Table 1: **p17**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK		human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes that this is an A*0301 epitope				
p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human(A3)	[Wilson (1996)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • KIRLRPGGR and RIRLRPGGR, naturally occurring variants, were found in mother, and are escape mutants				
p17(18–26)	p17(18–26)	KIRLRPGGK	*in vitro* stimulation	human(A3)	[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				
p17(18–26)	Gag(18–26)	KIRLRPGGK	HIV-1 infection	human(A3)	[Brodie (1999)]
	• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptive transfer • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively-infected CD4+ T cells, showing that CTL move to appropriate target sites and mediate anti-viral effects				
p17(18–26)	(18–26)	KIRLRPGGK	HIV infection	human(A3)	[Brodie (2000)]
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV Tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK	HIV-1 infection	SJL/J HLA transgenic mice(A3)	[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 • KIRLRPGGR and RIRLRPGGR were escape mutants • This epitope was recognized and many escape mutants were detected in an HLA A3 transmitting mother, and was recognized but invariant in an HLA A3 non-transmitting mother				
p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human(A3)	[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 (1997b)] is a review of immune escape that summarizes this study.				
p17(18–26)	p17( )	KIRLRPGGK	HIV-1 exposed seronegative	human(A3)	[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				
p17(18–26)	p17( )	KIRLRPGGK	HIV-1 infection	human(A3)	[Goulder (2000a)]
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK (this tally comes from the tables, not the text of the paper) • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPGGKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(18–26)	( )	KIRLRPGGK	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 moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
p17(18–27)	p17(18–27 LAI)	KIRLRPGGKK		human(B27)	[Brander & Walker(1996)]
	• D. Lewinsohn, pers. comm.				
p17(18–27)	p17(18–27)	KIRLRPGGKK	HIV-1 infection	human(B27)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(18–31)	p17(18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human(A3)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(18–31)	p17(18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human(B62)	[Lubaki (1997)]
	• Eighty two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of CTL response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a Polyclonal response • A subject who was HLA-B62+ had CTL that recognized this peptide, and p24 LGLNKIVRMYS, and one additional unknown epitope				
p17(18–42)	p17(18–42 IIIB)	KIRLRPGGKKKYKLK-HIVWASRELE	HIV-1 infection	human(A3)	[Jassoy (1992)]
	• Epitope recognized by CTL clone derived from CSF				
p17(18–42)	p17(18–42 PV22)	KIRLRPGGKKKYKLK-HIVWASRELE	HIV-1 infection	human(A3)	[Jassoy (1993)]
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(18–42)	p17(18–42 BH10)	KIRLRPGGKKKYKLK-HIVWASRELE	HIV-1 infection	human(Bw62)	[Johnson (1991)]
	• Gag CTL response was studied in three individuals				
p17(19–27)	p17(19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse(B*2705)	[Brander & Goulder(2001)]
	Noted by Brander to be B*2705 (Pers. Comm. D. Lewinsohn)				
p17(19–27)	p17(19–27 LAI)	IRLRPGGKK		human(B27)	[Brander & Walker(1996)]
p17(19–27)	p17(19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse(B27)	[McKinney (1999)]
	• Epitope-specific CTL were infused in infected human PBL-SCID mice, and transient decreases in viral load were observed, however virus was not eradicated and the HIV-specific CTL rapidly disappeared • No escape mutants were observed • Control CTL were long lived in both infected and uninfected mice, showing the rapid loss of CTL was due to target interaction				
p17(19–27)	p17( )	IRLRPGGKK	HIV-1 infection	human(B27)	[Goulder (2000a)]
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 2/3 individuals that were B27+ had a dominant response to this epitope • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17(20–28)	p17(20–28)	RLRPGGKKK	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 • Three of the four individuals that responded to SLYNTVATL recognized HIV epitopes, and one individual who was A*0201, A31 and B51 and B58w4 recognized this epitope (previously described as HLA A3.1), as well as one other				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A*03)	[Goulder (1997b), Goulder (1997a)]
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a response to Gag A3 epitope RLRPGGKKK, the other non-responder carried the sequence RLRPGGKKC • [Goulder (1997a)] is a review of immune escape that summarizes this study				
p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes that this is an A*0301				
p17(20–28)	p17( )	RLRPGGKKK	HIV-1 infection	human(A*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 moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (2000b)]
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC				
p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (1997f)]
	• A control CTL line that reacts with this peptide was included in the study				
p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Cao (1997)]
	• The consensus peptide of A, B, and D clade viruses is RLRPGGKKK • The consensus peptide of C clade viruses is RLRPGGKKH and is equally reactive				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(20–28)	p17( )	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (2000a)]
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK (this tally comes from the tables, not the text of the paper which stated 6/7 RLRPGGKKK) • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of x from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17(20–29)	p17(20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(A3)	[Goulder (2000b)]
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(A3.1)	[Brander & Walker(1995)]
	• Unpublished, C. Jassoy and Beatrice Culman, pers. comm.				
p17(20–29)	p17(20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human(A3.1)	[Wilkens & Ruhl(1999)]
	• Pers. comm., B. Wilkens and D. Ruhl				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(A30,A3.1)	[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 A30, and one was A3, and both responded to RLRPGGKKKY • The A2+ A3 individual also reacted with two other A3.1 epitopes				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(20–29)	p17(20–29 IIIB)	RLRPGGKKKY	HIV-1 infection	human(B42)	[Wilson (1996)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • RLRPGGKKRY, a naturally occurring variant, was found in non-transmitting mother and is recognized • Binds HLA-A3 and Bw62 as well				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV infection	human(B62)	[Brodie (2000)]
	• Study tracks and quantifies *in vivo* migration of neo-marked CD8 HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV Tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL *in vivo*				
p17(20–29)	p17(20–29 LAI)	RLRPGGKKKY		human(Bw62)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • Also P. Johnson, pers. comm.				
p17(20–30)	p17( )	RLRPGGKKKYK	HIV-1 infection	human( )	[Goulder (2000a)]
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – the dominant response in a Haitian immigrant living in Boston who was HLA A24/29 B7/B44 Cw6/7 was to this epitope, although the restricting element was not determined • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17(20–35)	p17(90–105 SF2)	CLRPGGKKKYKLKHIV	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI Gag • One of these 12 had CTL response to this peptide • The responding subject was HLA A-2, A-24, B-13, B-35				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(21–35)	Gag( )	LRPGGKKKYKLKHIV	HIV-infection	human( )	[Weekes (1999a)]
	• Peptide 703.3: Memory CTL-specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
p17(21–35)	p17(91–105 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI Gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A2, B50, B57				
p17(21–35)	Gag( )	LRPGGKKKYKLKHIV	HIV-infection	human(A3)	[Weekes (1999b)]
	• Peptide 703.3: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vβ responses was studied and was found to be highly focused, with one TCR β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vbeta13.1 and Vbeta5.2				
p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV		human(B8)	[Nixon & McMichael(1991)]
	• Two CTL epitopes defined (see also p24(191–205))				
p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV	HIV-1 infection	human(not B8)	[van Baalen (1996)]
	• Unknown HLA specificity, but not B8				
p17(21–40)	p17(21–40 Clade A)	LRPGGKKKYRLKHLV-WASRE	HIV-1 infection	human(Cw4)	[Dorrell (1999)]
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This epitope was defined in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTL from this patient were not A-B cross-reactive				
p17(22–31)	Gag(22–31)	RPGGKKRYKL	HIV-1 infection	human(B7)	[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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31)	GGKKKYKL		human(B8)	[Goulder (1997g)]
	• The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation • The predictions were experimentally confirmed • The anchors for HLA-B8 epitopes, as defined by peptide elution data, are P3 (K), P5 (K/R), and P8 (L) • Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe • Small hydrophobic residues at P2 may be favorable for binding • A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor				
p17(24–31)	p17(24–31 SF2)	GGKKKYKL	HIV-1 infection	human(B8)	[McAdam (1998)]
	• CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope				
p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Reid (1996)]
	• The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied • Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined • 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement • 7Q and 7R alter the TCR exposed surface, and retain some recognition • Reactivity of 5R depends on the T cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound • Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues				
p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Price (1997)]
	• A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual • Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present				
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes epitope to be presented by B*0801				
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Sutton (1993)]
	• Exploration of HLA-B8 binding motif through peptide elution				
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Rowland-Jones (1993)]
	• Study of an individual with partially defective antigen processing				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1994)]
	• Naturally occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1995)]
	• Naturally occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Nowak (1995)]
	• Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[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				
p17(24–32)	p17( )	GGKKKYKLK		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, and the B35 allele seems to be protective • HIV-2 sequence: GGKKKYKMK – no cross-reactivity [Phillips (1991)]				
p17(24–35)	p17(25–35 SF2)	GGKKKYKLKHIV	HIV-1 infection	human(B8)	[Phillips (1991), Goulder (1997a)]
	• Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time • [Goulder (1997a)] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients				
p17(24–35)	p17(25–35)	GGKKKYKLKHIV	HIV-1 infection	human(B8)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A*2402)	[Brander & Goulder(2001)]
	• Ikeda-Moore(1998) and D. Lewinsohn, pers. comm. • C. Brander notes that this is an A*2402 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(28–36)	p17(28–36 SF2)	KYKLKHIVW	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1998)]
	• Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+ • HLA A24 is very common in Japanese (70% carry it) and is common globally • This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.				
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A23)	[Goulder & Walker(1999)]
	• P. Goulder, pers. comm.				
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A24)	[Brander & Walker(1996)]
	• D. Lewinsohn, pers. comm.				
p17(36–44)	p17( )	WASRELERF	HIV-1 infection	human( )	[Goulder (2000a)]
	• The dominant response in an African American who was HLA A3/33 B35/B53 Cw4/7 was to this epitope, although the restricting element was not determined – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17(36–44)	p17(35–43 LAI)	WASRELERF	HIV-1 infection	human(B*3501)	[Goulder (1997e)]
	• Optimal epitope defined from within p17(30–44), LKHIVWASRELERFA • Dominant CTL response in an HIV+ asymptomatic donor was to this epitope • The Phe in the C-term anchor is distinct from the previously-defined Tyr for B*3501 C-term anchors				
p17(36–44)	p17(36–44 LAI)	WASRELERF		human(B*3501)	[Brander & Goulder(2001), Goulder (1997c)]
	• C. Brander notes this is a B*3501 epitope				
p17(36–44)	p17(36–44)	WASRELERF	HIV-1 infection	human(B35)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(69–93)	p17(69–93 BH10)	QTGSEELRSLYNTVAT-LYCVHQRIE	HIV-1 infection	human(A2)	[Johnson (1991)]
	• Gag CTL response studied in three individuals				
p17(71–79)	p17(71–79 LAI)	GSEELRSLY		human(A1)	[Brander & Walker(1996)]
	• P. Goulder, pers. comm.				
p17(71–79)	p17(71–79)	GSEELRSLY	HIV-1 infection	human(A1)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(71–85)	p17(71–85 SF2)	GSEELRSLYNTVATL	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI Gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A11, B8, B27				
p17(74–82)	p17( )	ELRSLYNTV		human(B*0801)	[Brander & Goulder(2001)]
	• Noted by Brander to be a B*0801 epitope				
p17(74–82)	p17( )	ELRSLYNTV		human(B8)	[Goulder (1997g)]
	• Defined in a study of the B8 binding motif				
p17(74–82)	p17(74–82)	ELRSLYNTV	HIV-1 infection	human(B8)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(76–86)	p17(74–86 LAI)	RSLYNTVATLY		human(A*3002)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*3002 epitope				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(76–86)	p17( )	RSLYNTVATLY	HIV-1 infection	human(A*3002)	[Goulder (2000a)]
	• The CTL-dominant response was focused on this epitope in an single HIV+ individual from Boston – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPGGKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*02)	[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 γ IFN producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT • 4/8 A*02 subjects had a positive response to this epitope indicating that it is a major epitope for CD8+ γ IFN production • In 3/3 HLA A*02, B*27 individuals, the dominant response in Gag measured by both γ IFN production and T cell lysis was a B27 epitope, p24(263–272), not the A2 SLYNTVATL epitope			
p17(77–85)	p17(77–85 HXB2)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Brander (1999)]
	• Epitope SL9: Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope • The substitution Y79F was an escape mutation in that it interfered with CTL recognition by one CTL clone from an A*0201 infected individual, clone 13010.B17, but it was still recognized by another CTL clone, 115.D4			
p17(77–85)	Gag( )	SLYNTVATL	HIV-1 infection	human(A*0201)	[Tan (1999)]
	• Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts			

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[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 • Individuals that did not respond to SLYNTVATL recognized other HIV epitopes, and 2/4 SLYNTVATL responders had stronger responses to epitopes restricted by other class I alleles • SLYNTVATL was the only response detected in one individual that was HLA A*0201, B44, B70				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Ogg (1999)]
	• Epitope SL9: CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SLYNTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient • Levels of CTL effectors typically decline for 5–7 days and then rebound, fluctuating during the first two weeks of therapy • After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Altman (1996)]
	• Epitope SL9: This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs – HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and quantitate HIV-specific CD8+ cell lines in freshly isolated PBMCs • Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%)				
p17(77–85)	Gag( )	SLYNTVATL	HIV-1 infection	human(A*0201)	[Gray (1999)]
	• Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL				
p17(77–85)	p17(77–85 SF2)	SLYNTVATL	HIV-1 infection	human(A*0201)	[McAdam (1998)]
	• Epitope SL9: CTL from a patient infected with clade B virus did not recognize the clade A analog of this epitope				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Wilson (1998a)]
	• Epitope SL9: HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T cells was followed *in vivo* • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases • An A2-Gag-specific line from one patient was found to be BV8, and at its highest level represented 17.5% of the patient's CD8+ T cells				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Ogg (1998b)]
	• Epitope SL9: HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load • Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity • No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells				
p17(77–85)	p17(77–85)	SLYNTVATL	none	human(A*0201)	[Walter (1997)]
	• Epitope SL9: HLA-A2 heavy chain and β2-microglobulin expressed in *E. coli* were refolded in the presence of this peptide • The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2 • Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Lalvani (1997)]
	• Epitope SL9: A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the test peptides for optimizing the protocol				
p17(77–85)	p17(76–84)	SLYNTVATL	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]
	• Epitope SL9: Slow dissociation rate is associated with immunogenicity • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Goulder (1997b), Goulder (1997a)]
	• Epitope SL9: Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a response to Gag A2 epitope SLYNTVATL, the other to Pol A2 epitope ILKEPVHGV • Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL • 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to Gag SLYNTVATL • Those individuals with a Pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL • An additional subject went from SLYNTVATL responder to non-responder coincident with a switch to the variant SLFNTVATL • [Goulder (1997a)] is a review of immune escape that summarizes this study				
p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Gray (1999)]
	• Epitope SL9: Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T cells • 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL • After HAART, the majority of the epitope-specific CTL were apparently memory cells				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85 Clade A)	SLFNTVATL	HIV-1 infection	human(A*0201)	[Dorrell (1999)]
	• Epitope SL9: CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This epitope is most commonly SLYNTVATL in B subtype, and CTL from the C subtype infection did not recognize B clade Gag or the 3Y form of the epitope, but do recognize the predominant A and C clade form, SLFNTVATL				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Brander (1998a)]
	• Epitope SL9: Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope • Only one subject had CTL against all three epitopes • There was significant heterogeneity in the CTL response to this immunodominant epitope • The overall variation in this epitope among the 17 who had a CTL response and 11 non-HLA A*0201 HIV-1+ individuals was similar, suggesting a lack of immune pressure • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area				
p17(77–85)	p17(77–85 HXB2)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Hay (1999)]
	• Epitope SL9: CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201 • The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted • Despite the initial narrow response to two epitopes, no other CTL responses developed • No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak • A variant of this epitope was observed *in vivo* (`--F----V-`), but this mutation is recognized by SLYNTVATL-specific CTL, and in this case the patient's cells could present the peptide to SLYNTVATL-specific CTL				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Kalams (1999b)]
	• Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV-specific *in-vivo* activated CTL such that by day 260 CTL activities were undetectable • ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant • Sporadic breakthrough in viremia resulted in transient increases in CTLp • Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Spiegel (2000)]
• High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T cell mediated effector activity was not seen • Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy					
p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Larsson (1999)]
• ELISPOT was used to assay the CD8 T cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia vectors in 19 HIV+ people • The highest CTL frequency was directed at epitopes Pol • In A*0201 individuals, higher numbers of spot-forming T cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2					
p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A*0201)	[Goulder (2000a)]
• The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa					
p17(77–85)	p17(77–85 LAI)	SLYNTVATL		human(A*0201)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*0201 epitope					
p17(77–85)	p17(77–85)	SLYNTVATL		human(A*0202)	[Brander & Goulder(2001)]
• C. Brander notes that this epitope can be presented by A*0201 and A*0202					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A*0202)	[Goulder (2000a)]
	• The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa				
p17(77–85)	p17(77–85 LAI)	SLYNTVATL		human(A*0205)	[Brander & Goulder(2001)]
	• C. Brander notes that this epitope can be presented by A*0201 and A*0202				
p17(77–85)	p17( )	SLYNTVATL	HIV-1 exposed seronegative	human(A*0214,A*0201)	[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 • The epitope variants SLYNTVATL and SLFNTVATL were both recognized				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	Gag(77–85)	SLYNTVATL	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 • SLYNTVATL was recognized by 5/16 HLA-A2 patients		
p17(77–85)	p17(77–85)	SLYNTVATL	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(A2)	[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 • Lack of response to SLYNTVATL led the authors to speculate that the immunodominance of this epitope in natural infections may not be recapitulated by vaccine antigen				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Birk (1998)]
	• Epitope SL9: A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Callan (1998)]
	• Epitope SL9: Included as a negative control in a tetramer study of A2-EBV CTL response				
p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A2)	[Wagner (1998a)]
	• Epitope SL9: CTL-specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				
p17(77–85)	p17(77–85 HXB2)	SLYNTVATL	HIV-1 infection	human(A2)	[Collins (1998)]
	• Epitope SL9: Two CTL clones recognize this epitope, but not the NL4–3 form of the epitope SLYNTIAVL • Nef down-regulates MHC class I molecules, which inhibits CTL killing, and this down-regulation can be partially compensated for by adding excess soluble peptide				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Durali (1998)]
	• Epitope SL9: Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype Gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Kundu (1998b)]
	• Epitope SL9: Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients • 1/6 showed increased Env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated • SLYNTVATL is a conserved HLA-A2 epitope included in this study – 3/6 patients had this sequence as their HIV direct sequence, one had the form SLYNTVAVL and all four of these had a detectable CTL response – the other two had either the sequence SLFSAVAVL or SLFSAVAAL and no detectable CTL response				
p17(77–85)	p17(77–85 IIIB)	SLYNTVATL	HIV-1 infection	human(A2)	[Sipsas (1997)]
	• Epitope SL9: HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • SLYNTVAVL, a variant found in HIV-1 MANC, was also recognized • SLFNTVAVL, a variant found in HIV-1 NY5CG, was also recognized				
p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A2)	[Rowland-Jones (1998a)]
	• Epitope SL9: A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is SLfNtvatL • The D subtype consensus is SLyNTvATL				
p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A2)	[Sewell (1997)]
	• Epitope SL9: Naturally occurring variants of this epitope escaped killing and acted as antagonists • The following variants were found in HIV-1 infected patients who mounted a strong response against this epitope: `--F------`, `--F----V-`, `--S------`, `-SF------`, `--L------`, `-----I---`, `-----I-V-`, `--F--I---`, `--F--I-V-`, `--F-A----` • All variants bound to A2 with at least half the affinity of SLYNTVATL except the triple mutant: `--F--I-V-` • Antagonism could be observed at low concentrations, abrogating lysis at an antagonist:agonist ratio of 1:10 – the antagonism was observed in one SLYNTVATL-specific CTL line but not another				
p17(77–85)	p17(77–85 HXB2)	SLYNTVATL	HIV-1 infection	human(A2)	[Yang (1997b)]
	• Epitope SL9: A chimeric universal T cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T cell receptor chain ζ, and transduced into CD8+ cells • The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency • A CTL clone specific for this epitope was used for the comparison				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85)	SLYNTVATL	*in vitro* stimulation	human(A2)	[Stuhler & Schlossman(1997)]
	• Epitope SL9: Keyhole limpit hemocyanin or tetanus toxoid Th epitope co-expression with peptide CTL epitopes on the same APC was required for induction of peptide-specific CTL				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Yang (1996)]
	• Epitope SL9: CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones • The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Yang (1997a)]
	• Epitope SL9: 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				
p17(77–85)	p17(77–85 LAI)	SLYNTVATL	HIV-1 infection	human(A2)	[Parker (1992), Parker (1994)]
	• Epitope SL9: Examined in the context of motifs important for HLA-A2 binding				
p17(77–85)	p17(77–85 LAI)	SLYNTVATL	HIV-1 infection	human(A2)	[McMichael & Walker(1994)]
	• Epitope SL9: Review of HIV CTL epitopes				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Tsomides (1994)]
	• Epitope SL9: CTL clones recognize naturally processed peptide				
p17(77–85)	p17(77–85)	SLYNTVATL	Peptide stimulation *in vitro*	human(A2)	[Stuhler & Schlossman(1997)]
	• Epitope SL9: A three cell-type cluster consisting of APCs, Th, and CTLs is the minimal regulatory unit required for Th cell-dependent induction of CTLs				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Cao (1997)]
	• Epitope SL9: The consensus peptides of B and D clade viruses and some Cs have the sequence SLYNTVATL • The consensus peptide of A, and some C strains have SLFNTVATL, a form that is cross-reactive				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Dyer (1999)]
	• Epitope SL9: CTL-specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Harrer (1998)]
	• Epitope SL9: Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL) • Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape				
p17(77–85)	p17( )	SLYNTVATL	HIV-1 exposure	human(A2, A*0202)	[Rowland-Jones (1998b)]
	• Epitope SL9: HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90–95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, SLFNTVATL, was preferentially recognized by CTL • This epitope was recognized by two different exposed seronegative prostitutes				
p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(B*0201)	[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 moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(B62)	[Goulder (1997a)]
	• Epitope SL9: This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY • As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form				
p17(84–91)	p17(83–91)	TLYCVHQR	HIV-1 infection	human(A11)	[Harrer (1998)]
	• Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL) • Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape • A Q90E substitution resulted in a loss of the ability of the peptide to induce lysis, a R91K substitution was still reactive, and a R91Q substitution show a reduced ability to stimulate lysis				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes that this is an A*1101 epitope				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A11)	[Brander & Walker(1995)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A11)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(87–105)	p17(91–105 SF2)	CRIDVKDTKEALEKIE	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
p17(88–115)	p17(88–115 ARV)	VHQRIEIKDTKEALDK-IEEEQNKSKKKA	HIV-1 infection	human(A2)	[Achour (1990)]
	• B cell epitope HGP-30 also serves as a CTL epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(88–115)	p17(88–115 ARV)	VHQRIEIKDTKEALDK-IEEEQNKSKKKA	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				
p17(90–101)	p17( )	RIDVKDTKEAL	HIV-1 infection	human( )	[Goulder (2000a)]
	• The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A23/68 B45/72 Cw2/16 – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17(91–105)	p17(91–105 SF2)	RIDVKDTKEALEKIE	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI Gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A3, A24, B8, B55				
p17(92–101)	p17(92–101)	IEIKDTKEAL	HIV-1 infection	human(B*4001)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*4001 epitope				
p17(92–101)	p17( )	IEIKDTKEAL	HIV-1 infection	human(B60)	[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-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(93–101)	p17( )	DVKDTKEAL	HIV-1 infection	human( )	[Goulder (2000a)]
	• The CTL-dominant response was focused on this epitope in an HIV+ Caucasian from Boston, who was A1/*0201 B8/63 Cw7/- – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71–85), SALSEGATPQDLNTMLNTVG (p24 41–60), and WEKIRLRPG-GKKKYKLK(p17 16–30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20–36), ELRSLYNTVATLYCV (p17Gag 74–88), SALSEGATPQDLNTMLNTVG (p24 41–60), FRDYVDRFFKTLRAEQA (p24 161–177), and SILDIKQGKEPFRDY (p24 149–164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa			
p17(93–101)	p17(93–101)	EIKDTKEAL	no CTL shown	human(B8)	[DiBrino (1994b)]
	• Examined in the context of motifs important for HLA-B8 binding, predicted epitope based on Achour *et al*.				
p17(93–101)	p17(93–101)	EIKDTKEAL	HIV-1 infection	human(B8)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(93–101)	p17(93–101 LAI)	EIKDTKEAL		human(B8,B60)	[Brander & Walker(1997)]
	• Pers. Comm. from A. Trocha and S. Kalams to C. Brander and B. Walker				
p17(121–132)	p17(121–132 HXB2R)	DTGHSNQVSQNY	HIV-1 infection	human(A33)	[Buseyne (1993b)]
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				
p17(121–132)	Gag(121–132 LAI)	DTGHSNQVSQNY	HIV-1 infection	human(A33)	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag				
p17(124–132)	p17(124–132 LAI)	NSSKVSQNY	HIV-1 or -2 infection	human(B*3501)	[Brander & Goulder(2001)]
	• Noted by Brander to be B*3501 epitope				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(124–132)	p17(124–132 LAI) • Review of HIV CTL epitopes	NSSKVSQNY	HIV-1 infection	human(B35)	[McMichael & Walker(1994)]
p17(124–132)	( ) • 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 moderatly 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	NSSKVSQNY	HIV-1 infection	human(B35)	[Wilson (2000)]
p17(124–132)	p17(124–132) • A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs	NSSKVSQNY	HIV-1 infection	human(B35)	[Birk (1998)]
p17(124–132)	p17(124–132 LAI) • Established by titration	NSSKVSQNY	HIV-1 or -2 infection	human(B35)	[Rowland-Jones (1995)]
p17(124–132)	p17(124–132 LAI) • A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors	NSSKVSQNY	none	human(B35)	[Lalvani (1997)]
p17(124–132)	p17( ) • CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive • HIV-2 version of this epitope is not conserved: PPSGKGGNY, but the CTLs are cross-reactive – this is one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]	NSSKVSQNY		human(B35)	[Rowland-Jones (1999)]