Table 3: **p24**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(8–20)	p24(140–152 IIIB)	GQMVHQAISPRTL	HIV-1 infection	human(Cw3)	[Littaua (1991)]
	• Fine specificity of human Cw3 restricted Gag CTL epitope				
p24(8–27)	p24(140–159)	GQMVHQAISPRTLNAWVKVV	HIV-1 infection	human(B14)	[Musey (1997)]
	• CTL specific for this epitope were found in the peripheral blood but not cervical mucosa of one donor				
p24(11–32)	p24(143–164 BH10)	VHQAISPRTLNAWVKVV-EEKAF	HIV-1 infection	human(Bw57)	[Johnson (1991)]
	• Gag CTL response studied in three individuals				
p24(12–20)	Gag(146–154)	HQAISPRTL	HIV-1 infection	chimpanzee(Patr-B*02)	[Balla-Jhagjhoorsingh (1999b)]
	• Certain HLA-alleles are have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57 • Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS • CTL responses were studied in two HIV-1 infected chimps that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57 • The human HLA protein which presents this Patr-B*02 epitope is HLA-B*5701 but the amino acid sequences in the binding pockets of HLA-B*5701 and Patr-B*02 are distinctive				
p24(13–23)	p24(145–155 LAI)	QAISPRTLNAW		human(A*2501)	[Kurane & West(1998)]
	• C. Brander notes that this is a A*2501 epitope in the 1999 database, Pers. Comm. I. Kurane and K. West				
p24(15–23)	p24(147–155 IIIB)	ISPRTLNAW	HIV-1 infection	human(B*5701, B*5801)	[Goulder (1996b)]
	• Five slow progressors made a response to this epitope, and in two it was the dominant response • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations • Described as B*5701 in C. Brander *et al*., this database, 1999				
p24(15–23)	Gag(147–155 LAI)	ISPRTLNAW	HIV-1 infection	human(B*5701 B*5801)	[Klein (1998)]
	• B57 has been associated with long term non-progression in the Amsterdam cohort • The most pronounced CTL response in HLA B*5701 LTS were to RT and Gag				
p24(16–24)	p24(148–156)	SPRTLNAWV		human(B7,B*0702)	[Brander & Walker(1997b)]
	• Optimal peptide mapped by titration, Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker • Noted in Brander 1999, this database, to be B*0702				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(16–24)	Gag( )	SPRTLNAWV	HIV-1 exposure	human(B7,B*8101)	[Rowland-Jones (1998b)]
	• HIV specific-CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B, and D clade viruses				
p24(19–27)	p24(151–159)	TLNAWVKVV	HIV-1 infection	human(A2)	[Parker (1992), Parker (1994)]
	• Study of sequence motifs preferred for peptide binding to class I HLA-A2				
p24(19–27)	p24( )	TLNAWVKVV	HIV-1 exposure	human(A2, A*0202)	[Rowland-Jones (1998b)]
	• HIV specific-CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
p24(21–40)	p24(153–172 SF2)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A2, B21				
p24(21–40)	p24(153–172 SF2)	NAWVKVVEEKAFSPEVIPMF	HIV-1 Pr55gag VLP with anchored gp120 or V3+CD4 linear domains	Macaca mulatta( )	[Wagner (1998b)]
	• A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains – gag and env specific CTL were stimulated in each case, and Ab response to gag and gp120 and was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner (1998b)] • CTL specific for this epitope could be found both before and after SHIV challenge				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(21–40)	Gag(153–172)	NAWVKVVEEKAFSPEVIPMF	HIV-1 infection	human(B57)	[Brodie (1999)]
• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptively transferring them • 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					
p24(21–42)	p24(153–174 BH10)	NAWVKVVEEKAFSPEVI-PMFSA	HIV-1 infection	human(Bw57)	[Johnson (1991)]
• Gag CTL response studied in three individuals					
p24(28–47)	p24(160–179)	EEKAFSPEVIPMFSALSEGA	HIV-1 infection	human(B27)	[Musey (1997)]
• Cervical and peripheral blood derived CTL clones from an HIV infected woman recognized this epitope					
p24(30–37)	p24(162–170 LAI)	KAFSPEVI	HIV-1 infection	human(B*5703,B57)	
• Described as B*5703 in C. Brander *et al*., this database, 1999, P. Goulder, submitted					
p24(30–40)	p24(162–172 LAI)	KAFSPEVIPMF	HIV-1 infection	human(B*5701)	[Goulder (1996b)]
• This peptide was recognized by CTL from five slow progressors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations • This epitope is highly conserved • Described as B*5701 in C. Brander *et al*., this database, 1999					
p24(30–40)	p24(162–172 LAI)	KAFSPEVIPMF	HIV-1 infection	human(B*5703,B57)	
• Described as B*5703 in C. Brander *et al*., this database, 1999, P. Goulder, submitted					
p24(31–50)	p24(163–182)	AFSPEVIPMFSALSEGATPQ	HIV infection	human( )	[Lieberman (1995)]
• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide					
p24(31–50)	p24(163–182 SF2)	AFSPEVIPMFSALSEGATPQ	HIV infection	human( )	[Lieberman (1997a)]
• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A2, B21					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(31–50)	p24(163–182 SF2)	AFSPEVIPMFSALSEGATPQ	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
p24(35–43)	p24(167–175 LAI)	EVIPMFSAL		human(A*2601)	[Goulder (1996a)]
	• Identified as optimal epitope within Gag sequence AFSPEVIPMFSALSEGATPQ • Relatively conserved epitope within B clade and in other clades • Suspected binding motif for HLA-A26 includes T or V anchor at position 2, negative charge at position 1 • C. Brander notes that this is a A*2601 epitope in the 1999 database				
p24(36–43)	p24(168–175 LAI)	VIPMFSAL		human(Cw*0102,Cw1)	[Goulder (1997c)]
p24(37–52)	p24(169–184 LAI)	IPMFSALSEGATPQDL	HIV-1 infection	human(B12(44))	[Buseyne (1993b)]
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV infected people				
p24(37–52)	Gag(169–184 LAI)	IPMFSALSEGATPQDL	HIV-1 infection	human(B12)	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activities against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic • Patient EM17 (CDC P2A+C+D2), had a CTL response to two epitopes in Gag				
p24(41–60)	p24(173–192 SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 subjects had CTL that could recognize vaccinia expressed LAI gag • Three of these 12 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B7, B14; and HLA-A2, A3, B14, B44				
p24(41–60)	p24(173–192 SF2)	SALSEGATPQDLNTMLNTVG	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(41–60)	p24(179–188 Clade A)	SALSEGATPQDLNMMLNIVG	HIV-1 infection	human(B*8101)	[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 CTL epitope is presented by B*8101 in one of the patients with an A subtype infection – B*8101 is a newly discovered HLA allele found in Africans, and the epitope has yet to be mapped precisely • This epitope is distinct in subtype A relative to subtypes B, C, and D which share the dominant sequence: SALSEGATPQDLNTML-NTVG					
p24(41–62)	p24(173–194 BH10)	SALSEGATPQDLNTMLN-TVGGH	HIV-1 infection	human(B14)	[Johnson (1991)]
• Gag CTL response studied in three individuals					
p24(44–52)	p24(176–184)	SEGATPQDL		human(B*4001,B60)	
• Noted by C. Brander *et al*., this database 1999, to be a B*4001,B60 epitope, Pers. Comm. A. Trocha and S. Kalams					
p24(47–58)	p24(181–192)	CTPYDINQMLNC	HIV-2 infection	human(B58)	[Bertoletti(1998)]
• HIV-2 epitope defined from an infection in the Gambia, Bertoletti, Pers. Comm.					
p24(48–56)	p24( )	TPQDLNQML		human(B53)	[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: TPYDINQML, no cross-reactivity, [Gotch (1993)]					
p24(48–56)	p24(180–188 IIIB)	TPQDLNTML	HIV-1 infection	human(B7,B*0702)	[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 • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope • Noted in Brander 1999, this database, to be B*0702					
p24(48–56)	p24(180–188 LAI)	TPQDLNTML	HIV-1 infection	human(B*8101,B81)	
• Defined as B*8101 in C. Brander, 1999, this database, P. Goulder, submitted					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(48–56)	Gag(173–181 HIV-2)	TPYDINQML	HIV-2	human(B*5301,B53)	[Gotch (1993)]
	• Noted in Brander 1999, this database, to be B*5301, B. Wilkes and D. Ruhl, Pers. Comm.				
p24(49–57)	p24(181–189 LAI)	PQDLNTMLN	HIV-1 infection	human(B14, Cw8)	[Lubaki (1997)]
	• 82 HIV-1-specific CTL clones from 5 long term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • Despite this being a well defined conserved epitope, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 RAEQASQEV • Christian Brander notes that B14 and Cw8 are in linkage disequilibrium, and that this epitope may be Cw8				
p24(51–59)	p24(183–191 LAI)	DLNTMLNTV	HIV-1 infection	human(C*0802, Cw8)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes – defined by B14 motif found within a larger peptide • Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication) • Described as C*0802 by C. Brander *et al*., 1999, this database				
p24(51–59)	p24(183–191 LAI)	DLNTMLNTV	HIV-1 infection	human(B14, Cw8)	[Nixon (1988), Johnson (1992)]
	• Recent evidence indicates this is a Cw8 eptiope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24(51–59)	p24( )	DLNTMLNTV	HIV-1 exposure	human(B14, Cw8)	[Rowland-Jones (1998a)]
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is identical to the B clade epitope • The D subtype consensus is dLNmMLNiV • Recent evidence indicates this is a Cw8 eptiope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(51–59)	p24( )	DLNTMLNTV	HIV-1 exposure	human(Cw8, B*1402)	[Rowland-Jones (1998b)]
	• HIV specific-CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, DLNNMLNIV, was preferentially recognized by CTL • Recent evidence indicates this is a Cw8 eptiope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)				
p24(51–70)	p24(183–202 SF2)	DLNTMLNTVGGHQAAMQMLK	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A26, A30, B38				
p24(61–69)	p24(193–201 LAI)	GHQAAMQML		human(B*3901,B39)	[Kurane & West(1998)]
	• Optimal peptide defined by titration, noted by C. Brander *et al*., this database 1999, to be a B*3901 epitope, I. Kurane and K. West, pers. comm.				
p24(61–71)	p24(193–203 BRU)	GHQAAMQMLKE	HIV-1 infection	human(A2)	[Claverie (1988)]
	• 1 of 4 epitopes first predicted, then shown to stimulate HLA-A2 restricted CTL line				
p24(61–80)	p24(193–212 SF2)	GHQAAMQMKETINEEAAEW	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A26, A30, B38				
p24(61–82)	p24(193–214 BH10)	GHQAAMQMLKETINEEA-AEWDR	HIV-1 infection	human(Bw52)	[Johnson (1991)]
	• Gag CTL response studied in three individuals				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(62–70)	p24(194–202 LAI)	HQAAMQMLK		human(B52)	[Brander & Walker(1997a)]
• P. Goulder, pers. comm.					
p24(65–73)	p24(199–207 SF2)	AMQMLKETI	DNA plasmid immunization	murine(H-2K^d)	[Selby (1997)]
• Murine CTL response to peptide observed after immunization with DNA plasmid containing HIV-1 (SF2) p55gag gene regulated by bacteriophage T7 promoter					
• CTL response required coadministration of rec vaccinia virus expressing T7 RNA polymerase or T7 RNA polymerase soluble protein					
p24(65–73)	p24(199–207 SF2)	AMQMLKETI	vaccinia expressing gag and pol	murine(H-2K^d)	[Doe & Walker(1997)]
• Immunodominant murine CTL response to this peptide observed after immunization with vaccine VVgagpol					
• Optimal peptide was defined					
p24(69–86)	Gag(201–218 LAI)	LKETINEEAAEWDRVPV	HIV-1 infection	human( )	[Buseyne (1993a)]
• Vertical transmission of HIV ranges from 13% to 39%					
• Primary assays showed cytotoxic activities 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 EM28 (CDC P2A) had a CTL response to four epitopes in Gag					
p24(71–80)	p24(203–212)	ETINEEAAEW	HIV-1 infection	human(A*2501)	[Klenerman (1996)]
• The epitope was defined through direct stimulation of PBMC with 20-mer peptides					
• It is in a conserved region, ETINEEAAEW is found in most B, D, and E subtype isolates					
• DTINEEAAEW is found in A and some D subtype sequences					
• C. Brander notes that this is a A*2501 epitope in the 1999 database					
p24(71–80)	p24(203–212)	ETINEEAAEW	HIV-1 infection	human(A*2501)	[van Baalen (1996)]
• Conserved between B and D subtypes, variable in other clades; a consensus of clades A,C, F, G, and H and a peptide of HIV-2ROD over this region were not recognized by CTL recognizing the index peptide					
• C. Brander notes that this is a A*2501 epitope in the 1999 database					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(71–80)	p24( )	ETINEEAAEW		human(A25)	[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: EIINEEAAEW, no cross-reactivity, [van Baalen (1996)]				
p24(71–90)	p24(203–222 SF2)	ETINEEAAEWDRVHPVVHAGP	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A2, B21				
p24(83–92)	p24(215–223 IIIB)	VHPVHAGPIA	HIV-1 infection	human(B55)	[Sipsas (1997)]
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • LHPVHAGPVA, a variant found in HIV-1 PH136, was also recognized • LHPVHAGPIA, a variant found in HIV-1 RF, was also recognized • LHPVHAGPIT, a variant found in HIV-1 MN, was also recognized • LHPAQAGPIA, a variant found in HIV-1 JH3, was recognized at high peptide concentrations				
p24(87–101)	p24(219–233 BRU)	HAGPIAPGQMREPRG	HIV-1 infection	human(A2)	[Claverie (1988)]
	• 1 of 4 epitopes predicted then shown to stimulate HLA-A2 restricted CTL line				
p24(87–101)	Gag(219–233 LAI)	HAGPIAPGQMREPRG	HIV-1 infection	human( )	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activities 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 EM28 (CDC P2A) had a CTL response to four epitopes in Gag				
p24(91–110)	p24(223–242 SF2)	IAPGQMREPRGSDIAGTTST	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A2, A24, B13, B35				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(101–120)	p24(233–252 SF2)	GSDIAGTTSTLQEQIGWMTN	HIV-1 infection	human( )	[Lieberman (1997a)]
• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A26, A30, B38					
p24(108–117)	p24(240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human(B*5701, B*5801)	[Goulder (1996b)]
• Response to this epitope was found in 4 slow progressing HLA-B*57 individuals, in 2 it was dominant or very strong • For one donor (from Zimbabwe) this was defined as the optimal peptide • This epitope can be presented in the context of the closely related HLA molecules B*5801 and B*57 • Described as B*5701 in C. Brander *et al*., this database, 1999					
p24(108–117)	p24(241–250)	TSTVEEQQIW	HIV-2 infection	human(B*5801,B58)	[Bertoletti(1998)]
• HIV-2 epitope defined from an infection in the Gambia, Bertoletti, Pers. Comm. • All HIV-2 sequences from the database are TSTVEEQIQW in this region, not TSTVEEQQW as in the paper • This epitope is specified as B*5801 in C. Brander *et al*., 1999, this database					
p24(108–117)	p24( )	TSTLQEQIGW	HIV exposure	human(B58)	[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: TSTVEEQIQW, CTL are cross-reactive, [Bertoletti (1998)]					
p24(108–117)	p24(233–252)	TSTLQEQIGW	HIV-1 infection	human(B57)	[Bernard (1998)]
• This study focuses on six rare long term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL was found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XSXXXXXXXW is a B57 binding motif, and CTL activity against TSTLQEQIGW has been found in two other B57 long term non-progressors					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(108–117)	p24(240–249)	TSTLQEQIGW	HIV-2 infection	human(B58)	[Bertoletti (1998)]
• CTL responses in HLA-B*5801 positive HIV-2 infected individuals have a dominant response to Gag and tolerate extensive substitution, thus HLA-B*5801+ individuals may have an enhanced potential for cross-protection between HIV-1 and HIV-2 • This can be an immunodominant eptiope in HLA-B57 and B*5801 infected individuals, and is associated with long term non-progression [Goulder (1996b)] • HIV-2 sequence: HIV-2 ROD has the epitope sequence TSTVEEQIQW, and the CTL from a person infected with HIV-2 was cross-reactive with HIV-1 epitopes • The epitope is TSTLQEQIGW in HIV-1 B clade, and TSTVEEQIQW in HIV-2 ROD • HLA B*5801 and B35 may preferentially select HIV-1 and HIV-2 cross-reactive epitopes					
p24(109–117)	Gag(241–249 LAI)	STLQEQIGW	HIV-1 infection	human(B*5701 B*5801)	[Klein (1998)]
• B57 has been associated with long term non-progression in the Amsterdam cohort • The most pronounced CTL response in HLA B*5701 LTS were to RT and Gag					
p24(121–135)	p24(253–267)	NPPIPVGEIYKRWII	HIV-1 infection	human(B8)	[Gotch (1990)]
• High frequency of memory and effector Gag specific CTL					
p24(121–135)	p24(255–274 SF2)	NPPIPVGEIYKRWII	HIV-1 infection	human(B8)	[Phillips (1991), Goulder (1997a)]
• Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time, in people with the appropriate HLA types • [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					
p24(121–140)	p24(253–272)	NPPIPVGEIYKRWIILGLNK	HIV infection	human( )	[Lieberman (1995)]
• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide					
p24(121–140)	p24(253–272 SF2)	NPPIPVGEIYKRWIILGLNK	HIV infection	human( )	[Lieberman (1997a)]
• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 subjects had CTL that could recognize vaccinia expressed LAI gag • Two of these 12 had CTL response to this peptide • The responding subjects were HLA-A2, A3, B8, B62, and HLA-A1, B8, B18					
p24(121–140)	p24(253–272 SF2)	NPPIPGEIKRWIILGNIK	HIV-1 infection	human( )	[Lieberman (1997b)]
• CTL expanded *ex vivo* were later infused into HIV-1 infected patients					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(121–140)	p24(255–274 SF2)	NPPIPVGEIYKRWIILGLNK	HIV-1 infection	human( )	[van Baalen (1993)]
• Gag CTL epitope precursor frequencies were estimated and peptide mapping was performed					
p24(121–142)	p24(253–274 BH10)	NPPIPVGEIYKRWIILGLNKIV	HIV-1 infection	human(B8)	[Johnson (1991)]
• Gag CTL response studied in three individuals					
p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	HIV-1 or -2 infection	human(B*3501,B35)	[Rowland-Jones (1995)]
• Defined as minimal peptide by titration curve, PPIPVGEIY and HIV-2 form NPVPVGNIY are also recognized					
• Noted in Brander 1999, this database, to be B*3501					
p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	none	human(B35)	[Lalvani (1997)]
• 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					
p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	HIV-1 infection	human(B35)	[McMichael & Walker(1994)]
• Review of HIV CTL epitopes					
p24(122–130)	p24( )	PPIPVGEIY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998b)]
• HIV specific-CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection					
• Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world					
• Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes					
• This epitope is conserved among B and D clade viruses					
• The Clade A version of the epitope, PPIPVGDIY, was preferentially recognized by CTL					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(122–130)	p24( )	PPIPVGDIY		human(B35)	[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 version of this epitope is not conserved: NPVPVGNIY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]				
p24(122–130)	p24(245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human(B*3501)	[Rowland-Jones (1995)]
p24(124–138)	p24(256–270 LAI)	IPVGEIYKRWIILGL	HIV-1 infection	human(B8)	[Buseyne (1993b)]
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV infected people				
p24(124–138)	Gag(256–270 LAI)	IPVEGEIYKRWIILGL	HIV-1 infection	human(B8)	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activities 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 • Two children, EM16 (CDC P2A+D2) and EM18 (CDC P2A), had a CTL response to this epitope, and it was shown to be presented by B8 in EM18				
p24(127–135)	p24(261–269)	GEIYKRWII	HIV-1 infection	human(B8)	[Sutton (1993)]
	• Predicted epitope based on B8 binding motifs, from larger peptide NPPIPVGEIYKRWII				
p24(127–135)	p24(259–267 LAI)	GEIYKRWII	HIV-1 infection	human(B8)	[Klenerman (1994)]
	• Naturally occurring variant GDIYKRWII may act as antagonist				
p24(127–135)	p24(259–267)	GEIYKRWII	HIV-1 infection	human(B8)	[Nowak (1995)]
	• Longitudinal study of CTL response and study of immune escape – GDIYKRWII could also stimulate CTL, reactivity fluctuated				
p24(127–135)	p24(259–267)	GEIYKRWII	HIV-1 infection	human(B8)	[McAdam (1995)]
	• Equivalent sequence GDIYKRWII also recognized by CTL from some donors				
p24(127–135)	p24(259–267 SF2)	GDIYKRWII	HIV-1 infection	human(B*0801)	[McAdam (1998)]
	• GDIYKRWII specific CTL clone also recognized GEIYKRWII				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(127–135)	p24(259–267)	GEIYKRWII	*in vitro* stimulation	human(B8)	[Zarling (1999)]
	• HIV and influenza virus CTL epitopes were used to study the relative abilities of different antigen presenting cells (macrophages, immature dendritic cells (iDC) and mature dendritic cells (mDC)) to prime CD8+ lymphocytes • Both types of dendritic cells were superior to macrophages in the primary stimulation of CTL				
p24(128–135)	p24(260–267 LAI)	EIYKRWII		human(B*0801,B8)	[Goulder (1997g)]
	• Defined in a study of the B8 binding motif • Noted in Brander 1999, this database, to be B*0801				
p24(129–136)	p24(263–270 SF2)	IYKRWIIL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins, (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • IYKRWIIL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
p24(129–138)	p24(263–272 SF2)	IYKRWIILGL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
	• Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins, (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • IYKRWIILGL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
p24(130–148)	p24(265–280 BRU)	YKRWIILGLNKIVRMYSPT	HIV-1 infection	human(B27)	[Dadaglio (1991)]
	• Used as a positive control for HLA specificity				
p24(131–139)	Gag(265–273)	KRWIILGLN	HIV-1 infection	chimpanzee(Patr-B*03)	[Balla-Jhagjhoorsingh (1999b)]
	• Certain HLA-alleles are have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57 • Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS • CTL responses were studied in two HIV-1 infected chimps that have strong CTL responses, and they were found to respond to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57 • The human HLA protein which presents this Patr-B*03 epitope is HLA B*2705 but the amino acid sequences in the binding pockets of HLA-B*2705 and Patr-B*03 are distinctive				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(131–140)	p24(260–269 HIV-2)	RRWIQLGLQK		human(B*2703,B27)	[Brander & Walker(1997a)]
	• HIV-2, HLA-B*2703, S. Rowland-Jones, Pers. Comm. • Noted in Brander 1999, this database, to be B*2703, Pers. Comm. S. Rowland-Jones				
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[Fan (1997)]
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				
p24(131–140)	p24(263–272 SF2)	KRWIILGLNK	HIV-1 infection	human(B*27)	[McAdam (1998)]
	• Epitope invariant across clades A, B, C, and D				
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[Wilson (1998a)]
	• 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				
p24(131–140)	p24( )	KRWIILGLNK	HIV infection	human(B27)	[Rowland-Jones (1997)]
	• Described in this review as the first identified HIV CTL epitope				
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B*2705,B27)	[Goulder (1997e), Goulder (1997a)]
	• HLA-B*2705 is associated with slow HIV disease progression • 11/11 HLA-B*2705 donors make a response to this epitope, usually an immunodominant response • This is a highly conserved epitope • The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position • [Goulder (1997a)] is a review on CTL immune escape that discusses this epitope in the context of the difficulty in detection of immune escape – KRWIILGLNK and a R2K change, KKWIILGLNK, show little difference in titration curves, yet the K2 variants fail to bind to targets for more than 1 hour, while the R2 form can sensitize lysis by CTL for over 24 hours – minigene transfection experiments confirmed the importance of this for the CTL response				
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B*2705,B27)	[Buseyne (1993b)]
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV infected people • Noted in Brander 1999, this database, to be B*2705, Pers. Comm.				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes				
p24(131–140)	p24(263–272)	KRWIIMGLNK	HIV-1 infection	human(B27)	[Klenerman (1994)]
	• Naturally occurring variant KRWIILGLNK may act as antagonist				
p24(131–140)	p24(263–272)	KRWIIMGLNK	HIV-1 infection	human(B27)	[Klenerman (1995)]
	• Naturally occurring variant KRWIILGLNK may act as antagonist				
p24(131–140)	p24(265–274)	KRWIILGLNK	HIV infection	human(B27)	[Moss (1995)]
	• In one individual, TCR usage changed over time indicating that new populations of CTL can be recruited • TCR usage showed a CTL clonal response to this epitope that persisted over 5 years • CTL clones specific for HIV epitopes may represent between 0.2 and 1% of the total CD8+ population of T cells				
p24(131–140)	p24(265–276)	KRWIILGLNK		human(B27)	[Carreno (1992)]
	• Included in HLA-B27 binding peptide competition study				
p24(131–140)	p24(265–274 SF2)	KRWIILGLNK	HIV-1 infection	human(B27)	[Phillips (1991), Goulder (1997a)]
	• Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to B8 epitope • [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				
p24(131–140)	p24(263–272)	KRWIILGLNK	HIV-1 infection	human(B27)	[Nietfeld (1995), Goulder (1997a)]
	• Single point mutations were introduced and viral viability and CTL recognition tested – an Arg to Lys change at anchor position P2 abrogates binding to B27, but doesn‘t change viral viability *in vitro* • [Goulder (1997a)] is a review of immune escape that summarizes this study				
p24(131–140)	p24(263–272)	KRWIIMGNK	HIV-1 infection	human(B27)	[Nowak (1995)]
	• Longitudinal study of CTL response and immune escape – the form KRWIILGNK was also found, and both forms stimulate CTL				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(131–140)	p24(263–272)	KRWIILGNK	HIV-1 infection	human(B27)	[Durali (1998)]
	• 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 • One of the patients was shown to react to this epitope: KRWIILGNK				
p24(131–140)	p24(263–272)	KRWIIMGLNK	HIV-1 infection	human(B27)	[Goulder (1997f), Goulder (1997a)]
	• Six HLA-B27 donors studied make a strong response to this epitope • In 4/6 cases, this was the immunodominant or only CTL response • Two of the cases had an epitope switch to the form KKWIIMGLNK during a period of rapid decline to AIDS, following their asymptomatic period • The arginine to lysine switch is in an anchor residue, and results in immune escape due to severely diminished binding to the B27 molecule • [Goulder (1997a)] is a review of immune escape that summarizes this study in the context of CTL escape to fixation				
p24(131–140)	p24( )	KRWIILGLNK		human(B27)	[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: RRWIQLGLQK – this epitope was not HIV-1 and HIV-2 cross-reactive				
p24(131–140)	Gag( )	KRWILGLNK	none, computer prediction	(B27)	[Schafer (1998)]
	• This study uses EpiMatrix for T-cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using a T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule • 2 of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV • This peptide sequence is not conserved between clades, but is found in most B clade isolates				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(131–140)	p24(263–282)	KRWIILGLNK	HIV-1 infection	human(B27)	[Bernard (1998)]
	• This study focuses on six rare long term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL was found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XRXXXXXXXK is a B*2705 binding motif				
p24(131–140)	Gag(263–272 LAI)	KRWILLGLNK	HIV-1 infection	human( )	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activities 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 EM28 (CDC P2A) had a CTL response to four epitopes in Gag				
p24(131–142)	p24(265–276)	KRWIILGLNKIV	no CTL shown	human(B27)	[Jardetzky (1991)]
	• Epitope examined in the context of peptide binding to HLA-B27				
p24(131–142)	p24(263–274 LAI)	KRWIILGLNKIV	HIV-1 infection	human(B27)	[Fan (1997)]
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				
p24(131–145)	p24(266–277)	KRWIILGLNKIVRMY	rec gag-vaccinia	human(B27)	[Nixon (1988)]
	• Gag CTL epitope mapped with rec gag-vaccinia and synthetic peptides • This was the first HIV-1 epitope to be mapped				
p24(131–145)	p24(263–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human(A33)	[Buseyne (1993b)]
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV infected people				
p24(131–145)	p24(266–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human(B27)	[Meyerhans (1991)]
	• Longitudinal study showing persistence of epitope despite CTL activity				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(131–145)	p24(265–279)	KRWIILGLNKIVRMY	HIV-1 infection	human(B27)	[Nixon (1990), Rowland-Jones (1999)]
	• HIV-1 and HIV-2 cross-reactive CTL clone, highly conserved epitope • Reviewed in Rowland-Jones99, notes that it did not appear cross-reactive with HIV-2 in Rowland-Jones98, HIV-2 form: RRWIQL-GLQK				
p24(131–146)	p24(265–279)	KRWIILGLNKIVRMYC	HIV-1 infection	human(B27)	[Bouillot (1989)]
	• HLA-B27 restricted epitope also binds to HLA-A2 and HLA-B37 in solid phase assay				
p24(131–150)	p24(265–284 SF2)	KRWIILGLNKIVRMYSPTSI	HIV-1 infection	human(Bw62?)	[van Baalen (1993)]
	• Gag CTL epitope precursor frequencies estimated				
p24(131–150)	p24(263–282 SF2)	KRWIILGLNKIVRMYSPTSI	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 subjects had CTL that could recognize vaccinia expressed LAI gag • One of these 12 A-2 had CTL response to this peptide • The responding subject was HLA-A3, A32, B51, B62				
p24(131–152)	p24(263–284 BH10)	KRWIILGLNKIVRMYSPTSILD	HIV-1 infection	human(Bw62)	[Johnson (1991)]
	• Gag CTL response studied in three individuals				
p24(134–143)	p24( )	IILGLNKIVR	HIV-1 exposure	human(A33)	[Rowland-Jones (1998b)]
	• HIV specific-CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
p24(136–145)	p24(268–277 LAI)	LGLNKIVRMY	Predicted from larger peptide	human(Bw62)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • Also P. Johnson, Pers. Comm.				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(136–146)	p24(271–281)	LGLNKIVRMYS	HIV-1 infection	human(B62)	[Lubaki (1997)]
• 82 HIV-1-specific CTL clones from 5 long term non-progressors were isolated and analyzed for breadth of 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 B62+ had CTL that recognized this peptide, p17 KIRLRPGGKKKYKL, and one additional unknown epitope • The two clones that recognized this epitope used two different Vβ genes, further demonstrating a polyclonal response					
p24(137–145)	p24(272–280 LAI)	GLNKIVRMY	HIV-1 infection	human(B62,B*1501)	[Goulder (1997a)]
• 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 dominanted 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 • Noted in Brander 1999, this database, to be B*1501, Pers. Comm. P. Goulder					
p24(143–150)	p24(273–283 IIIB)	RMYSPTSI	HIV-1 infection	human(B*5201,B52)	[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 • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope • Noted in Brander 1999, this database, to be B*5201, B. Wilkes and D. Ruhl, Pers. Comm.					
p24(151–170)	p24(283–302 SF2)	LDIRQGPKEPFRDYVDRFYK	HIV-1 infection	human( )	[McAdam (1998)]
p24(155–177)	p24(287–309)	QGPKEPFRDYVDRFYKT-LRAEQA	Peptide vaccination	murine( )	[Nakamura (1997)]
• Mice immunized with this synthetic peptide generated specific CTLs, a proliferative response, and antibodies • The amino acids shown in the epitope field were based on the numbering provided by Nakamura *et al*., and may not be correct • The CTL epitope was shown to be located in positions 291-300					
p24(157–178)	p24(290–309)	PKEPFRDYVDRFYKTLRAEQAS	HIV-1 infection	human(B14)	[Musey (1997)]
• Cervical and peripheral blood derived CTL clones from an HIV infected woman recognized this epitope					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(161–170)	p24( )	FRDYVDRFYK	HIV-1 infection	human(B*1801)	[Ogg (1998a)]
	• Noted in Brander 1999, this database, to be B*1801, FRDYVDRFY				
p24(161–180)	p24(293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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-A2, A3, B8, B62				
p24(161–180)	p24(293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
p24(161–180)	p24(293–312 SF2)	FRDYVDRFYKTLRAEQASQD	HIV-1 infection	human(B71)	[McAdam (1998)]
p24(162–172)	p24(293–312 LAI)	RDYVDRFYKTL	HIV-1 infection	human(B*4402,B44,A26 or B70)	[Ogg (1998a)]
	• Noted in C. Brander *et al*., 1999, this database, to be B*4402				
p24(162–172)	p24(296–306 Clade A)	RDYVDRFFKTL	HIV-1 infection	human(A*2402)	[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 is similar to the A24 DYVDRYFKT epitope found for B subtype, but CTL from this A subtype infection required the additional Arg – the B clade sequence change from F to Y diminished CTL reactivity • C. Brander notes that this is a A*2402 epitope in the 1999 database				
p24(164–172)	p24(298–306 Clade A)	YVDRFFKTL	HIV-1 infection	human(A26 or B70)	[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 CTL epitope is conserved in A and C subtype, and B clade sequences tend to have a change from F to Y, YVDRFYKTL – both variants showed strong CTL reactivity • CTL reacted with targets presenting either in the context A26 or B70 – the epitope has the HLA-26 motif of Val at position 2 and Leu at the carboxy terminus, and the B70 anchor residue motif is unknown				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(166–174)	p24(298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human(B14)	[Wilson (1996)]
• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • DRFYKILRA, a naturally occurring variant, was found in mother, and is recognized although less reactive • DQFYKTLRA, a naturally occurring variant, was found in infant and is not recognized					
p24(166–174)	p24(298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human(B14)	[Cao (1997)]
• The consensus peptide for clades B and D is DRFYKTLRA • The consensus peptide for clades A and C is DRFFKTLRA and it is equally reactive					
p24(166–174)	p24(298–306 HXB2)	DRFYKTLRA	HIV-1 infection	human(B14)	[Yang (1997b)]
• 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 transducing into CD8+ cells • The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* was comparable to the natural occuring 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					
p24(166–174)	p24( )	DRFWKTLRA	HIV-1 exposure	human(B14)	[Rowland-Jones (1998a)]
• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The D subtype consensus is identical to the B clade epitope • The A subtype consensus is drFfKtLRA					
p24(166–174)	p24(298–306 LAI)	DRFYKTLRA	HIV-1 infection	human(B*1402,B14)	[Harrer (1996b)]
• Noted in Brander 1999, this database, to be B*1402					
p24(166–174)	p24(298–306)	DRFYKTLRA	HIV-1 infection	human(B14)	[Yang (1996)]
• CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones • The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production					
p24(166–174)	p24(298–306)	DRFYKTLRA	HIV-1 infection	human(B14)	[Yang (1997a)]
• CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo* • CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation • CTL suppress HIV replication more efficiently in HLA-matched cells					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(166–174)	p24(298–306)	DRFYKTLRA	*in vitro* stimulation	human(B14)	[Zarling (1999)]
• HIV and influenza virus CTL epitopes were used to study the relative abilities of different antigen presenting cells (macrophages, immature dendritic cells (iDC) and mature dendritic cells (mDC)) to prime CD8+ lymphocytes • Both types of dendritic cells were superior to macrophages in the primary stimulation of CTL					
p24(166–174)	p24( )	DRFYKTLRA	HIV-1 exposure	human(B14, B*1402)	[Rowland-Jones (1998b)]
• HIV specific-CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope, DRFFKLTRA , was preferentially recognized by CTL • This epitope was recognized by two different exposed and uninfected prostitutes					
p24(166–174)	p24( )	DRFYKLTRA		human(B14)	[Rowland-Jones (1999)]
• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: DRFYKSLRA is cross-reactive, [T (1993)]					
p24(166–174)	p24(298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human(B14)	[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 • DRFYKILRA and DQFYKTLRA were escape mutants					
p24(166–175)	p24(298–306 HX10)	DRFYKTLRAE	HIV-1 infection	human(B14)	[Wagner (1999)]
• The immunodominant CTL response in a long term survivor was to this highly conserved and functionally relevant epitope • By testing mutations in an HXB2 background, it was found that all mutations within the epitope that abrogated CTL recognition also abolished viral infectivity • The epitope in this study overlaps the major homology region for which highly conserved residues exist in all known lenti- and onco-viruses and yeast transposons • Patient was part of the study in [Harrer (1996a)]					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 infection	human(Cw8)	[Johnson (1991)]
• Originally reported as HLA-B14 restricted, but subsequently found not to be presented by cells transfected with B14 • Thought to be HLA-Cw8 restricted (C. Brander and B. Walker)					
p24(173–181)	p24( )	RAEQASQEV	HIV-1 exposure	human(Cw8)	[Rowland-Jones (1998a)]
• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A subtype consensus is RAeQAtQEV • The D subtype consensus is RAEQsQdV • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)					
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 infection	human(B14?)	[Price (1995)]
• Study of cytokines released by HIV-1 specific activated CTL • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)					
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 infection	human( )	[Lubaki (1997)]
• 82 HIV-1-specific CTL clones from 5 long term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • Despite this being a well defined conserved epitope, and thought to be presented by B14, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 PQDLNTMLN • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)					
p24(174–184)	p24(306–316 LAI)	AEQASQDVKNW		human(B*4402,B44)	[Brander & Walker(1997b)]
• Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker, C Brander *et al*., this database, 1999					
p24(174–184)	Gag(306–316)	AEQASQEVKNW	HIV-1 infection	human(B44)	[Brodie (1999)]
• The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptively transferring them • 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(175–186)	p24(307–318)	EQASQEVKNWMT	HIV-1 infection	human(B44)	[Quayle (1998)]
	• HIV is found in semen both as cell-associated and cell-free forms, and HIV-specific CTL could be found in the semen of 5/5 men with CD4 greater than 500 – 3 of the men were analyzed in detail and had broad CTL to gag, env and pol • Two CTL lines from one donor recognized this eptiope • Isolation of CTLs specific to HIV in both male and femal urinal tracts provide evidence that virus-specific lymphocytes come from the urogenital mucosa, and the authors speculate that CTL in mucosal tissues may be correlated with lower viral load in semen and reduced transmission				
p24(176–184)	p24(309–317 LAI)	QASQEVKNW	HIV-1 infection	human(B*5701)	[Goulder (1996b)]
	• Recognition of this peptide by two long term non-progressors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations • Described as B*5701 in C. Brander *et al*., this database, 1999				
p24(176–184)	p24(308–316 LAI)	QASQEVKNW	HIV-1 infection	human(B53)	[Buseyne (1997)]
	• Minimal sequence determined through epitope mapping • This is a relatively conserved epitope • HLA-Cw*0401 was defined as the restricting element, but cells that carry Cw*0401 varied in their ability to present this epitope – this could be the result of diminished cell-surface expression of Cw*0401 in some cells • The HLA presenting molecule for this epitope was originally described as Cw*0401, but subsequent experiments with a HLAB53+C4- cell line and with C1R cells transfected with HLA-B53 have shown that the HLA restricting element is HLA-B53 (Pers. Comm., Dr. Florence Buseyne, 2000)				
p24(181–190)	p24(313–322 LAI)	VKNWMTETLL		human(B8)	[Brander & Walker(1997a)]
	• P. Johnson pers. comm.				
p24(191–205)	p24(323–337)	VQNANPDCKTILKAL	HIV-1 infection	human(B8)	[Nixon & McMichael(1991)]
	• Two CTL epitopes defined (see also p17(21-35))				
p24(191–205)	p24(325–339 SF2)	VQNANPDCKTILKAL	HIV-1 infection	human(B8)	[Phillips (1991), Goulder (1997a)]
	• Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to the B8 epitopes, which varied over time, in people with the appropriate HLA types • [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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(191–210)	p24(323–342 SF2)	VQNANPDCKTILKALGPAAT	HIV-1 infection	human( )	[Lieberman (1997a)]
• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 subjects had CTL that could recognize vaccinia expressed LAI gag • Three of these 12 had CTL response to this peptide • The responding subjects were HLA-A3, A24, B8, B55; HLA-A1, A11, B8, B27					
p24(191–210)	p24(323–342 SF2)	VQNANPDCKTILKALGPAAT	HIV-1 infection	human( )	[Lieberman (1997b)]
• CTL expanded *ex vivo* were later infused into HIV-1 infected patients					
p24(193–201)	Gag(327–335 SF2)	NANPDCKTI	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]
• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS while HLA-B35,-B8,-B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996; Lancet 22:1187, 1986; Hum Immunol 22:73, 1988; Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, NANPDCKTI is conserved					
p24(193–201)	p24(324–335 IIIB)	NANPDCKTI	HIV-1 infection	human(B51)	[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 • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope					
p24(195–202)	p24(323–342)	NPDCKTIL	HIV-1 infection	human(B35)	[Bernard (1998)]
• This study focuses on six rare long term survivor HIV-infected people who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL was found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XPXXXXXL is a B35 binding motif					
p24(197–205)	p24(329–337 LAI)	DCKTILKAL		human(B*0801,B8)	[Sutton (1993)]
• Predicted epitope based on B8 binding motifs, from larger peptide VQNANPDCKTILKAL • Noted in Brander 1999, this database, to be B*0801					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(197–205)	p24(329–337)	DCKTILKAL	HIV-1 infection	human(B8)	[Nowak (1995)]
	• In a longitudinal study of CTL response and immune escape – the variant DCRTILKAL was also found, binds to B8, but is not recognized				
p24(197–205)	p24(329–337)	DCKTILKAL		human(B8)	[McAdam (1995)]
	• Defined as minimal epitope by titration and binding studies				
p24(197–205)	p24(197–205)	DCKTILKAL		human(B8)	[Goulder (1997g)]
	• Included in a study of the B8 binding motif				
p24(211–230)	p24(345–364 SF2)	LEEMMTACQGVGGPGHKARV	HIV-1 infection	human( )	[van Baalen (1993)]
	• Gag CTL epitope precursor frequencies estimated, peptide mapping				
p24(211–230)	p24(343–362 SF2)	LEEMMTACQGVGGPGHKARV	HIV-1 infection	human(B7)	[McAdam (1998)]
p24(211–231)	p24(343–362 SF2)	LEEMMTACQGVGGPGHK-ARVL	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 12 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				
p24(217–227)	p24(349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human(A11)	[Sipsas (1997)]
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB • ACQGVGGPSHK, a variant found in HIV RF, was also recognized • C. Brander notes that this is a A*1101 epitope in the 1999 database				
p24(223–231)	p24(355–363 LAI)	GPGHKARVL	HIV-1 infection	human(B7)	[Goulder (1997b), Goulder (1997a)]
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a strong response to this peptide, the other a weak response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
p24(369–377)	p24(369–377)	IEELRQHLL		human(B*4001,B60)	
	• Noted by C. Brander *et al*., this database 1999, to be a B*4001,B60 epitope, Pers. Comm. P. Goulder and M. Altfeld				