Table 9: **RT**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(3–12)	RT( )	SPIETVPVKL	HIV-1 infection	human(A2, B61)	[van der Burg (1997)]
	• Recognized by CTL from a long-term survivor, EILKEPVGHGV was also recognized • Highly conserved across clades				
RT(5–29)	RT(160–184 HXB2)	IETVPVKLKPGMDGP-KVKQWPLTEE	HIV-1 infection	human(B8)	[Walker (1989)]
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT(18–26)	RT(185–193 LAI)	GPKVKQWPL		human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
RT(18–26)	RT(18–26)	GPKVKQWPL	HIV-1 infection	human(B8)	[Meier (1995), Menendez-Arias (1998)]
	• HIV proteins with mutations in this epitope allowed transactive inhibition of specific CTL-mediated lysis • Article Reviewed in [Menendez-Arias (1998)], with a discussion of antagonism				
RT(18–26)	RT(173–181)	GPKVKQWPL		human(B8)	[Goulder (1997g), Menendez-Arias (1998)]
	• Included in a study of the B8 binding motif • Article Reviewed in [Menendez-Arias (1998)], with a discussion of antagonism				
RT(18–26)	RT(185–193 LAI)	GPKVKQWPL		human(B8)	[Sutton (1993)]
	• Predicted epitope based on B8-binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE				
RT(18–26)	RT(185–193 LAI)	GPKVKQWPL	HIV-1 infection	human(B8)	[Klenerman (1995), Menendez-Arias (1998)]
	• Naturally occurring antagonist GPRVKQWPL found in viral PBMC DNA and RNA • Article Reviewed in [Menendez-Arias (1998)] with a discussion of antagonism				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(18–26)	RT(18–26)	GPKVKQWPL	*in vitro* stimulation	human(B8)	[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				
RT(33–41)	RT(33–41 LAI)	ALVEICTEM	HIV-1 infection	human(A*0201)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0201 epitope				
RT(33–41)	RT(33–41)	ALVEICTEM	HIV-1 infection	human(A2)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(33–43)	RT(33–43)	ALVEICTEMEK	HIV-1 infection	human(A*0301)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • C. Brander notes that this is an A*0301 epitope in the 1999 database, G. Haas pers. comm.				
RT(33–43)	RT(33–43)	ALVEICTEMEK	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
RT(38–52)	RT(205–219)	CTEMEKEGKISKIGP	HIV-1 infection	human(broad)	[Hosmalin (1990), Menendez-Arias (1998)]
	• Murine and human helper and CTL epitope • Epitope noted in a Review by [Menendez-Arias (1998)] to be located in the “fingers” domain of RT and is a helper and CTL epitope				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(38–52)	RT(205–219 BRU)	CTEMEKEGKISKIGP	recRT injection	murine(H2^k)	[De Groot (1991), Menendez-Arias (1998)]
	• Murine and human helper and CTL epitope • Epitope noted in a Review by [Menendez-Arias (1998)] to be located in the "fingers" domain of RT and is a helper and CTL epitope				
RT(39–47)	RT(206–214)	TEMEAEGKI	peptide on pulsed irradiated splenocytes	C3H/HeJ mice( )	[Leggatt (1997)]
	• Ala-substituted nonamer-peptide used to test a non-radioactive assay for murine CTL recognition of peptide-MHC class I complexes • The new assay is CTL adherence assay (CAA), and is based on the discovery that CTL develop adhesive properties upon TCR triggering • Substitutions in TEMEAEGKI that reduce cytolytic activity were correctly detected by CAA				
RT(39–47)	RT( )	TEMEKEGKI		murine(H-2K^k)	[Leggatt (1998)]
	• Epitope variants were examined for CTL response in concert with H-2K^k MHC class I binding – all of the following combinations were observed: (i) two single mutations which did not alone abrogate CTL activity did abrogate activity when combined, (ii) loss of recognition of a single substitution could be restored by an additional substitution, and (iii) sometimes there was recognition of two single substitutions as well as the combination of those substitutions • 2E and 9I are anchor residues for H-2K^k – if you have M in the third position, it enhances H-2K^k binding 10-fold, but Polymorphism at this site is important for the overall conformation of the peptide and can influence T cell recognition				
RT(42–50)	RT(42–50 LAI)	EKEGKISKI	HIV-1 infection	human(B*5101)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5101 epitope				
RT(42–50)	RT(42–50 LAI)	EKEGKISKI	HIV-1 infection	human(B51)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(93–101)	( )	GIPHPAGLK		(A3)	[Brander & Goulder(2001), Altfeld(2000)]

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(98–113)	RT(252–266)	AGLKKKKSVTVLDVG-D	HIV-1 infection	human(Cw4)	[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 were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs				
RT(103–117)	RT(257–251)	KKSVTVLDVGDAYFS	HIV-1 infection	human(Cw4)	[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 were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs				
RT(107–115)	RT(262–270 IIIB)	TVLDVGDAY		(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
RT(107–115)	RT(262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human(B35)	[Wilson (1996), Menendez-Arias (1998)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • TVLDMGDAC is a naturally occurring variant that is less reactive • [Menendez-Arias (1998)], in a Review, notes that this epitope includes a catalytic residue (Asp-110) in the active site of RT				
RT(107–115)	Pol(262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human(B35)	[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 • An additional variant that gave a positive CTL response: TVLDMGDAC				
RT(108–118)	RT(267–277)	VLDVGDAYFSV	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]
	• High dissociation rate, but immunogenic in primary CTL induction after repeated stimulations with peptide • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(108–118)	RT(267–277)	VLDVGDAYFSV	HIV-1 infection	human(A2)	[Kundu (1998b)]
	• 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 • VLDVGDAYFSV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, but only one of these had a detectable CTL response – the other two had the sequences EEDVGDAYFSV and ELDVGDAYFSV and no detectable CTL response				
RT(108–118)	RT(267–277)	VLDVGDAYFSV	*in vitro* stimulation	human(A2)	[van der Burg (1995)]
	• Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor • VLDVGDAYFSV is in a functional domain				
RT(108–122)	RT(257–251)	VLDVGDAYFSVPLDE	HIV-1 infection	human(Cw4)	[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 were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs				
RT(113–120)	Pol(268–275 SF2)	DAYFSVPL	HIV-1 infection	human(B*5101, B24)	[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, DAYFSVPL is conserved				
RT(118–127)	RT(273–282 SF2)	VPLDKDFRKY	HIV-1 infection	human(B*3501)	[Tomiyama (1997), Menendez-Arias (1998)]
	• A CTL clone responsive to this epitope was obtained • 4/7 B35-positive individuals had a CTL response to this epitope • A K to E substitution at position 5 abrogates specific lysis, and reduces binding to B*3501 • [Menendez-Arias (1998)], in a Review, notes that a Glu to Lys (E to K) change abrogates CTL activity, but that both VPLDEDFRKY and VPLDKDFRKY can serve as HLA-B35 epitopes, so the change must alter T cell receptor binding – residues in this epitope may be important for Polymerase activity				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B*3501,B35)	[Shiga (1996)]
	• Binds HLA-B*3501				
RT(118–127)	( )	VPLDKDFRKY	HIV-1 infection	human(B35)	[Kawana (1999)]
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation • `-----E----` was found in 8/10 of the B35+ individuals, and three of the B35- individuals – the D ⟶ E substituted peptide had similar binding affinity to B35 and was equally susceptible to a CTL clone				
RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B35)	[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 • VPLDKDFRKY, a variant found in HIV MN, was not recognized • VPHDEDFRKY, a variant found in HIV YU2, was not recognized • This epitope was type-specific and conserved in only one other B subtype sequence				
RT(126–135)	RT(293–302 HXB-nPLAP)	KYTAFTIPSI	HIV-1 infection	human(A2)	[Shankar (1998)]
	• A novel CTL clone was defined with a panel of recombinant vaccinia-RT-infected B-LCL target cells using PBMCs donated by a patient who was HIV-seropositive for 6 years and had not received any antiretroviral therapy • There is evidence that some CTL epitopes are poorly presented on the surface of infected cells, but this RT epitope was recognized as effectively on HIV-infected cells as on peptide-pulsed targets				
RT(128–135)	RT(295–302 IIIB)	TAFTIPSI	HIV-1 infection	human(B*5101)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5101 epitope				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(128–135)	Pol(283–290 SF2)	TAFTIPSI	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, but TAFTIPSI is somewhat variable				
RT(128–135)	RT(295–302 IIIB)	TAFTIPSI	HIV-1 infection	human(B51)	[Sipsas (1997), Menendez-Arias (1998)]
	• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • TAFTIPST, a variant found in HIV-1 CAM1, was also recognized but 100-fold more peptide was needed • TAFTIPSV, a variant found in HIV-1 VE1RT, was also recognized, but 10-fold more peptide was needed • TVFTIPSI, a variant found in HIV-1 MANC, was also recognized • [Menendez-Arias (1998)], in a Review, notes that this epitope includes a region near the active site of RT – the substitution of the position two conservative change from A to V decreases CTL recognition				
RT(128–135)	RT(295–302)	TAFTIPSI	HIV-1 infection	human(B51)	[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 additional HIV epitopes, and all three were also HLA B51 and recognized this epitope as well as other epitopes				
RT(151–159)	Pol(306–314 SF2)	QGWKGSPAI	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]
	• HLA-B27, -B51, and -B57 are associated with slow progression to AIDS • 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, QGWKGSPAI is conserved				
RT(153–165)	RT(308–320)	WKGSPAIFQSSMT	HIV-1 infection	human(B7)	[Brander & Walker(1995)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(156–164)	RT(311–319 SF2)	SPAIFQSSM	HIV-1 infection	human(B*3501)	[Tomiyama (1997), Menendez-Arias (1998)]
• A CTL clone responsive to this epitope was obtained • Only 1/7 B35-positive individuals had a CTL response to this epitope • [Menendez-Arias (1998)], in a Review, notes that this epitope is near the active site of RT					
RT(156–164)	RT(311–319 SF2)	SPAIFQSSM	HIV-1 infection	human(B35)	[Shiga (1996), Menendez-Arias (1998)]
• Binds HLA-B*3501 • [Menendez-Arias (1998)], in a Review, notes that this epitope includes catalytic residues in the active site of RT					
RT(156–164)	Pol(156–164 HXB2)	SPAIFQSSM	HIV-1 infection	human(B7)	[Hay (1999)]
• 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 • Variants of this epitope were observed *in vivo* (`------C--, --S------`), but the binding motifs for B7 were preserved (P2, and C-term aromatic or hydrophobic)				
RT(156–165)	RT(311–319 SF2)	SPAIFQSSMT		human(B7)	[Brander & Walker(1997), Menendez-Arias (1998)]
• Pers. Comm. from C. Hey and D. Ruhl to C. Brander and B. Walker • [Menendez-Arias (1998)], in a Review, notes that this epitope includes catalytic residues in the active site of RT					
RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*0301 epitope					
RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*1101 epitope					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(158–166)	RT(325–333)	AIFQSSMTK	HIV-1 infection	human(A*1101, A3, A*0301, A*6801)	[Threlkeld (1997), Menendez-Arias (1998)]
	• Study of the fine specificity of an A3-like super-type epitope (the A3 super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801) • A3 super-type is characterized by a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position • While most lines were specific, promiscuous cloned CTL lines were also derived from HIV+ donors that could recognize epitope presented by either A3 or A11 or A*6801 • Alanine substitutions throughout the epitope and natural variants indicate that the same amino acid positions are critical for presentation by either MHC molecule, A3 or A11 • AIFQSSMTK is presented by three members of the A3 superfamily: A*0301, A*1101, and A*6801, and the naturally occurring variants A1S and K9R are recognized with similar efficiency to wild type epitope – AIFQRSMTR can also bind to two additional members of the A3 superfamily, A*3101 and A*3301				
RT(158–166)	RT( )	AIFQSSMTK	HIV-1 infection	human(A11)	[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				
RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	No CTL shown	human(A11)	[Zhang (1993), Menendez-Arias (1998)]
	• Exploration of A11 binding motif, based on Nixon *et al.* 1991				
RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A11)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes				
RT(158–166)	RT(325–333 IIIB)	AIFQSSMTK	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 • AIFQSSMTR and AILQSSMTK, naturally occurring variants, were found in infant, and are recognized • TISQSSMTK, a naturally occurring variant, was found in infant and is not recognized				
RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A3)	[Cao (1997)]
	• The consensus peptide of B and D clade viruses is AIFQSSMTK • The consensus peptide of a subset of As is AIFQASMTK and it is less able to stimulate the CTL clone • The consensus peptide of a subset of As is SIFQSSMTK and is as reactive as the originally defined epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(158–166)	Pol(325–333 IIIB)	AIFQSSMTK	HIV-1 infection	human(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 • One variant found in an infant gave a positive CTL response: AIFQSSMTR • AIFLSSMTK and TISQSSMTK were escape mutants					
RT(158–166)	RT(325–333)	AIFQSSMTK	HIV-1 infection	human(A3.1)	[Brander & Walker(1995)]
• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study					
RT(158–166)	RT(325–333)	AIFQSSMTK	HIV-1 infection	human(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 HLA A3 and reacted with this epitope as well as two other A3.1 epitopes					
RT(158–166)	RT(325–333 LAI)	AIFQSSMTK		human(A33)	[Rowland-Jones(1995)]
• Defined as minimal peptide by titration curve, S. Rowland-Jones, Pers. Comm.					
RT(158–166)	( )	AIFQSSMTK	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 moderately 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				
RT(158–182)	RT(325–349 PV22)	AIFQSSMTKILEPFRKQ-NPDIVIYQ	HIV-1 infection	human(A11)	[Jassoy (1993)]
• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(158–182)	RT(325–349)	AIFQSSMTKILEPFRKQ-NPDIVIYQ	HIV-1 infection	human(A11)	[Price (1995)]
	• Study of cytokines released by HIV-1 specific activated CTL				
RT(173–181)	RT(173–181 LAI)	KQNPDIVIY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001)]
	• C. Brander notes this is an A*3002 epitope				
RT(175–183)	RT(328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human(B*3501)	[Tomiyama (1997)]
	• A CTL clone responsive to this epitope was obtained • 3/7 B35-positive individuals had a CTL response to this epitope • D to E, or V to I, substitutions at positions 3 or 5, respectively, reduces CTL activity and binding to B*3501				
RT(175–183)	RT(328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
RT(175–183)	RT(342–350 LAI)	HPDIVIYQY	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
RT(175–183)	RT(342–350 LAI)	HPDIVIYQY	HIV-1 infection	human(B35)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes				
RT(175–183)	RT(329–337)	HPDIVIYQY	HIV-1 infection	human(B35)	[Rowland-Jones (1995)]
	• NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized				
RT(175–183)	( )	NPDIVIYQY	HIV-1 infection	human(B35)	[Kawana (1999)]
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation • `--E------` was found in 8/10 of the B35+ individuals, and two of the B35- individuals – the D ⟶ E substituted peptide had reduced binding affinity to B35 and may be an escape mutant				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(175–183)	RT(329–337)	HPDIVIYQY	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					
RT(175–183)	RT(328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human(B35)	[Shiga (1996), Menendez-Arias (1998)]
• Binds HLA-B*3501 • CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding [Menendez-Arias (1998)]					
RT(175–183)	RT(328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human(B35)	[Sipsas (1997), Menendez-Arias (1998)]
• HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • NPDIIIYQY, a variant found in HIV-1 JRCSF, was also recognized • NPEIVIYQY, was also recognized • NPDLVIYQY, was also recognized • [Menendez-Arias (1998)], in a Review, notes that the YXDD motif, highly conserved among Polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding					
RT(175–183)	RT( )	NPDIVIYQY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998a), Menendez-Arias (1998)]
• 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 HPDIVIYQY • The D subtype consensus is NPEIVIYQY • [Menendez-Arias (1998)], in a Review, notes that the YXDD motif, highly conserved among Polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(175–183)	Pol( )	NPDIVIYQY	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 • Clade A version of epitope HPDIVIYQY, Clade D NPEIVIYQY				
RT(175–183)	Pol( )	HPDIVIYQY		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: NPDVILIQY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]				
RT(175–183)	( )	HPDIVIYQY	HIV-1 infection	human(B35)	[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 moderately 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			
RT(175–199)	RT(342–366 LAI)	NPDIVIYQYMDDLYV-GSDLEIGQHR	HIV-1 infection	human(A11)	[Walker (1989), Menendez-Arias (1998)]
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT(179–187)	RT( )	VIYQYMDDL	Polyepitope encoding DNA in VVA	human(A*0201)	[Hanke (1998b), Hanke (1998a)]
	• This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(179–187)	RT( )	VIYQYMDDL	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 • Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable				
RT(179–187)	Pol(346–354)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Sewell (1999)]
	• Proteasome regulation influences epitope processing and could influence patterns of immunodominance • The proteasome is inhibited by lactacystin treatment, and γ IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome • IFN-γ induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within Pol proteins, showing the two epitopes are processed by different pathways • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants				
RT(179–187)	RT(346–354 LAI)	VIYQYMDDL	HIV infection	human(A*0201)	[Harrer (1996a), Menendez-Arias (1998)]
	• The substitution VIYQYVDDL abrogates CTL response and confers drug resistance • [Menendez-Arias (1998)], in a Review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT				
RT(179–187)	RT(346–354 LAI)	VIYQYMDDL	HIV infection	human(A*0201)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0201 epitope				
RT(179–187)	RT(346–354)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Brander (1998a), Menendez-Arias (1998)]
	• 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 or evidence of immune escape • Only one subject had CTL against all three epitopes • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area • In the Review [Menendez-Arias (1998)] the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) – substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC – substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(179–187)	RT( )	VIYQYMMDL	HIV-1 exposure	human(A2)	[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 and D consensus sequences are both VIYQYMMDL					
RT(179–187)	Pol(346–354)	VIYQYMDDL	HIV-1 infection (human) or HIV A2-Polyepitope (Polytope) DNA vaccine with vaccinia boost (rVV.HIV.pt) (mouse)	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 • VIYQYMDDL was recognized by 3 of the HLA-A2 patients					
RT(179–187)	RT(179–187)	VIYQYMDDL	HIV-1 infection	human(A2)	[Schmitt (2000)]
• The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL • 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL • This suggests immunotherapy stimulating anti-VIYQYVDDL responses maybe helpful for reducing lamivudine escape					
RT(179–187)	RT(179–187)	VIYQYMDDL	HIV infection	human(A2)	[Haas (1998)]
• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(179–187)	Pol( )	VIYQYMMDL	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				
RT(180–189)	RT( )	IYQYMDDLYV	HIV-1 infection	human(A*0201)	[van der Burg (1997), Menendez-Arias (1998)]
	• Recognized by CTL from a progressor, spans important RT functional domain • A previous study determined that this was an epitope recognized by a long-term survivor				
RT(192–201)	RT(192–201)	DLEIGQHRTK	HIV-1 infection	human(A3)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(192–216)	RT(359–383 HXB2)	DLEIGQHRTKIEELRQ-HLLRWGLTT	HIV-1 infection	human(Bw60)	[Walker (1989), Menendez-Arias (1998)]
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT(192–216)	RT(191–215)	DLEIGQHRTKIEELRQ-HLLRWGFTT	HIV-1 infection	human(Polyclonal)	[Haas (1997), Menendez-Arias (1998)]
	• Polyclonal CTL recognition switched from RT 191–215 to RT 514–524 when AZT therapy selected for the resistance mutation, and presumably the escape variant, RT T215Y				
RT(201–209)	RT(201–209)	KIEELRQHL	HIV-1 infection	human(A2)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(202–210)	RT(202–210 LAI)	IEELRQHLL		human(B*4001)	[Brander & Goulder(2001), Altfeld (2000)]
	• C. Brander notes this is a B*4001 epitope				
RT(203–212)	RT( )	EELRQHLLRW	HIV-1 infection	human(B44)	[van der Burg (1997), Menendez-Arias (1998)]
	• The only epitope recognized by CTL from a long-term survivor in two samples taken six years apart • Recognized by CTL from a progressor, EILKEPVGHGV and TWETWWTEYW were also recognized				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(209–220)	RT(209–220)	LLRWGLTTPDKK	HIV-1 infection	human(A2)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(243–252)	RT( )	PIVLPEKDSW	HIV-1 infection	human(B*5701)	[van der Burg (1997), Menendez-Arias (1998)]
	• Recognized by CTL from a progressor and a long-term survivor, KITTESIVIW was also recognized				
RT(243–252)	RT( )	PIVLPEKDSW	HIV-1 infection	human(B*5701)	[van der Burg (1997), Menendez-Arias (1998)]
	• Recognized by CTL from long-term survivor, whose CTL response persisted for more than 10 years – the substitution V3M reduced affinity but was well recognized, on the other hand V3T and D8G did not reduce affinity, but abrogate CTL response				
RT(244–252)	RT(399–407)	IVLPEKDSW		human(B*5701)	[Brander & Goulder(2001)]
	• Subtype of B57 not determined • C. Brander notes this is a B*5701 epitope				
RT(244–252)	RT(244–252 LAI)	IVLPEKDSW	HIV-1 infection	human(B*5701, B*5801)	[Klein (1998)]
	• This peptide was defined as the optimal epitope • B57 has been associated with long-term non-progression in the Amsterdam cohort. • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag • B57 restricted CTL responses are targeted at multiple proteins, but one LTS had a response that was dominated by reactivity to the epitope – two variants were found in this LTS: ITLPEKESW, which bound to B*5701 with similar affinity as the index peptide but was an escape mutant that was not recognized by CTL, and IMLPEKDSW, which bound to B*5701 with reduced affinity but could still be recognized • In an additional HIV+ LTS, only the variant IELPEKDSW was found, and this epitope was recognized by CTL but had less affinity for B*5701 than the index peptide • This epitope was recognized in the context of both HLA-B*5701 and B*5801				
RT(244–252)	RT(399–407)	IVLPEKDSW		human(B57)	[van der Burg (1997)]
RT(260–271)	RT(415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human(B*1501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*1501 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(260–271)	RT(415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human(Bw62)	[Brander & Walker(1996), Menendez-Arias (1998)]
	• P. Johnson, Pers. Comm.				
RT(263–271)	RT(263–271 LAI)	KLNWASQIY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001)]
	• C. Brander notes this is an A*3002 epitope				
RT(269–277)	( )	QIYPGIKVR		(A3)	[Brander & Goulder(2001), Altfeld(2000)]
RT(271–279)	( )	YPGIKVRQL	HIV-1 infection	human(B*4201)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*4201 epitope				
RT(271–279)	RT(438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human(B42)	[Wilson (1996), Menendez-Arias (1998)]
	• YAGIKVRQL and YPGIKVKQL are naturally occurring variants that are both reactive • YHKIKVRQL is a naturally occurring variant that has not been tested • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
RT(271–279)	Pol(438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human(B42)	[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 • An additional variant that gave a positive CTL response: YPGIKVKQL, YAGIKVRQL • YHGIKVRQL was an escape mutant				
RT(293–301)	RT(448–456 SF2)	IPLTEEAEL	HIV-1 infection	human(B*3501)	[Tomiyama (1997), Menendez-Arias (1998)]
	• A CTL clone responsive to this epitope was obtained • Only 1/7 B35-positive individuals had a CTL response to this epitope • An E to K substitution at position 5 abrogates specific lysis, but not binding to B*3501 • An I to V substitution at position 1, P to Q at position 2, and E to K at 5, abrogates specific lysis and binding to B*3501 • An I to V substitution at position 1 did not alter reactivity • Reviewed in [Menendez-Arias (1998)], this epitope lies in the thumb region of RT				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(293–301)	( )	IPLTEEAEL	HIV-1 infection	human(B35)	[Kawana (1999)]
• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals but this was one of the six that had no B35 associated pattern of mutation					
RT(293–301)	RT(448–456 SF2)	IPLTEEAEL	HIV-1 infection	human(B35, B51)	[Shiga (1996), Menendez-Arias (1998)]
• Binds HLA-B*3501 and B*5101 • Reviewed in [Menendez-Arias (1998)], this epitope lies in the thumb region of RT					
RT(294–318)	RT(461–485 HXB2)	PLTEEAELELAENREIL-KEPVHGVY	HIV-1 infection	human(A2)	[Walker (1989), Menendez-Arias (1998)]
• One of five epitopes defined for RT-specific CTL clones in this study					
RT(308–317)	RT( )	EILKEPVGHV	HIV-1 infection	human(A*0201)	[van der Burg (1997), Menendez-Arias (1998)]
• Recognized by CTL from a long-term survivor, SPIETVPVKL was also recognized • Recognized by CTL from a progressor, EELRQHLLRW and TWETWWTEYW were also recognized					
RT(309–317)	RT(476–484)	ILKEPVHGV	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 gamma interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT					
RT(309–317)	Pol(476–484)	ILKEPVHGV	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					
RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Loing (2000)]
• The ILKEPVHGV was modified by the addition of an N-palmitoyl-lysine residue at the P0, P1 or P10 positions of the parent peptide to create a lipopeptide for direct antigen delivery to the cytoplasm for processing • The N-terminal modification increased the life span for functional CTL recognition up to 48 hours in comparison to the parent peptide					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(309–317)	( )	ILKEPVHGV	HIV-1 infection	human(A*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 moderately 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			
RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Sewell (1999)]
• Proteasome regulation influences epitope processing and could influence immunodominance • The proteasome is inhibited by lactacystin treatment, and γ-IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome • IFN-γ induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within Pol proteins, showing the two epitopes are processed by different pathways • ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway • This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants					
RT(309–317)	Pol(510–518)	ILKEPVHGV	Rec pox vectors (vaccinia and canarypox) expressing HIV-1 genes (Gag, Pol, Nef or Env)	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 or canarypox 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[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				
RT(309–317)	RT(476–484)	ILKEPVHGV	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 • 2/11 of the A2+ individuals responded to ILKEPVHGV, and neither of these two responded to SLYNTVATL				
RT(309–317)	Pol( )	ILKEPVHGV	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				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Ogg (1998b), Menendez-Arias (1998)]
	• 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				
RT(309–317)	RT( )	ILKEPVHGV	Polyepitope encoding DNA in VVA	human(A*0201)	[Hanke (1998b), Hanke (1998a)]
	• This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans				
RT(309–317)	RT(476–484)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[Konya (1997), Menendez-Arias (1998)]
	• This epitope was included as a positive control • Binding affinity to A*0201 was measured, $C_{1/2}\max \mu M = 12$				
RT(309–317)	RT(468–476)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]
	• Immunogenic in humans, slow dissociation rate, and associated with immunogenicity in transgenic HLA-A*0201/K^b mice • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(309–317)	RT(468–476)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[van der Burg (1995)]
	• Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Pogue (1995), Menendez-Arias (1998)]
	• Mutational study: position 1 I to Y increases complex stability with HLA-A*0201				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Goulder (1997b), Goulder (1997a), Menendez-Arias (1998)]
	• 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 • [Goulder (1997a)] is a review of immune escape that summarizes this study				
RT(309–317)	RT(309–317)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Altman (1996)]
	• 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 quantify 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%) • The A2-Pol CD8+ clones were CD45RO positive and HLA-DR and CD38 negative, suggesting a memory rather than effector phenotype				
RT(309–317)	RT(476–484)	ILKEPVHGV	none	human(A*0201)	[Walter (1997), Menendez-Arias (1998)]
	• 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				
RT(309–317)	RT(464–472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Gray (1999)]
	• 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
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Brander (1998a), Brander & Goulder(2001)]
	• 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 or evidence of immune escape • Only one subject had CTL against all three epitopes • Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area • C. Brander notes this is an A*0201 epitope				
RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Ogg (1999)]
	• CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVANTVATL 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				
RT(309–317)	Pol(476–484)	ILKEPVHGV	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 • ILKEPVHGV was recognized by 2 of the patients				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Collins (1998)]
	• Nef down-regulates MHC class I molecules, which inhibits CTL killing of HIV-infected targets • The anti-RT CTL clone killed Nef- cells less efficiently than anti-Gag clones, correlated with the reduced expression of RT				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Kolowos (1999)]
	• TCR usage in CTL-specific for this epitope was examined in three patients and identical Vβ6.1 and Vα2.5 gene segments were used and two of the patients had very similar complementarity-determining regions – clonal expansion of RT-HIV-specific CTL can contribute to the skewed TCR repertoire in HIV-1 infected patients • CTL clones from all three patients showed similar sensitivity to mutation in the epitope, `-------E-` was well recognized (the sequence from SF2), `---D-----` was not (the common A clade form)				
RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A2)	[Fan (1997)]
	• The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				
RT(309–317)	RT(464–472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Kundu (1998b)]
	• 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 • ILKEPVHGV is a conserved HLA-A2 epitope included in this study – 5/6 patients had this sequence as their HIV direct sequence, and these had a detectable CTL response– one person carried the form ILREPVHGV and had no detectable CTL				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Tsomides (1994), Menendez-Arias (1998)]
	• CTL clones recognize naturally processed peptide – peptide abundance corresponded to level of CTL killing				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 exposure	human(A2)	[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 ILKDPVHGV • The D subtype consensus is identical to the epitope ILKEPVHGV				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Cao (1997), Menendez-Arias (1998)]
	• The consensus peptides of B and D clade viruses and some As have the sequence ILKEPVHGV • The consensus peptide of a subset of A clade viruses, ILKDPVHGV, is not cross-reactive				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[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
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Yang (1996), Menendez-Arias (1998)]
	• 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				
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Musey (1997), Menendez-Arias (1998)]
	• Cervical CTL clones from an HIV-infected woman recognized this epitope				
RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A2)	[Tsomides (1991), Menendez-Arias (1998)]
	• Precise identification of the nonamer that binds to A2				
RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	no CTL shown	human(A2)	[Connan (1994), Menendez-Arias (1998)]
	• Promotes assembly of HLA-A2 molecules in T2 cell lysates				
RT(309–317)	RT(510–518)	ILKEPVHGV	none	human(A2)	[Parker (1992)]
	• Studied in the context of HLA-A2 peptide binding				
RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[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				
RT(309–317)	RT(476–484)	ILKEPVHGV	*in vitro* stimulation	human(A2)	[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				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(309–317)	RT( )	ILKEPVHGV	none – computer prediction	(A2)	[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 T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV • This sequence is not conserved between clades, but is found only in a small number of B clade isolates				
RT(309–317)	Pol( )	ILKEPVHGV	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 B and D clade viruses • Clade A version of the epitope, ILKDPVHGV, was preferentially recognized by CTL				
RT(309–317)	Pol( )	ILKEPVHGV	DNA multi-epitope vaccine	SJL/J HLA transgenic mice(A2.1)	[Ishioka (1999)]
	• A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed • The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans • HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection				
RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Brander & Goulder(2001)]
	• C. Brander notes this is a A*0201 epitope				
RT(309–318)	RT(476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human(B*1501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*1501 epitope				
RT(309–318)	RT(476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human(Bw62)	[McMichael & Walker(1994), Menendez-Arias (1998)]
	• Review of HIV CTL epitopes				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(328–352)	RT(495–515 LAI)	EIQKQGQGQWTYQIY-QEPFKNLKTG	HIV-1 infection	human(A11)	[Walker (1989), Menendez-Arias (1998)]
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT(340–350)	RT(507–516)	QIYQEPFKNLK	HIV-1 infection	human( )	[Price (1995), Menendez-Arias (1998)]
	• Study of cytokines released by HIV-1 specific activated CTL				
RT(340–352)	RT(507–519 LAI)	QIYQEPFKNLKTG	HIV-1 infection	human(A11)	[Johnson & Walker(1994), Menendez-Arias (1998)]
	• This epitope was listed in a Review				
RT(341–350)	RT(508–516)	IYQEPFKNLK	HIV-1 infection	human(A*1101)	[Culmann(1998)]
	• C. Brander notes that this is an A*1101 epitope in the 1999 database				
RT(341–350)	RT(508–517 LAI)	IYQEPFKNLK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*1101 epitope				
RT(364–372)	RT(518–526 U455)	DVKQLTEVV		human(A28, A*6802)	[Dong (1998), Menendez-Arias (1998)]
	• Predicted on binding motif, no truncations analyzed • Reacts with clade A consensus (U455), and with the peptide DVKQLAEAV, from the D clade				
RT(364–372)	RT(470–478 Clade A)	DVKQLTEVV	HIV-1 infection	human(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 response was defined in a patient with an A subtype infection • Bulk cultures from this patient gave a CTL response that could recognize the subtype D form of this epitope, with two substitutions (DVKQLAEAV), though a CTL line from these cultures didn't recognize the B clade variant (DVKQLTEAV)				
RT(374–383)	RT( )	KITTESIVIW	HIV-1 infection	human(B*5701)	[van der Burg (1997), Menendez-Arias (1998)]
	• Patients studied were from the Amsterdam cohort • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS); no differences could be found in the degree of conservation between them • Epitope recognized by LTS and by a progressor				
RT(374–383)	RT( )	KITTESIVIW	HIV-1 infection	human(B*5701)	[van der Burg (1997)]
	• Recognized by CTL from a progressor and a long-term survivor, PIVLPEKDSW was also recognized				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(375–383)	RT(375–383 LAI)	ITTESIVIW	HIV-1 infection	human(B*5701 B*5801)	[Klein (1998)]
	• Another patient recognized the ten-mer version of this epitope, KITTESIVIW [van der Burg (1997)] • B57 has been associated with long-term non-progression in the Amsterdam cohort • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag • The patient that recognized ITTESIVIW also recognized IVLPEKDSW				
RT(392–401)	RT(559–568 LAI)	PIQKETWETW		human(A*3201)	[Harrer (1996b), Menendez-Arias (1998)]
	• Reviewed in [Menendez-Arias (1998)], suggest the epitope is HLA B53/Cw2 • C. Brander notes that this is an A*3201 epitope in the 1999 database				
RT(392–401)	RT(559–568 LAI)	PIQKETWETW		human(A*3201)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*3201 epitope				
RT(397–406)	RT( )	TWETWWTEYW	HIV-1 infection	human(B44)	[van der Burg (1997), Menendez-Arias (1998)]
	• Recognized by CTL from two progressors, EILKEPVGHGV and EELRQHLLRW were also recognized by one, and RETKLGKAGY was also recognized by the other				
RT(421–429)	RT(421–429)	PLVKLWYQL	HIV-1 infection	human(A2)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(432–440)	RT(587–597 SF2)	EPIVGAETF	HIV-1 infection	human(B*3501)	[Tomiyama (1997), Menendez-Arias (1998)]
	• A CTL clone responsive to this epitope was obtained • 5/7 B35-positive individuals had a CTL response to this epitope • An E to D substitution at position 1, and V to I at position 4, reduces activity but not binding to B*3501 • [Menendez-Arias (1998)] note in their Review that this epitope is near the protease cleavage site and conservation of this region is important for proper viral maturation				
RT(432–440)	Pol(587–595)	EPIVGAETF	HIV-1 infection	human(B35)	[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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(432–440)	( )	EPIVGAETF	HIV-1 infection	human(B35)	[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 moderately 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			
RT(432–440)	RT(587–596 SF2)	EPIVGAETF	HIV-1 infection	human(B35, B51)	[Shiga (1996)]
	• Binds HLA-B*3501, and is also presented by B51 – but CTL could not kill RT-vaccinia virus infected cells that expressed B51				
RT(432–441)	RT(587–597 SF2)	EPIVGAETFY	HIV-1 infection	C3H/HeJ mice(B35)	[Shiga (1996), Menendez-Arias (1998)]
	• Binds HLA-B*3501, but not presented by B51, in contrast to the peptide EPIVGAETF • [Menendez-Arias (1998)] note in their Review that this epitope is located near the protease cleavage site and conservation of this region is important for viral maturation • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(432–441)	RT(587–597 SF2)	EPIVGAETFY	HIV-1 infection	human(B35)	[Kawana (1999)]
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation				
RT(434–447)	RT( )	IVGAETFYVDGAAS	HIV-1 infection	human(A*6802)	[van der Burg (1997), Menendez-Arias (1998)]
	• Recognized by CTL from a long-term survivor that recognized a set of 5 overlapping peptides spanning IVGAETFYVDGAAS as well as PIVLPEKDSW and KITTESIVIW • A*6802 is a subset of HLA-A28 • This epitope spans the Pol p66 RT – p15 (RNAse) domain				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(436–445)	RT(591–600 IIIB)	GAETFYVDGA	HIV-1 infection	human(B45)	[Menendez-Arias (1998)]
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(436–445)	Pol(591–600 IIIB)	GVETFYVDGA	HIV-1 infection	human(B45)	[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 who had a CTL response to it • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(437–447)	RT(592–602 LAI)	AETFYVDGAAN		human(A28)	[Brander & Walker(1996), Menendez-Arias (1998)]
	• P. Johnson, pers. comm. • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(438–448)	RT(593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human(A26)	[Menendez-Arias (1998)]
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(438–448)	Pol(593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human(A26)	[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 • One other variant was found that gave a positive, though reduced, CTL response: ETYYVNGAANR • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(448–457)	RT( )	RETKLGKAGY	HIV-1 infection	human(A29)	[van der Burg (1997)]
	• Patients studied were from the Amsterdam cohort • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS) and no differences could be found in the degree of conservation between them • Epitope recognized by a LTS • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(481–505)	RT(648–672)	AIYLALQDSGLEVNIV-TDSQYALGI	HIV-1 infection	human( )	[Price (1995), Menendez-Arias (1998)]
	• Study of cytokines released by HIV-1 specific activated CTL • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(481–505)	RT(648–672 PV22)	AIYLALQDSGLEVNIV-TDSQYALGI	HIV-1 infection	human(B14)	[Kalams (1994), Menendez-Arias (1998)]
	• A CTL response used to study gene usage in HLA-B14 response • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(485–493)	RT(640–648 HXB2R)	ALQDSGLEV	no CTL shown	human(A2)	[Brander (1995)]
	• Epitope studied in the context of inclusion in a synthetic vaccine • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(485–493)	RT(640–648 HXB2R)	ALQDSGLEV	peptide vaccine	human(A2.1)	[Brander (1996), Brander (1995)]
	• This epitope was recognized by PBMC from 3/14 HIV+ asymptomatic patients • This epitope was used along with Env CTL epitope TLTSCNTSV and a tetanus toxin T helper epitope for a synthetic vaccine • This vaccine failed to induce a CTL response, although a helper response was evident • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(485–505)	RT(648–672)	ALQDSGLEVVTDSQY-ALGI	HIV-1 infection	human(B14)	[Brander & Walker(1995)]
	• Unpublished, S. Kalams • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(496–505)	Pol( )	VTDSQYALGI	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 A, B and D clade viruses				
RT(496–505)	RT(663–672 IIIB)	VTDSQYALGI	HIV-1 infection	human(Cw8)	[Brander & Walker(1996)]
	• Unpublished, P. Johnson • Published in this database in 1995 as B14, but B14 transfected cells did not present the peptide and it is thought to be presented by the genetically linked Cw8 molecule instead [Brander & Walker(1996)] • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(496–505)	RT( )	VTDSQYALGI	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 and D subtype consensus are identical to the B clade epitope • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication) • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(516–525)	RT(516–525)	ELVNQIIEQL	HIV-1 infection	human(A2)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(520–528)	Pol(520–528 LAI)	QIIEQLIKK		human(A*1101)	[Brander & Goulder(2001), Fukada (1999)]
	• C. Brander notes this is an A*1101 epitope				
RT(532–540)	RT(532–540)	YLAWVPAHK	HIV-1 infection	human(B7)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against Pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				