYK	Koenig *et al.*, 1990; Culmann *et al.*, 1991
A*0301 (A3)	Nef	84–92	AVDLSHFLK	Yu *et al.*, 2002a

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

HLA	Protein	AA	Sequence	Reference
A*1101 (A11)			2 C **K** V I F Y	Zhang *et al.*, 1993; Rammensee *et al.*, 1995
A*1101 (A11)	p17	84–92	TLYCVHQRI	Harrer *et al.*, 1998
A*1101 (A11)	p24	217–227	ACQGVGGPGHK	Sipsas *et al.*, 1997
A*1101 (A11)	RT	158–166	AIFQSSMTK	Johnson & Walker, 1994; Zhang *et al.*, 1993; Threlkeld *et al.*, 1997
A*1101 (A11)	RT	341–350	IYQEPFKNLK	Culmann, 1999
A*1101 (A11)	RT	520–528	QIIEQLIKK	Fukada *et al.*, 1999
A*1101 (A11)	Integrase	179–188	AVFIHNFKRK	Fukada *et al.*, 1999
A*1101 (A11)	gp160	199–207	SVITQACPK	Fukada *et al.*, 1999
A*1101 (A11)	Nef	73–82	QVPLRPMTYK	Buseyne, 1999
A*1101 (A11)	Nef	75–82	PLRPMTYK	Culmann *et al.*, 1991
A*1101 (A11)	Nef	84–92	AVDLSHFLK	Culmann *et al.*, 1991
A23	gp41	74–82	RYLKDQQLL	Cao *et al.*, 2003
A*2402 (A24)			2 C **Y** **I** **L** **F**	Maier *et al.*, 1994
A*2402 (A24)	p17	28–36	KYKLKHIVW	Ikeda-Moore *et al.*, 1998; Lewinsohn, 1999
A*2402 (A24)	p24	162–172	RDYVDRFFKTL	Dorrell *et al.*, 1999; Rowland-Jones, 1999
A*2402 (A24)	gp160	52–61	LFCASDAKAY	Lieberman *et al.*, 1992; Shankar *et al.*, 1996
A*2402 (A24)	gp160	585–593	RYLKDQQLL	Dai *et al.*, 1992
A*2402 (A24)	Nef	134–141	RYPLTFGW	Goulder *et al.*, 1997a; Ikeda-Moore *et al.*, 1998
A*2501 (A25)	p24	13–23	QAISPRTLNAW	Kurane & West, 1999
A*2501 (A25)	p24	71–80	ETINEEAAEW	Klenerman *et al.*, 1996; van Baalen *et al.*, 1996
A*2601 (A26)			12 6 C **V** **Y** **T** **F** **I** **L** **F** D I E L V	Dumrese *et al.*, 1998
A*2601 (A26)	p24	35–43	EVIPMFSAL	Goulder *et al.*, 1996a
A*2601 (A26)	RT	449–457	ETKLGKAGY	Sabbaj *et al.*, 2003
A29	Nef	120–128	YFPDWQNYT	Draenert *et al.*, 2004a
A*2902 (A29)	p17	78–86	LYNTVATLY	Masemola *et al.*, 2004
A*2902 (A29)	gp160	209–217	SFEPIPIHY	Altfeld, 2000

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

HLA	Protein	AA	Sequence	Reference
A30	p17	34–44	LVWASRELERF	Masemola *et al.*, 2004
A*3002 (A30)			12 C **Y** **Y** **F** **L** **V** R	Rammensee *et al.*, 1999
A*3002 (A30)	p17	76–86	RSLYNTVATLY	Goulder *et al.*, 2001
A*3002 (A30)	RT	173–181	KQNPDIVIY	Goulder *et al.*, 2001
A*3002 (A30)	RT	263–271	KLNWASQIY	Goulder *et al.*, 2001
A*3002 (A30)	RT	356–365	RMRGAHTNDV	Sabbaj *et al.*, 2003
A*3002 (A30)	Integrase	219–227	KIQNFRVYY	Sabbaj *et al.*, 2003; Rodriguez *et al.*, 2004
A*3002 (A30)	gp160	310–318	HIGPGRAFY	Sabbaj *et al.*, 2003
A*3002 (A30)	gp160	704–712	IVNRNRQGY	Goulder *et al.*, 2001
A*3002 (A30)	gp160	794–802	KYCWNLLQY	Goulder *et al.*, 2001
A*3101 (A31)			2 C **R** L V Y F	Falk *et al.*, 1994; Rammensee *et al.*, 1999
A*3101 (A31)	gp160	770–780	RLRDLLLIVTR	Safrit *et al.*, 1994a,b
A*3201 (A32)	RT	392–401	PIQKETWETW	Harrer *et al.*, 1996b
A*3201 (A32)	gp160	419–427	RIKQIINMW	Harrer *et al.*, 1996b
A33	Nef	133–141	TRYPLTFGW	Cao, 2002
A*3303 (A33)	gp41	187–196	VFAVLSIVNR	Hossain *et al.*, 2001
A*3303 (A33)	gp41	320–327	EVAQRAYR	Hossain *et al.*, 2001
A*3303 (A33)	Vpu	29–37	EYRKILRQR	Addo *et al.*, 2002
A*6801 (A68)	Tat	39–49	ITKGLGISYGR	Oxenius *et al.*, 2002
A*6801 (A68)	Vpr	52–62	DTWAGVEAIIR	Sabbaj *et al.*, 2004
A*6802 (A68)	RT	436–445	GAETFYVDGA	Rathod & Kiepiela, 2005
A*6802 (A68)	Protease	3–11	ITLWQRPLV	Rowland-Jones, 1999
A*6802 (A68)	Protease	30–38	DTVLEEWNL	Rowland-Jones, 1999
A*6802 (A68)	Vpr	48–57	ETYGDTWTGV	Rathod & Kiepiela, 2005
A*6802 (A68)	gp160	777–785	IVTRIVELL	Wilkes, 1999
A*7401 (A19)	Protease	3–11	ITLWQRPLV	Rowland-Jones, 1999

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

HLA	Protein	AA	Sequence	Reference
B7	p24	84–92	HPVHAGPIA	Yu *et al.*, 2002a
B7	RT	156–164	SPAIFQSSM	Frahm & Brander, 2005
B*0702 (B7)			123 C **P** **L** A R **F** R K	Englehard *et al.*, 1993; Rammensee *et al.*, 1999
B*0702 (B7)	p24	16–24	SPRTLNAWV	Lewinsohn, 1999
B*0702 (B7)	p24	48–56	TPQDLNTML	Wilson, 1999; Wilkes *et al.*, 1999; Jin *et al.*, 2000; Wilson *et al.*, 1997
B*0702 (B7)	p24	223–231	GPGHKARVL	Goulder, 1999
B*0702 (B7)	Vpr	34–42	FPRIWLHGL	Altfeld *et al.*, 2001a
B*0702 (B7)	Vif	48–57	HPRVSSEVHI	Altfeld *et al.*, 2001a
B*0702 (B7)	gp160	298–307	RPNNNTRKSI	Safrit *et al.*, 1994b
B*0702 (B7)	gp160	843–851	IPRRIRQGL	Wilkes & Ruhl, 1999
B*0702 (B7)	Nef	68–77	FPVTPQVPLR	Haas *et al.*, 1996; Maier & Autran, 1999
B*0702 (B7)	Nef	68–76	FPVTPQVPL	Bauer *et al.*, 1997; Frahm & Goulder, 2002
B*0702 (B7)	Nef	71–79	TPQVPLRPM	Goulder, 1999
B*0702 (B7)	Nef	77–85	RPMTYKAAL	Bauer *et al.*, 1997
B*0702 (B7)	Nef	106–115	RQDILDLWIY	Goulder, 1999
B*0702 (B7)	Nef	128–137	TPGPGVRYPL	Culmann-Penciolelli *et al.*, 1994; Haas *et al.*, 1996
B8	gp160	848–856	RQGLERALL	Cao, 2002
B*0801 (B8)			23 5 C **K** **K** **L** **R** PR L	Hill *et al.*, 1992; Sutton *et al.*, 1993; DiBrino *et al.*, 1994b
B*0801 (B8)	p17	24–32	GGKKKYKLK	Reid *et al.*, 1996; Goulder *et al.*, 1997d
B*0801 (B8)	p17	74–82	ELRSLYNTV	Goulder *et al.*, 1997d
B*0801 (B8)	p24	128–135	EIYKRWII	Sutton *et al.*, 1993; Goulder *et al.*, 1997d
B*0801 (B8)	p24	197–205	DCKTILKAL	Sutton *et al.*, 1993
B*0801 (B8)	RT	18–26	GPKVKQWPL	Walker *et al.*, 1989; Sutton *et al.*, 1993
B*0801 (B8)	gp160	2–10	RVKEKYQHL	Sipsas *et al.*, 1997
B*0801 (B8)	gp160	586–593	YLKDQQLL	Johnson *et al.*, 1992; Shankar *et al.*, 1996
B*0801 (B8)	Nef	13–20	WPTVRERM	Goulder *et al.*, 1997d
B*0801 (B8)	Nef	90–97	FLKEKGGL	Culmann-Penciolelli *et al.*, 1994; Price *et al.*, 1997
B13	Nef	106–114	RQDILDLWI	Harrer *et al.*, 2005
B14	p2p7p1p6	42–50	CRAPRKKGC	Yu *et al.*, 2002b
B*1402 (B14)			23 5 C **R** **R** **L** **K** **H** L Y F	DiBrino *et al.*, 1994a
B*1402 (B14)	p24	166–174	DRFYKTLRA	Harrer *et al.*, 1996b
B*1402 (B14)	gp160	584–592	ERYLKDQQL	Johnson *et al.*, 1992

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

HLA	Protein	AA	Sequence	Reference
B*1501 (B62)			2 C	
			Q Y	Barber *et al.*, 1997
			L F	Barber *et al.*, 1997
			M	Barber *et al.*, 1997
B*1501 (B62)	p24	137–145	GLNKIVRMY	Johnson *et al.*, 1991; Goulder, 1999
B*1501 (B62)	RT	260–271	LVGKLNWASQIY	Johnson, 1999
B*1501 (B62)	RT	309–318	ILKEPVHGVY	Johnson *et al.*, 1991; Johnson, 1999
B*1501 (B62)	Nef	117–127	TQGYFPDWQNY	Culmann, 1999
B*1503 (B72)	p24	24–32	VKVIEEKAF	Honeyborne & Kiepiela, 2005
B*1503 (B72)	p24	164–172	YVDRFFKTL	Masemola *et al.*, 2004
B*1503 (B72)	RT	496–505	VTDSQYALGI	Sabbaj *et al.*, 2003
B*1503 (B72)	Integrase	135–143	IQQEFGIPY	Honeyborne & Kiepiela, 2005
B*1503 (B72)	Integrase	185–194	FKRKGGIGGY	Honeyborne, 2003
B*1503 (B72)	Integrase	263–271	RKAKIIRDY	Cao *et al.*, 2003
B*1503 (B72)	Tat	38–47	FQTKGLGISY	Novitsky *et al.*, 2001
B*1503 (B72)	Nef	183–191	WRFDSRLAF	Cao, 2002
B*1510 (B71)	p24	12–20	HQAISPRTL	Day, 2005
B*1510 (B71)	p24	61–69	GHQAAMQML	Day, 2003
B*1510 (B71)	Vif	79–87	WHLGHVSI	Honeyborne, 2003
B*1516 (B63)			2 9	Barber *et al.*, 1997; Seeger *et al.*, 1998
			T Y	
			S I	
			V	
			F	
B*1516 (B63)	gp160	375–383	SFNCGGEFF	Wilson *et al.*, 1997; Wilson, 1999
B*1801 (B18)	p24	161–170	FRDYVDRFYK	Ogg *et al.*, 1998
B*1801 (B18)	Vif	102–111	LADQLIHLHY	Altfeld *et al.*, 2001a
B*1801 (B18)	Nef	135–143	YPLTFGWCY	Culmann *et al.*, 1991; Culmann-Penciolelli *et al.*, 1994
B27	Vpr	31–39	VRHFPRIWL	Addo & Rathod, 2004
B*2703 (B27)	p24	131–140	RRWIQLGLQK	Rowland-Jones *et al.*, 1998; Rowland-Jones, 1999
B*2705 (B27)			12 C	Jardetzky *et al.*, 1991; Rammensee *et al.*, 1995
			R L	
			F	
			K K	
			R R	
			G I	
			A	
B*2705 (B27)	p17	19–27	IRLRPGGKK	McKinney *et al.*, 1999; Lewinsohn, 1999
B*2705 (B27)	p24	131–140	KRWIILGLNK	Nixon *et al.*, 1988; Buseyne *et al.*, 1993; Goulder *et al.*, 1997c
B*2705 (B27)	gp160	786–795	GRRGWEALKY	Lieberman *et al.*, 1992; Lieberman, 1999
B*2705 (B27)	Nef	105–114	RRQDILDLWI	Goulder *et al.*, 1997b

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

HLA	Protein	AA	Sequence	Reference
B*3501 (B35)			2 C **P Y** A F V M S L I	Hill *et al.*, 1992; Rammensee *et al.*, 1999
B*3501 (B35)	p17	36–44	WASRELERF	Goulder *et al.*, 1997a
B*3501 (B35)	p17	124–132	NSSKVSQNY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	p24	122–130	PPIPVGDIY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	p24	122–130	NPVPVGNIY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	RT	107–115	TVLDVGDAY	Wilkes & Ruhl, 1999; Wilson *et al.*, 1999
B*3501 (B35)	RT	118–127	VPLDEDFRKY	Sipsas *et al.*, 1997; Shiga *et al.*, 1996
B*3501 (B35)	RT	175–183	NPDIVIYQY	Sipsas *et al.*, 1997; Shiga *et al.*, 1996
B*3501 (B35)	RT	175–183	HPDIVIYQY	Rowland-Jones *et al.*, 1995
B*3501 (B35)	gp160	42–52	VPVWKEATTTL	Wilkes & Ruhl, 1999
B*3501 (B35)	gp160	78–86	DPNPQEVVL	Shiga *et al.*, 1996
B*3501 (B35)	gp160	606–614	TAVPWNASW	Johnson *et al.*, 1994
B*3501 (B35)	Nef	74–81	VPLRPMTY	Culmann *et al.*, 1991; Culmann-Penciolelli *et al.*, 1994
B*3701 (B37)			2 C **D F** **E M** **L** **I**	Falk *et al.*, 1993
B*3701 (B37)	Nef	120–128	YFPDWQNYT	Culmann *et al.*, 1991; Culmann, 1999
B*3801 (B38)	Vif	79–87	WHLGQGVSI	Sabbaj *et al.*, 2004
B*3801 (B38)	gp160	104–112	MHEDIISLW	Cao, 2002
B*3901 (B39)			2 C **R L** **H**	Falk *et al.*, 1995a
B*3901 (B39)	p24	61–69	GHQAAMQML	Kurane & West, 1999
B*3910 (B39)	p24	48–56	TPQDLNTML	Honeyborne & Kiepiela, 2005
B*4001 (B60)			2 C **E L**	Falk *et al.*, 1995b
B*4001 (B60)	p17	92–101	IEIKDTKEAL	Altfeld *et al.*, 2000
B*4001 (B60)	p24	44–52	SEGATPQDL	Altfeld *et al.*, 2000
B*4001 (B60)	p2p7p1p6	118–126	KELYPLTSL	Yu *et al.*, 2002b
B*4001 (B60)	RT	5–12	IETVPVKL	Draenert, 2004
B*4001 (B60)	RT	202–210	IEELRQHLL	Altfeld *et al.*, 2000
B*4001 (B60)	gp160	805–814	QELKNSAVSL	Altfeld *et al.*, 2000
B*4001 (B60)	Nef	37–45	LEKHGAITS	Draenert, 2004
B*4001 (B60)	Nef	92–100	KEKGGLEGL	Altfeld *et al.*, 2000

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

HLA	Protein	AA	Sequence	Reference
B*4002 (B61)	p17	11–19	GELDRWEKI	Sabbaj *et al.*, 2003
B*4002 (B61)	p24	70–78	KETINEEAA	Sabbaj *et al.*, 2003
B*4002 (B61)	p24	78–86	AEWDRVHPV	Sabbaj *et al.*, 2003
B*4002 (B61)	p2p7p1p6	64–71	TERQANFL	Sabbaj *et al.*, 2003
B*4002 (B61)	Nef	92–100	KEKGGLEGL	Sabbaj *et al.*, 2003; Altfeld *et al.*, 2000
B42	Integrase	260–268	VPRRKAKII	Kiepiela & Goulder, 2002
B*4201 (B42)	p24	48–56	TPQDLNTML	Goulder *et al.*, 2000a
B*4201 (B42)	RT	271–279	YPGIKVRQL	Wilkes & Ruhl, 1999
B*4201 (B42)	Nef	128–137	TPGPGVRYPL	Goulder, 1999
B44	Protease	34–42	EEMNLPGRW	Rodriguez *et al.*, 2004
B*4402 (B44)			2 C **E F** **Y**	Rammensee *et al.*, 1999
B*4402 (B44)	p24	162–172	RDYVDRFYKTL	Ogg *et al.*, 1998
B*4402 (B44)	p24	174–184	AEQASQDVKNW	Lewinsohn, 1999
B*4402 (B44)	gp160	31–40	AENLWVTVYY	Borrow *et al.*, 1997
B*4403 (B44)	p17	78–86	LYNTVATLY	Masemola *et al.*, 2004
B*4415 (B12)	p24	28–36	EEKAFSPEV	Bird *et al.*, 2002
B*4501 (B45)	p2p7p1p6	1–10	AEAMSQVTNS	Sabbaj *et al.*, 2004
B50	Nef	37–45	LEKHGAITS	Draenert, 2004
B51	Vif	57–66	IPLGDAKLII	Bansal *et al.*, 2004
B51	Vpr	29–37	EAVRHFPRI	Cao *et al.*, 2003
B*5101 (B51)			2 C **A F** **P I** **G**	Falk *et al.*, 1995a
B*5101 (B51)	RT	42–50	EKEGKISKI	Haas *et al.*, 1998; Haas, 1999
B*5101 (B51)	RT	128–135	TAFTIPSI	Sipsas *et al.*, 1997
B*5101 (B51)	gp160	416–424	LPCRIKQII	Tomiyama *et al.*, 1999
B*5201 (B52)			2 C **I** **V** Q	Rammensee *et al.*, 1999
B*5201 (B52)	p24	143–150	RMYSPTSI	Wilkes & Ruhl, 1999; Wilson *et al.*, 1997

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

HLA	Protein	AA	Sequence	Reference
B53	Nef	135–143	YPLTFGWCF	Kiepiela & Goulder, 2002
B*5301 (B53)			2 C **P** **L**	Hill *et al.*, 1992
B*5301 (B53)	p24	48–56	TPYDINQML	Gotch *et al.*, 1993
B*5301 (B53)	p24	176–184	QASQEVKNW	Buseyne *et al.*, 1996, 1997; Buseyne, 1999
B*5301 (B53)	Tat	2–11	EPVDPRLEPW	Addo *et al.*, 2001
B*5301 (B53)	Nef	135–143	YPLTFGWCY	Sabbaj *et al.*, 2003
B*5501 (B55)			2 C **P** A	Barber *et al.*, 1995
B*5501 (B55)	gp160	42–51	VPVWKEATTT	Shankar *et al.*, 1996; Lieberman, 1999
B57	p24	32–40	FSPEVIPMF	Frahm *et al.*, 2005a
B57	Protease	70–77	KAIGTVLV	Frahm *et al.*, 2005a
B57	Integrase	123–132	STTVKAACWW	Rodriguez *et al.*, 2004; Addo & Rathod, 2004
B57	Nef	116–124	HTQGYFPDW	Draenert, 2002
B57	Nef	127–135	YTPGPGIRY	Frahm *et al.*, 2005a
B57	Nef	137–145	LTFGWCFKL	Frahm *et al.*, 2005a
B*5701 (B57)			12 C **A** **F** **T** **W** **S** K Y	Barber *et al.*, 1997
B*5701 (B57)	p24	15–23	ISPRTLNAW	Johnson *et al.*, 1991; Goulder *et al.*, 1996b
B*5701 (B57)	p24	30–40	KAFSPEVIPMF	Goulder *et al.*, 1996b
B*5701 (B57)	p24	108–118	TSTLQEQIGWF	Goulder *et al.*, 1996b
B*5701 (B57)	p24	176–184	QASQEVKNW	Goulder *et al.*, 1996b
B*5701 (B57)	RT	244–252	IVLPEKDSW	van der Burg *et al.*, 1997; Hay, 1999
B*5701 (B57)	Integrase	173–181	KTAVQMAVF	Goulder *et al.*, 1996b; Hay, 1999
B*5701 (B57)	Vpr	30–38	AVRHFPRIW	Altfeld *et al.*, 2001a
B*5701 (B57)	Vif	31–39	ISKKAKGWF	Altfeld *et al.*, 2001a
B*5701 (B57)	Rev	14–23	KAVRLIKFLY	Addo *et al.*, 2001
B*5701 (B57)	Nef	116–125	HTQGYFPDWQ	Culmann *et al.*, 1991
B*5701 (B57)	Nef	120–128	YFPDWQNYT	Culmann *et al.*, 1991
B*5703 (B57)	p24	30–37	KAFSPEVI	Goulder *et al.*, 2000b
B*5703 (B57)	p24	30–40	KAFSPEVIPMF	Goulder *et al.*, 2000b
B58	p17	76–86	RSLYNTVATLY	Frahm *et al.*, 2005a
B58	Tat	2–11	EPVDPRLEPW	Frahm & Brander, 2005

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

HLA	Protein	AA	Sequence	Reference
B*5801 (B58)			12 C **A** **F** **T** **W** **S** K V I	Barber *et al.*, 1997; Falk *et al.*, 1995b
B*5801 (B58)	p24	108–117	TSTVEEQQIW	Bertoletti *et al.*, 1998
B*5801 (B58)	p24	108–117	TSTLQEQIGW	Goulder *et al.*, 1996b
B*5801 (B58)	RT	375–383	IAMESIVIW	Kiepiela & Goulder, 2002
B*5801 (B58)	Rev	14–23	KAVRLIKFLY	Addo *et al.*, 2001
B62	Nef	19–27	RMRRAEPAA	Cao, 2002
B63	p17	76–86	RSLYNTVATLY	Frahm *et al.*, 2005a
B63	p24	15–23	ISPRTLNAW	Frahm *et al.*, 2005a
B63	p24	30–40	KAFSPEVIPMF	Frahm *et al.*, 2005a
B63	Rev	14–23	KAVRLIKFLY	Frahm *et al.*, 2005a
B63	Nef	127–135	YTPGPGIRY	Frahm *et al.*, 2005a
B63	Nef	137–145	LTFGWCFKL	Frahm *et al.*, 2005a
B81	Pol	715–723	LFLDGIDKA	Addo, 2002
B*8101 (B81)	p24	48–56	TPQDLNTML	Goulder *et al.*, 2000a
B*8101 (B81)	Vpr	34–42	FPRIWLHGL	Altfeld *et al.*, 2001a

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

HLA	Protein	AA	Sequence	Reference
Cw*0102 (Cw1)			23 C **A L** **L** P	Barber *et al.*, 1997
Cw*0102 (Cw1)	p24	36–43	VIPMFSAL	Goulder *et al.*, 1997a
Cw3	Nef	83–91	AALDLSHFL	Draenert, 2004
Cw*0303 (Cw9)	p24	164–172	YVDRFFKTL	Honeyborne, 2003
Cw*0304 (Cw10)	p24	164–172	YVDRFFKTL	Honeyborne, 2003
Cw*0304 (Cw10)	gp41	46–54	RAIEAQQHL	Currier *et al.*, 2002; Trocha, 2002
Cw*0401 (Cw4)			2 6 C **Y L** **P F** **F M** V I L	Falk *et al.*, 1994
Cw*0401 (Cw4)	gp160	375–383	SFNCGGEFF	Wilson *et al.*, 1997; Johnson *et al.*, 1993
Cw5	Gag p24	174–185	AEQASQEVKNWM	Draenert, 2004
Cw6	Nef	120–128	YFPDWQNYT	Frahm & Brander, 2005
Cw7	Nef	105–115	KRQEILDLWVY	Kiepiela & Goulder, 2002
Cw7	Nef	105–115	RRQDILDLWIY	Yu *et al.*, 2002a
Cw*0802 (Cw8)	p24	48–56	TPQDLNTML	Goulder *et al.*, 2000a; Honeyborne & Kiepiela, 2005
Cw*0802 (Cw8)	Nef	83–91	AAVDLSHFL	Cao *et al.*, 2003
Cw*0804 (Cw8)	p17	33–31	HLVWASREL	Masemola *et al.*, 2004
Cw12	Tat	30–37	CCFHCQVC	Cao *et al.*, 2003; Nixon *et al.*, 1999
Cw14	p17	78–85	LYNTVATL	Horton & Havenar-Daughton, 2005
Cw15	gp41	46–54	RAIEAQQHL	Trocha, 2002
Cw18	p24	161–169	FRDYVDRFF	Honeyborne & Kiepiela, 2005
Cw*1801 (Cw18)	Integrase	165–172	VRDQAEHL	Rathod & Kiepiela, 2005

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

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