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)	IETVPVKLKPGMDGPKV-KQWPLTEE	HIV-1 infection	human(B8)	[Walker (1989)]
• One of five epitopes defined for RT specific CTL clones in this study					
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(B*0801,B8)	[Sutton (1993)]
• Predicted epitope based on B8 binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE • Noted in Brander 1999, this database, to be B*0801					
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					
RT(18–26)	RT(18–26)	GPKVKQWPL	*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					
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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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 a A*0301 epitope in the 1999 database, G. Haas pers. comm.					
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(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					
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-2Kk)	[Leggatt (1998)]
• Epitope variants were examined for CTL response in concert with H-2Kk MHC class I binding – all of the following combinations were observed: (i) two single mutations which did not alone abrograted 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 substitions as well as the combination of those substitutions • 2E and 9I are anchor residues for H-2 Kk. If you have M in the third position, it enhances H-2Kk 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,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 • Noted in Brander 1999, this database, to be B*5101					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(98–113)	RT(252–266)	AGLKKKKSVTVLDVGD	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 was 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 • No direct CTL was 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	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, note 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 • Other variants found that gave a positive CTL response: TVLDMGDAC				
RT(107–115)	RT(262–270 IIIB)	TVLDVGDAY		(B*3501,B35)	
	• Noted in Brander 1999, this database, to be B*3501, Pers. Comm. B. Wilkes and D. Ruhl				
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 was 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 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B*3501,B35)	[Shiga (1996)]
• Binds HLA-B*3501					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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 note 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				
RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B*3501,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 • Noted in Brander *et al*., this database 1999, to be B*3501				
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,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, note 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 • Noted in Brander 1999, this database, to be B*5101				

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(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				
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, note that this epitope includes catalytic residues in the active site of RT				
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, note that this epitope is near the active site of RT				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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 an 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 quicly 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 epitopes were observed *in vivo* (`------C--, --S------`), but the binding motifs for B7 were preserved (P2, C term aromatic or hydrophobic)				
RT(156–165)	RT(311–319 SF2)	SPAIFQSSMT		human(B7)	[Brander & Walker(1997b), Menendez-Arias (1998)]
• Pers. Comm. from C. Hey and D. Ruhl to C. Brander and B. Walker • [Menendez-Arias (1998)], in a review, note that this epitope includes catalytic residues in the active site of RT					
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( )	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					

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, that the naturally occuring variants A1S and K9R are recognized with similar efficiency to wild type epitope, and AIFQRSMTR can also bind to two additional members of the A3 superfamily, A*3101 and A*3301					
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					
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 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 LAI)	AIFQSSMTK		human(A33)	[Rowland-Jones(1995)]
• Defined as minimal peptide by titration curve, S. Rowland-Jones, Pers. Comm.					

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(158–182)	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				
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(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 infection	human(B*3501,B35)	[Rowland-Jones (1995)]
	• NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized • Noted in Brander *et al*., this database 1999, to be B*3501				
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(B*3501,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 be found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding [Menendez-Arias (1998)] • Noted to be B*3501 by Brander *et al*., this database 1999				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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,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, a variant found in HIV-1 JRU2RF, was also recognized • NPDLVIYQY, was also recognized • [Menendez-Arias (1998)], in a review, note 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 be found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding • Noted to be B*3501 by Brander *et al*., this database 1999					
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, note 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 be found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding					
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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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(175–199)	RT(342–366 LAI)	NPDIVIYQYMDDLYVGS-DLEIGQHR	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( )	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)	RT( )	VIYQYMDDL	Multi-epitope gene 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(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, note that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT • noted to be an A*0201 epitope in Brander *et al*., 1999				
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(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 for immune escape • Only one subject had CTL against all three • Subjects were part of the San Fransisco City Clinic Cohort, the ARIEL project and from the Boston area • In the review [Menendez-Arias (1998)] the authors note that substitution is 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 inhibiors				
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(191–215)	DLEIGQHRTKIEELRQH-LLRWGFTT	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 215 T to Y				
RT(192–216)	RT(359–383 HXB2)	DLEIGQHRTKIEELRQH-LLRWGLTT	HIV-1 infection	human(Bw60)	[Walker (1989), Menendez-Arias (1998)]
	• One of five epitopes defined for RT specific CTL clones in this study				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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(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				
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 affinty, but abrogated CTL response				
RT(244–252)	RT(244–252 LAI)	IVLPEKDSW	HIV-1 infection	human(B*5701, B*5801)	[Klein (1998)]
	• This peptide was defined as the optiomal epitope • 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 • 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(B*5701,B57)	[van der Burg (1997)]
	• Described as B*5701 in C. Brander *et al*., this database, 1999, C. Hays Pers. Comm.				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(260–271)	RT(415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human(B*1501,Bw62)	[Brander & Walker(1997a), Menendez-Arias (1998)]
	• P. Johnson, Pers. Comm. • Noted in Brander 1999, this database, to be B*1501, Pers. Comm. P. Johnson				
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 • Other variants found that gave a positive CTL response: YPGIKVKQL, YAGIKVRQL • YHGIKVRQL was an escape mutant				
RT(271–279)	Pol(438–446 LAI)	YPGIKVRQL		human(B*4201,B42)	
	• B. Wilkes, D. Ruhl, Pers. Comm.				
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(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				
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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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*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)	[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	Multi-epitope gene 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	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					
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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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	*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, $C_{1/2}\text{max}\mu M = 12$					
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 peptide 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(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					
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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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(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)	[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					
RT(309–317)	RT(309–317)	ILKEPVHGV	HIV infection	human(A2)	[Moss (1995), Menendez-Arias (1998)]
• Two clones were obtained with different TCR usage, V_β1 and V_β21					
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 quantitate HIV-specific CD8+ cell lines in freshly isolated PBMCs • The highest frequency of tetramer staining was found to the Pol epitope, 0.77% of the CD8+ lymphocytes in one patient who also had cells specific for the Gag epitope (0.28%) – three other patients only stained the Gag epitope, not the Pol • The A2-Pol CD8+ clones were CD45RO+ and HLA-DR and CD38 negative, suggesting a memory rather than effector phenotype					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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)	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(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)	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 CTL 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					
RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Dyer (1999)]
• CTL specific responses were measured over a 1.5- to 1.3-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)]
• 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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( )	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 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 sequence is not conserved between clades, but is found only in a small number of B clade isolates					
RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Brander (1998a)]
• 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 for immune escape • Only one subject had CTL against all three • Subjects were part of the San Fransisco City Clinic Cohort, the ARIEL project and from the Boston area					
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 typcially 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(309–318)	RT(476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human(B*1501,Bw62)	[McMichael & Walker(1994), Menendez-Arias (1998)]
	• Review of HIV CTL epitopes • Noted in Brander 1999, this database, to be B*1501, Pers. Comm. P. Johnson				
RT(328–352)	RT(495–515 LAI)	EIQKQGQGQWTYQIYQE-PFKNLKTG	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 a A*1101 epitope in the 1999 database				
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 subtitutions (DVKQLAEAV), though a CTL line from these cultures didn‘t recognize the B clade varient (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) of which no differences could be found in the degree of conservation between them • Epitope recognized by LTS and by a Progressor				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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				
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 response 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 a A*3201 epitope in the 1999 database				
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 epitopes near the protease cleavage site and conservation of this region is important for proper viral muturation				
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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(432–440)	Pol(587–595)	EPIVGAETF	HIV-1 infection	human(B35)	[Dyer (1999)]
• CTL specific responses were measured over a 1.5- to 1.3-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(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 muturation • This epitope spans the Pol p66 RT – p15 (RNAse) domain					
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					
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(1997a), 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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(448–458)	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 PV22)	AIYLALQDSGLEVNIVT-DSQYALGI	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(481–505)	RT(648–672)	AIYLALQDSGLEVNIVT-DSQYALGI	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					
RT(485–493)	RT(640–648 HXB2R)	ALQDSGLEV	no CTL shown	human(A2)	[Brander (1995b)]
• 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 (1995a)]
• 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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(485–505)	RT(648–672)	ALQDSGLEVVTDSQYALGI	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(1997a)]
	• 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(1997a)] • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
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(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				