Table 4: **RT**

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(71-79 LAI)	RT(59-67)	ITLWQRPLV		human(A*6802, A*7401)	[Dong98]
	NOTES: • Predicted on binding motif, no truncations analyzed • Clade A/B/D consensus, HLA-A28 subtype, S. Rowland-Jones, pers. comm.				
RT(71-79 LAI)	RT(59-67)	ITLWQRPLV		human(A19)	[Dong98]
	NOTES: • Clade A/B/D consensus, HLA-A*7401, S. Rowland-Jones, pers. comm.				
Pr(85-93 Clade D)	RT(86-94)	DTVLEEMNL		human(A*6802)	[Dong98]
	NOTES: • Predicted on binding motif, no truncations analyzed				
Pr(75-84 MN)	RT(131-140)	VLVGPTPVNI	*In vitro* stimulation	human(A*0201)	[Konya97]
	NOTES: • Peptide predicted to be reactive based on HLA-A*0201 binding motif • Peptide could stimulate CTL in PBMC from 5/6 seronegative donors • Peptide located in a highly conserved region of protease • Both 9-mer and 10-mer could stimulate CTL: VLVGPTPVNI and LVGPTPVNI • Binding affinity to A*0201 was measured, $C_{1/2max}\mu M$ = 6 for 10-mer, 3 for 9-mer • MAL variant of Pr(75-84 MN), with substitutions V77, G78, and P79 gave reduced binding and CTL recognition				
RT(LAI)	RT(158-167)	SPIETVPVKL	HIV-1 infection	human(A2,B61)	[vanderBurg97]
	NOTES: • Recognized by CTL from a long term survivor, EILKEPVGHGV was also recognized • Highly conserved across clades				
RT(160-184 HXB2)	RT(160-184)	IETVPVKLKPGMDGPKV-KQWPLTEE	HIV-1 infection	human(B8)	[Walker89]
	NOTES: • One of five epitopes defined for RT specific CTL clones in this study				
RT(18-26)	RT(173-181)	GPKVKQWPL	HIV-1 infection	human(B8)	[Meier95]
	NOTES: • HIV proteins with mutations in this epitope allowed transactive inhibition of specific CTL mediated lysis				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(173-181)	RT(173-181)	GPKVKQWPL		human(B8)	[Goulder97c]
	NOTES:				
	• Included in a study of the B8 binding motif				
RT(185-193 LAI)	RT(173-181)	GPKVKQWPL	no CTL shown	human(B8)	[Sutton93]
	NOTES:				
	• Predicted epitope based on B8 binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE				
RT(185-193 LAI)	RT(173-181)	GPKVKQWPL	HIV-1 infection	human(B8)	[Klenerman95]
	NOTES:				
	• Naturally occurring antagonist GPRVKQWPL found in viral PBMC DNA and RNA				
RT(33-41)	RT(188-196)	ALVICTEM	HIV-1 infection	human(A2)	[Haas98]
	NOTES:				
	• 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 was defined as optimal by peptide titration assays (per. comm., G. Haas)				
RT(33-43)	RT(188-198)	ALVICTEMEK	HIV-1 infection	human(A3)	[Haas98]
	NOTES:				
	• 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 was defined as optimal by peptide titration assays (per. comm., G. Haas)				
RT(191-215)	RT(?)		HIV-1 infection	human(polyclonal)	[Haas97]
	NOTES:				
	• Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably escape variant RT 215 T to Y				
RT(205-219 BRU)	RT(193-207)	CTEMEKEGKISKIGP	recRT injection	murine($H2^k$)	[DeGroot91]
	NOTES:				
	• Murine and human helper and CTL epitope				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(205-219)	RT(193-207)	CTEMEKEGKISKIGP	HIV-1 infection	human(broad)	[Hosmalin90]
	NOTES: • Murine and human helper and CTL epitope				
RT(206-214)	RT(194-202)	TEMEAEGKI	peptide on pulsed irradiated splenocytes	C3H/HeJ mice	[Leggatt97]
	NOTES: • 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(42-50)	RT(197-205)	EKEGKISKI	HIV-1 infection	human(B51)	[Haas98]
	NOTES: • 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 was defined as optimal by peptide titration assays (per. comm., G. Haas)				
RT(262-270 IIIB)	RT(262-270)	TVLDVGDAY	HIV-1 infection	human(B35)	[Walkerpercom96]
	NOTES: • 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				
RT(267-277)	RT(263-273)	VLDVGDAYFSV	*in vitro* stimulation	human(A*0201)	[vanderBurg96]
	NOTES: • 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				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(267-277)	RT(263-273)	VLDVGDAYFSV	HIV-1 infection	human(A2)	[Kundu98]
NOTES: • 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(267-277)	RT(263-273)	VLDVGDAYFSV	*in vitro* stimulation	human(A2)	[vanderBurg95]
NOTES: • Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor • VLDVGDAYFSV is in a functional domain					
RT(273-282 IIIB)	RT(273-282)	VPLDEDFRKY	HIV-1 infection	human(B35)	[Shiga96]
NOTES: • Binds HLA-B*3501					
RT(273-282 SF2)	RT(273-282)	VPLDKDFRKY	HIV-1 infection	human(B*3501)	[Tomiyama97]
NOTES: • 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					
RT(273-282 IIIB)	RT(273-282)	VPLDEDFRKY	HIV-1 infection	human(B35)	[Sipsas97]
NOTES: • 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					

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(295-302 IIIB)	RT(283-290)	TAFTIPSI	HIV-1 infection	human(B51)	[Sipsas97]
	NOTES: • 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 • TAFTIPSV, a variant found in HIV-1 VE1RT, was also recognized • TVFTIPSI, a variant found in HIV-1 MANC, was also recognized				
RT(308-320)	RT(308-320)	WKGSPAIFQSSMT	HIV-1 infection	human(B7)	[Brander95a]
	NOTES: • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
RT(311-319 SF2)	RT(311-319)	SPAIFQSSM	HIV-1 infection	human(B35)	[Shiga96]
	NOTES: • Binds HLA-B*3501				
RT(311-319 SF2)	RT(311-319)	SPAIFQSSM	HIV-1 infection	human(B*3501)	[Tomiyama97]
	NOTES: • A CTL clone responsive to this epitope was obtained • Only 1/7 B35 positive individuals had a CTL response to this epitope				
RT(311-319 SF2)	RT(311-319)	SPAIFQSSMT		human(B7)	[Brander97]
	NOTES: • Per. comm. from C. Hey and D. Ruhl to C. Brander and B. Walker				
RT(325-333 IIIB)	RT(313-321)	AIFQSSMTK	HIV-1 infection	human(A3)	[Walkerpercom96]
	NOTES: • 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				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT	RT(313-321)	AIFQSSMTK	HIV-1 infection	human(A11)	[Wagner98b]
	NOTES: • 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(325-333)	RT(313-321)	AIFQSSMTK	HIV-1 infection	human(A11, A3, A*6801)	[Threlkeld97]
	NOTES: • 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				
RT(325-333 LAI)	RT(313-321)	AIFQSSMTK	HIV-1 infection	human(A3)	[Cao97]
	NOTES: • 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(325-333)	RT(313-321)	AIFQSSMTK	HIV-1 infection	human(A3.1)	[Brander95a]
	NOTES: • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
RT(325-333 LAI)	RT(313-321)	AIFQSSMTK	No CTL shown	human(A11)	[Zhang93]
	NOTES: • Exploration of A11 binding motif, based on Nixon et al. 1991				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(325-333 LAI)	RT(313-321)	AIFQSSMTK	HIV-1 infection	human(A11)	[McMichael94]
	NOTES: • Review of HIV CTL epitopes				
RT(325-333 LAI)	RT(313-321)	AIFQSSMTK		human(A33)	[Rowland-JonesPerCom95]
	NOTES: • Defined as minimal peptide by titration curve, S. Rowland-Jones, per. comm.				
RT(325-349 PV22)	RT(313-337)	AIFQSSMTKILEPFRKQ-NPDIVIYQ	HIV-1 infection	human(A11)	[Jassoy93]
	NOTES: • HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
RT(325-349)	RT(313-337)	AIFQSSMTKILEPFRKQ-NPDIVIYQ	HIV-1 infection	human(A11)	[Price95]
	NOTES: • Study of cytokines released by HIV-1 specific activated CTL				
RT(342-366 LAI)	RT(330-354)	NPDIVIYQYMDDLYVGS-DLEIGQHR	HIV-1 infection	human(A11)	[Walker89]
	NOTES: • One of five epitopes defined for RT specific CTL clones in this study				
RT(342-350 LAI)	RT(330-338)	HPDIVIYQY	HIV-1 infection	human(B35)	[McMichael94]
	NOTES: • Review of HIV CTL epitopes				
RT(329-337)	RT(330-338)	HPDIVIYQY	HIV infection	human(B35)	[RowlandJones95]
	NOTES: • NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(329-337)	RT(330-338)	HPDIVIYQY	none	human(B35)	[Lalvani97]
	NOTES: • 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(328-336 IIIB)	RT(330-338)	NPDIVIYQY	HIV-1 infection	human(B35)	[Shiga96]
	NOTES: • Binds HLA-B*3501				
RT(328-336 IIIB)	RT(330-338)	NPDIVIYQY	HIV-1 infection	human(B*3501)	[Tomiyama97]
	NOTES: • 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(328-336 IIIB)	RT(330-338)	NPDIVIYQY	HIV-1 infection	human(B35)	[Sipsas97]
	NOTES: • 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				
RT	RT(330-338)	NPDIVIYQY	HIV-1 exposure	human(B35)	[RowlandJones98]
	NOTES: • 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				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT	RT(334-342)	VIYQYMMDL	HIV-1 exposure	human(A2)	[RowlandJones98]
	NOTES: • 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	RT(334-342)	VIYQYMDDL	Multi-epitope gene in VVA	human(A*0201)	[Hanke98c, Hanke98b]
	NOTES: • 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(346-354 LAI)	RT(334-342)	VIYQYMDDL	HIV infection	human(A2)	[Harrer96]
	NOTES: • The substitution VIYQYVDDL abrogates CTL response and confers drug resistance				
RT(179-187)	RT(334-342)	VIYQYMDDL	HIV infection	human(A2)	[Haas98]
	NOTES: • 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(LAI)	RT(335-344)	IYQYMDDLYV	HIV-1 infection	human(A*0201)	[vanderBurg97]
	NOTES: • 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(191-215)	RT(347-371)	DLEIGQHRTKIEELRQH-LLRWGFTT?	HIV-1 infection	human(polyclonal)	[Haas97]
	NOTES: • Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably escape variant RT 215 T to Y				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(359-383 HXB2)	RT(347-371)	DLEIGQHRTKIEELRQH-LLRWGLTT	HIV-1 infection	human(Bw60)	[Walker89]
	NOTES: • One of five epitopes defined for RT specific CTL clones in this study				
RT(192-201)	RT(347-356)	DLEIGQHRTK	HIV-1 infection	human(A3)	[Haas98]
	NOTES: • 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(201-209)	RT(356-364)	KIEELRQHL	HIV-1 infection	human(A2)	[Haas98]
	NOTES: • 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(LAI)	RT(358-367)	EELRQHLLRW	HIV-1 infection	human(B44)	[vanderBurg97]
	NOTES: • 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(364-375)	LLRWGLTTPDKK	HIV-1 infection	human(A2)	[Haas98]
	NOTES: • 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(LAI)	RT(398-407)	PIVLPEKDSW	HIV-1 infection	human(B*5701)	[vanderBurg97]
	NOTES: • Recognized by CTL from a progressor and a long term survivor, KITTESIVIW was also recognized				
RT(415-426 IIIB)	RT(415-426)	LVGKLNWASQIY	HIV-1 infection	human(Bw62)	[Brander96]
	NOTES: • P. Johnson, pers. comm.				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(438-446 IIIB)	RT(426-434)	YPGIKVRQL	HIV-1 infection	human(B42)	[Walkerpercom96]
	NOTES: • 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(448-456 SF2)	RT(448-456)	IPLTEEAEL	HIV-1 infection	human(B35,B51)	[Shiga96]
	NOTES: • Binds HLA-B*3501 and B*5101				
RT(448-456 SF2)	RT(448-456)	IPLTEEAEL	HIV-1 infection	human(B*3501)	[Tomiyama97]
	NOTES: • 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				
RT(461-485 HXB2)	RT(449-473)	PLTEEAELELAENREIL-KEPVHGVY	HIV-1 infection	human(A2)	[Walker89]
	NOTES: • One of five epitopes defined for RT specific CTL clones in this study				
RT(LAI)	RT(463-472)	EILKEPVGHV	HIV-1 infection	human(A*0201)	[vanderBurg97]
	NOTES: • Recognized by CTL from a long term survivor, SPIETVPVKL was also recognized • Recognized by CTL from a progressor, EELRQHLLRW and TWETWWTEYW were also recognized				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Pol(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Wilson98]
	NOTES: • 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				
Pol(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Ogg98]
	NOTES: • 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	RT(464-472)	ILKEPVHGV	Multi-epitope gene in VVA	human(A*0201)	[Hanke98c, Hanke98b]
	NOTES: • 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(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Collins98]
	NOTES: • 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				
Pol(476-484 LAI)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Fan97]
	NOTES: • The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(464-472)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Kundu98]
	NOTES: • 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(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Tsomides94]
	NOTES: • CTL clones recognize naturally processed peptide – peptide abundance corresponded to level of CTL killing				
RT(476-484)	RT(464-472)	ILKEPVHGV	*In vitro* stimulation	human(A*0201)	[Konya97]
	NOTES: • This epitope was included as a positive control • Binding affinity to A*0201 was measured, $C_{1/2max}\mu M$ = 12				
RT(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 exposure	human(A2)	[Konya97]
	NOTES: • 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(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Cao97]
	NOTES: • 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				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(468-476)	RT(464-472)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[vanderBurg96]
	NOTES: • Immunogenic in humans, slow dissociation rate, associated with immunogenicity in transgenic HLA-A*0201/K^b mice • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				
RT(468-476)	RT(464-472)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[vanderBurg95]
	NOTES: • Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor				
RT(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Pogue95]
	NOTES: • Mutational study: position 1 I to Y increases complex stability with HLA-A*0201				
pol(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Goulder97, Goulder97e]
	NOTES: • 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 SLYNT-VATL • Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL • [Goulder97e] is a review of immune escape that summarizes this study				
RT(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Yang96]
	NOTES: • 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				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Yang97]
NOTES: • 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(464-472)	ILKEPVHGV	HIV infection	human(A2)	[Moss95]
NOTES: • Two clones were obtained with different TCR usage, $V_\beta 1$ and $V_\beta 21$					
RT(309-317)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Altman96]
NOTES: • 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 • Reviewed in [McMichael98]					
RT(476-484)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Musey97]
NOTES: • Cervical CTL clones from an HIV infected woman recognized this epitope					
RT(476-484)	RT(464-472)	ILKEPVHGV	none	human(A*0201)	[Walter97]
NOTES: • 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					

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(476-484 LAI)	RT(464-472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Tsomides91]
	NOTES: • Precise identification of the nonamer that binds to A2				
RT(476-484 LAI)	RT(464-472)	ILKEPVHGV	no CTL shown	human(A2)	[Connan94]
	NOTES: • Promotes assembly of HLA-A2 molecules in T2 cell lysates				
RT(510-518)	RT(464-472)	ILKEPVHGV	none	human(A2)	[Parker92]
	NOTES: • Studied in the context of HLA-A2 peptide binding				
RT(476-485 LAI)	RT(464-473)	ILKEPVHGVY	HIV-1 infection	human(Bw62)	[McMichael94]
	NOTES: • Review of HIV CTL epitopes • Also: P. Johnson 1991 and pers. comm. P. Johnson				
RT(495-515 LAI)	RT(483-507)	EIQKQGQGQWTYQIYQE-PFKNLKTG	HIV-1 infection	human(A11)	[Walker89]
	NOTES: • One of five epitopes defined for RT specific CTL clones in this study				
RT(507-519 LAI)	RT(495-507)	QIYQEPFKNLKTG	HIV-1 infection	human(A11)	[Johnson94b]
	NOTES: • This epitope was listed in a review				
RT(507-516)	RT(495-505)	QIYQEPFKNLK	HIV-1 infection	human	[Price95]
	NOTES: • Study of cytokines released by HIV-1 specific activated CTL				
RT(508-516)	RT(496-505)	IYQEPFKNLK	HIV-1 infection	human(A11)	[CulmannPerCom]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(518-526 U455)	RT(519-527)	DVKQLTEVV		human(A*6802)	[Dong98]
	NOTES: • Predicted on binding motif, no truncations analyzed • Reacts with clade A consensus (U455), and with the peptide DVKQLAEAV, from the D clade				
RT(518-526 U455)	RT(519-527)	DVKQLTEVV		human(B70)	[Dorrell98]
RT(LAI)	RT(529-538)	KITTESIVIW	HIV-1 infection	human(B*5701)	[vanderBurg97]
	NOTES: • Recognized by CTL from a progressor and a long term survivor, PIVLPEKDSW was also recognized				
RT(559-568 LAI)	RT(547-556)	PIQKETWETW		human(A32)	[Harrer96b]
RT(LAI)	RT(552-561)	TWETWWTEYW	HIV-1 infection	human(B44)	[vanderBurg97]
	NOTES: • 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(576-584)	PLVKLWYQL	HIV-1 infection	human(A2)	[Haas98]
	NOTES: • 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(587-597 SF2)	RT(587-596)	EPIVGAETFY	HIV-1 infection	human(B35)	[Shiga96]
	NOTES: • Binds HLA-B*3501, but not presented by B51, in contrast to the peptide EPIVGAETF				
RT(587-597 SF2)	RT(587-595)	EPIVGAETF	HIV-1 infection	human(B*3501)	[Tomiyama97]
	NOTES: • 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				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(587-596 SF2)	RT(587-595)	EPIVGAETF	HIV-1 infection	human(B35,B51)	[Shiga96]
	NOTES: • Binds HLA-B*3501, and presented by B51 – CTL could not kill RT-vaccinia virus infected cells that expressed B51				
RT(LAI)	RT(589-602)	IVGAETFYVDGAAS	HIV-1 infection	human(A*6802)	[vanderBurg97]
	NOTES: • Recognized by CTL from a long term survivor that recognized a set of 5 overlapping peptides spanning IVGAET-FYVDGAAS as well as PIVLPEKDSW and KITTESIVIW • A*6802 is a subset of HLA-A28				
RT(591-600 IIIB)	RT(591-600)	GAETFYVDGA	HIV-1 infection	human(B45)	[Walkerpercom96]
	NOTES: • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • GVETFYVDGA, a naturally occurring variant, was recognized				
RT(592-602 LAI)	RT(592-602)	AETFYVDGAAN		human(A28)	[Brander96]
	NOTES: • P. Johnson pers. comm.				
RT(593-603 IIIB)	RT(593-603)	ETFYVDGAANR	HIV-1 infection	human(A26)	[Walkerpercom96]
	NOTES: • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • ETYYVNGAANR, a naturally occurring variant, was found in non-transmitting mother and is recognized but less reactive				
RT(648-672 PV22)	RT(636-660)	AIYLALQDSGLEVNIVT-DSQYALGI	HIV-1 infection	human(B14)	[Kalams94]
	NOTES: • A CTL response used to study gene usage in HLA-B14 response				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(648-672)	RT(636-660)	AIYLALQDSGLEVNIVT-DSQYALGI	HIV-1 infection	human	[Price95]
	NOTES: • Study of cytokines released by HIV-1 specific activated CTL				
RT(648-672)	RT(640-660)	ALQDSGLEVVTDSQYALGI	HIV-1 infection	human(B14)	[Brander95a]
	NOTES: • Unpublished, S. Kalams				
RT(640-648 HXB2R)	RT(640-648)	ALQDSGLEV	no CTL shown	human(A2)	[Brander95]
	NOTES: • Epitope studied in the context of inclusion in a synthetic vaccine				
RT(640-648 HXB2R)	RT(640-648)	ALQDSGLEV	peptide vaccine	human(A2.1)	[Brander96b, Brander95b]
	NOTES: • 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				
RT(663-672 IIIB)	RT(651-660)	VTDSQYALGI	HIV-1 infection	human(Cw8)	[Brander96]
	NOTES: • 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 [Brander96]				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT	RT(651-660)	VTDSQYALGI	HIV-1 exposure	human(Cw8)	[RowlandJones98]
	NOTES: • 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)				
RT(516-525)	RT(671-680)	ELVNQIIEQL	HIV-1 infection	human(A2)	[Haas98]
	NOTES: • 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(532-540)	RT(687-695)	YLAWVPAHK	HIV-1 infection	human(B7)	[Haas98]
	NOTES: • 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(797-804 SF2)	RT(797-804)	GYIEAEVI	HIV-1 infection	human(A*2402)	[IkedaMoore97]
	NOTES: • Defined using reverse immunogenetics – 59 HLA-A*2402 binding peptides were predicted by searching for A*2402 anchors in HIV proteins, (Tyr at 2, and Phe, Leu or Ile at the C term) – 53 of the 59 peptides bound A*2402 • This peptide induced CTL in 1/4 HIV-1+ people tested • GYIEAEVI bound to A*2402 weakly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
In(823-831)	RT(811-819)	ETAYFILKL		human(A*6802)	[Rowland-JonesPerCom98]
	NOTES: • Epitope found in clade A, B, and D – per. comm. S. Rowland-Jones and T. Dong				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(956-964)	RT(956-964)	LLWKGEGAV	HIV-1 infection	human(A2)	[Kundu98]
	NOTES: • 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 • LLWKGEGAV is a conserved HLA-A2 epitope included in this study – 6/6 patients had this sequence as their HIV direct sequence, but only four of these had a detectable CTL response				
RT(956-964 HXB2R)	RT(956-964)	LLWKGEGAV	no CTL shown	human(A2)	[Parker92, Parker94]
	NOTES: • Studied in the context of HLA-A2 peptide binding				
RT(956-964 HXB2R)	RT(956-964)	LLWKGEGAV	no CTL shown	human(A2)	[Brander95]
	NOTES: • No CTL activity found in HIV infected subjects, epitope studied in the context of inclusion in a synthetic vaccine				
RT(576-584)	RT(956-964)	LLWKGEGAV	*in vitro* stimulation	human(A*0201)	[vanderBurg96]
	NOTES: • Slow dissociation rate, associated with immunogenicity in transgenic HLA-A*0201/K^b mice • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				
RT(gag/pol)	RT		DNA gag/pol, vif, and env vaccine	murine	[Kim97]
	NOTES: • A gag/pol, vif or gp160 DNA vaccine, when delivered in conjuction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice • When IL-12 was present, CTL response could be detected even without *in vitro* stimulation				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
RT(pol)	RT(pol)		HIV infection	human	[Trickett98]
	NOTES: • 12 HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection • Improvement in CD4+ and CD8+ T cells were seen in 7/12, and an increase in the CTL response to Pol was seen in one patient				
RT(gag/pol)	RT		DNA gag/pol, and env vaccine	murine	[Kim97b]
	NOTES: • A gag/pol or env DNA vaccine, when delivered in conjuction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice • When CD86 was present, CTL response could be detected even without *in vitro* stimulation				
Pol	RT		HIV-1 infection	human	[Froebel97]
	NOTES: • Two HIV-1 infected children with contrasting disease courses were followed longitudinally – one died of AIDS, the other is a long term non-progressor • Reactivity against Gag, Pol, Env and Tat proteins was tested by PBMC bulk cultured cells reacting with protein expressed in vaccinia constructs in autologous EBV transformed B cells • The child who progressed consistently had CTL against Pol and Tat • The long term non-progressing child had no detectable CTL, but was heterozygous for a mutation in the CCR5 receptor and for HLA-B49, which has been shown to be associated with slower progression				
Pol(Pol IIIB)			HIV-1 infection	human	[Betts97]
	NOTES: • 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia expressed Gag, Pol and Env proteins • A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients				
Pol			HIV-1 infection	human	[DeMaria97]
	NOTES: • CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T-cell function • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels				