Table 10: **Nef**

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(13-20 LAI)	Nef(13-20)	WPTVRERM	HIV-1 infection	human(B8)	[Goulder97c]
	NOTES:				
	• Unusual epitope for HLA-B8, but compatible with crystal structure predictions				
Nef(61-80)	Nef(60-79)	EEEEVGFPVTPQVPLRPMTY	HIV infection	human	[Lieberman95]
	NOTES:				
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
Nef(61-80 SF2)	Nef(60-79)	EEEEVGFPVTPQVPLRPMTY	HIV infection	human	[Lieberman97]
	NOTES:				
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein				
	• 12 subjects had CTL that could recognize vaccinia expressed LAI Nef				
	• Two of these 12 had CTL response to this peptide				
	• The responding subjects were HLA-A11, A24, B8, B35, and HLA not determined				
Nef(61-80 SF2)	Nef(60-79)	EEEEVGFVTPQVPLRPMTY	HIV-1 infection	human	[Lieberman97b]
	NOTES:				
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(66-80 BRU)	Nef(64-78)	VGFPVTPQVPLRMT	HIV-1 infection	human(A1,B8)	[Hadida92]
	NOTES:				
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(68-77 LAI)	Nef(66-75)	FPVTPQVPLR	HIV-1 infection	human(B7)	[Haas96]
	NOTES:				
	• There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection				
Nef(72-80 SF2)	Nef(66-74)	FPVRPQVPL	HIV-1 infection	human(B35)	[Shiga96]
	NOTES:				
	• Binds HLA-B*3501				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(72-80 SF2)	Nef(66-74)	FPVRPQVPL	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 • An R to T substitution at position 4 abrogates specific lysis, but not binding to B*3501					
Nef(75-85 SF2)	Nef(69-79)	RPQVPLRPMTY	HIV-1 infection	human(B35)	[Shiga96]
NOTES: • Binds HLA-B*3501					
Nef(75-85 SF2)	Nef(69-79)	RPQVPLRPMTY	HIV-1 infection	human(B*3501)	[Tomiyama97]
NOTES: • A CTL clone responsive to this epitope was obtained • 4/7 B35 positive individuals had a strong CTL response to this epitope • An R to T substitution at position 1 abrogates specific lysis, but not binding to B*3501 • An R to H substitution at position 7 did not alter reactivity					
Nef(71-90 SF2)	Nef(70-89)	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human	[Lieberman97]
NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53					
Nef(71-90 SF2)	Nef(70-89)	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human	[Lieberman97b]
NOTES: • CTL expanded *ex vivo* were later infused into HIV-1 infected patients					
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK		human(B27)	[CulmannPerCom]
NOTES: • Optimal epitope mapped by peptide titration					

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali98]
	NOTES: • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: QVPLRPMTYK			
Nef(73-82 NL43)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig90]
	NOTES: • Tyr is critical for binding to A3.1				
Nef(73-82 BRU)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3,A11, B35)	[Culmann91]
	NOTES: • Nef CTL clones from HIV+ donors				
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A2?)	[Robertson93]
	NOTES: • Development of a retroviral vector (pNeoNef) to generate autologous CTL targets • [Hunziker98] suggests that HLA-A2 does not in fact present this epitope, in spite of the suggestion in this study that it did – also see [Brander98b]				
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin94, Goulder97e]
	NOTES: • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder97e] is a review of immune escape that summarizes this study				
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin95]
	NOTES: • Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder97, Goulder97e]
	NOTES:				
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII				
	• Both had a response to this epitope				
	• [Goulder97e] is a review of immune escape that summarizes this study				
Nef(73-82)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki97]
	NOTES:				
	• 82 HIV-1-specific CTL clones from 5 long term non-progressors were isolated and analyzed for breadth of response				
	• A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response				
	• An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being specific for this epitope, isolated at two time points, 1 year apart				
Nef(73-82)	Nef(71-80)	QVPLRPMTYK	HIV infection	human	[Garcia97]
	NOTES:				
	• The anti-Nef CTL line P1 specific for this epitope is able to kill target cells via two mechanisms				
	• First: Ca^{2+}-dependent, perforin-dependent Nef-specific lysis				
	• Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-specific targets				
	• Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice				
	• CTL mediated CD95-dependent apoptosis may play a role in pathogenesis				
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig95]
	NOTES:				
	• Alanine substitutions L76A, R77A, M79A, T80A significantly decreased immunogenicity of peptide				
	• Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health				
	• Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression				
Nef(73-82)	Nef(72-80)	VPLRPMTYK	no CTL shown	human(A11)	[Zhang93]
	NOTES:				
	• Exploration of A11 binding motif				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82 LAI)	Nef(72-79)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael94]
	NOTES: • Review of HIV CTL epitopes – defined by B35 motif found within a larger peptide				
Nef(73-82 LAI)	Nef(72-79)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[RowlandJones95]
	NOTES: • VPLRPMTY also recognized by CTL from HIV-2 seropositives, epitope is conserved				
Nef	Nef(72-79)	VPLRPMTY	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 and D subtype consensus are identical to the B clade epitope				
Nef(75-82)	Nef(72-79)	VPLRPMTY	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				
Nef(75-82)	Nef(72-79)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith96]
	NOTES: • Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex				
Nef(74-82)	Nef(72-79)	VPLRPMTY		human(A3)	[Carreno92]
	NOTES: • Included in HLA-A3 binding peptide competition study				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(75-82 LAI)	Nef(73-80)	PLRPMTYK	HIV-1 infection	human(A11)	[McMichael94]
	NOTES:				
	• Review of HIV CTL epitopes				
Nef(77-85 LAI)	Nef(75-83)	RPMTYKAAL	HIV-1 infection	human(B7)	[Bauer97]
	NOTES:				
	• Structural constraints on the Nef protein may prevent escape				
Nef(81-100 SF2)	Nef(80-99)	KAAVDLSHFLKEKGGLEGLI	HIV-1 infection	human	[Lieberman97]
	NOTES:				
	• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein				
	• 11 subjects had CTL that could recognize vaccinia expressed LAI Nef				
	• Three of these 11 had CTL response to this peptide				
	• The responding subjects were HLA-A1, A2, B8, B14; HLA-A11, A24, B8, B53				
Nef(83-94 BRU)	Nef(81-92)	AAVDLSHFLKEK	HIV-1 infection	human(A11)	[Culmann91]
	NOTES:				
	• Epitope defined by boundaries of overlapping peptides that stimulate Nef CTL clones				
Nef(84-92 LAI)	Nef(82-90)	AVDLSHFLK	HIV-1 infection	human(A11)	[McMichael94]
	NOTES:				
	• Review of HIV CTL epitopes				
Nef(84-92 LAI)	Nef(82-90)	AVDLSHFLK	HIV-1 infection	human(A11)	[Couillin94, Goulder97e]
	NOTES:				
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response				
	• [Goulder97e] is a review of immune escape that summarizes this study				
Nef(84-92 LAI)	Nef(82-90)	AVDLSHFLK	HIV-1 infection	human(A11)	[Couillin95]
	NOTES:				
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(84-91 LAI)	Nef(82-89)	AVDLSHFL	HIV-1 infection	human(Bw62)	[CulmannPenciolelli94]
Nef(86-100 LAI)	Nef(84-98)	DLSHFLKEKGGLEGL	HIV-1 infection	human(B35)	[Buseyne93]
Nef(86-100 LAI)	Nef(84-98)	DLSHFLKEKGGLEGL	HIV-1 infection	human(A2)	[Robertson93]
	NOTES: • Development of a retroviral vector (pNeoNef) to generate autologous targets				
Nef(84-92 LAI)	Nef(84-92)	DLSHFLKEK	HIV-1 infection	human(A3.1)	[McMichael94]
	NOTES: • Review of HIV CTL epitopes				
Nef(89-97 LAI)	Nef(88-95)	FLKEKGGL	HIV-1 infection	human(B8)	[Price97]
	NOTES: • CTL escape variants appeared over time in HLA-B8 HIV-1+ individual, providing evidence for immune escape • Most variants appear at position 5, an anchor residue • FLKE(ENQ)GGL showed reduced binding efficiency and recognition • Double mutants (FIKENGGL, FLEENGGL, and FLKGNGGL) completely escaped recognition • [Goulder97e] is a review of immune escape that summarizes this study in the context of CTL escape to fixation				
Nef	Nef(88-95)	FLKEKGGL	Multi-epitope gene in VVA	human(B8)	[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				
Nef(88-95)	Nef(88-95)	FLKEKGGL	HIV-1 infection	human(B8)	[Goulder97c]
	NOTES: • Natural variants for this epitope have been observed in several donors • Substitutions Q5, N5, E5 that alter anchor position 5 are not well recognized • Substitution I2 binds well to B8 and is recognized				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(93-106 BRU)	Nef(91-104)	EKGGLEGLIHSQRR	HIV-1 infection	human(A1,B8)	[Hadida92]
	NOTES: • HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(102-115 LAI)	Nef(100-113)	HSQRRQDILDLWIY	HIV-1 infection	human(B7)	[Goulder97, Goulder97e]
	NOTES: • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • One had a strong response to this peptide, the other did not • [Goulder97e] is a review of immune escape that summarizes this study				
Nef(101-120 SF2)	Nef(100-119)	HSQRRQDILDLQIYHTQGYF	HIV-1 infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • Two of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, A3, B8, B62 and HLA-A2, B21				
Nef(103-127 PV22)	Nef(101-125)	SQRRQDILDLWIYHTQG-YFPDWQNY	HIV-1 infection	human(B13)	[Jassoy93]
	NOTES: • HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
Nef(105-114 LAI)	Nef(103-112)	RRQDILDLWI	HIV-1 infection	human(B*2705)	[Goulder97d]
	NOTES: • Defined as optimal epitope from within reactive peptide HSQRRQDILDLWIYHTQGYF [Nef(102-121 LAI)] • HLA-B*2705 is associated with slow HIV disease progression • The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position				
Nef(111-132)	Nef(110-131)	LWIYHTQGYFPDWQNYT-PGPGV	HIV infection	human	[Lieberman95]
	NOTES: • HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(111-132 SF2)	Nef(110-131)	LWIYHTQGYFPDWQNYT-PGPGV	HIV infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • Four of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, B21; HLA-A1, A3, B7, B15; HLA-A2, A26, B7, B38				
Nef(111-132 SF2)	Nef(110-131)	LWIYHTQGYFPDWQNYT-PGPGV	HIV-1 infection	human	[Lieberman97b]
	NOTES: • CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(113-128 BRU)	Nef(111-126)	WIYHTQGYFPDWQNYT	HIV-1 infection	human(A1)	[Hadida92]
	NOTES: • HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(113-125 BRU)	Nef(111-123)	WIYHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann89]
	NOTES: • Nef CTL clones from HIV+ donors				
Nef(115-125 BRU)	Nef(113-123)	YHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann91]
	NOTES: • Nef CTL clones from HIV+ donors				
Nef(116-125 BRU)	Nef(114-123)	HTQGYFPDWQ	HIV-1 infection	human(B57)	[Culmann91]
	NOTES: • Nef CTL clones from HIV+ donors, optimal peptide mapped				
Nef(117-128 BRU)	Nef(115-126)	TQGYFPDWQNYT	HIV-1 infection	human(B17,B37)	[Culmann91]
	NOTES: • Nef CTL clones from HIV+ donors				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(117-127 LAI)	Nef(115-125)	TQGYFPDWQNY	HIV-1 infection	human(Bw62)	[CulmannPerCom]
	NOTES: • Optimal peptide defined by titration, B. Culmann, per. comm.				
Nef(118-127 LAI)	Nef(116-125)	QGYFPDWQNY		human(Bw62)	[McMichael94]
	NOTES: • Review of HIV CTL epitopes				
Nef(120-128 IIIB)	Nef(118-126)	YFPDWQNYT	HIV-1 infection	human	[Walkerpercom96]
	NOTES: • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • FFPDWKNYT, a naturally occurring variant, was found in mother and infant and was recognized • LFPDWKNYT, a naturally occurring variant, was found in infant and is not recognized				
Nef(120-128 LAI)	Nef(118-126)	YFPDWQNYT	HIV-1 infection	human(B37,B57)	[CulmannPerCom]
	NOTES: • Nef CTL clones from HIV+ donors – optimum peptide mapped by titration				
Nef(120-144 SF2)	Nef(118-142)	YFPDWQNYTPGPGIRYP-LTFGWCYK	HIV-1 infection	human(A24)	[Jassoy92]
	NOTES: • Epitope recognized by CTL clone derived from CSF				
Nef(121-140 SF2)	Nef(120-139)	PDWQNYTPGPGVRYPLTFGW	HIV-1 infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A2, B21; HLA-A3, A24, B7, B38				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(123-137 IIIB)	Nef(121-135)	QWQNYTPGPGVRYPL	HIV-1 infection	human	[Walkerpercom96]
	NOTES: • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • FFPDYTPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in mother and are not recognized • LFPDYKPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in infant and are not recognized				
Nef(126-138 BRU)	Nef(124-136)	NYTPGPGVRYPLT	HIV-1 infection	human(B7)	[Culmann91]
	NOTES: • Nef CTL clones from HIV+ donors				
Nef(128-137 LAI)	Nef(126-135)	TPGPGVRYPL	HIV-1 infection	human(B7)	[Haas96, Haas97]
	NOTES: • There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection • The epitope position was taken from [Haas97]				
Nef	Nef(126-135)	TPGPGVRYPL	HIV-1 exposure	human(B7)	[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 D subtype consensus is identical to the B clade epitope • The A subtype consensus is TPGPGIRYPL				
Nef(130-143 LAI)	Nef(128-141)	GPGVRYPLTFGWCY	HIV-1 infection	human(B*57)	[Goulder96]
	NOTES: • CTL response to this epitope observed in 4 long term survivors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(132-147 BRU)	Nef(130-145)	GVRYPLTFGWCYKLVP	HIV-1 infection	human(A1,B8)	[Hadida92]
	NOTES: • HIV-1 specific CTLs detected in lymphoid organs				
Nef(132-147 BRU)	Nef(130-145)	GVRYPLTFGWCYKLVP	HIV-1 infection	human(B18)	[Culmann91]
	NOTES: • Nef CTL clones from HIV+ donors				
Nef(133-148 LAI)	Nef(131-146)	VRYPLTFGWCYKLVPV		human(B57)	[Brander96]
	NOTES: • P. Goulder, pers. comm.				
Nef(134-144 LAI)	Nef(132-142)	RYPLTFGWCYK	HIV-1 infection	human(B18)	[Couillin94, Goulder97e]
	NOTES: • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder97e] is a review of immune escape that summarizes this study				
Nef(138-147 SF2)	Nef(132-141)	RYPLTFGWCF	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 3/4 HIV-1+ people tested • RYPLTFGWCF bound to A*2402 strongly, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained				
Nef(134-141 LAI)	Nef(132-139)	RYPLTFGW		human(B27)	[CulmannPerCom]
	NOTES: • Optimal peptide defined by titration				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(139-147 SF2)	Nef(133-141)	YPLTFGWCF	HIV-1 infection	human(B35)	[Shiga96]
	NOTES: • Binds HLA-B*3501				
Nef	Nef(133-141)	YPLTFGWCY	HIV-1 exposure	human(B49)	[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 identical to the B clade epitope • The D subtype consensus is YPLTFGWCf				
Nef(135-143)	Nef(133-141)	YPLTFGWCY	HIV-1 exposure	human(B18)	[Culmann91, CulmannPenci-olelli94]
	NOTES: • Nef CTL clones from HIV+ donors				
Nef(136-145)	Nef(134-143)	PLTFGWCFKL	HIV-1 infection	human(A2)	[Durali98]
	NOTES: • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFG-WCFKL				
Nef(161-180)	Nef(160-179)	TSLLHPVSLHGMDDPEREVL	HIV infection	human	[Lieberman95]
	NOTES: • HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(161-180 SF2)	Nef(160-179)	TSLLHPVSLHGMDDPEREVL	HIV infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide				
Nef(101-120 SF2)	Nef(160-179)	TSLLHPVSLHGMDDPEREVL	HIV-1 infection	human	[Lieberman97b]
	NOTES: • CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(161-180 SF2)	Nef(160-179)	TSLLHPVSLHGMDDPEREVL	HIV infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide				
Nef(171-190 SF2)	Nef(170-189)	GMDDPEREVLEWRFDSRLAF	HIV-1 infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, B21				
Nef(180-189 LAI)	Nef(178-187)	VLEWRFDSRL	HIV-1 infection	human(A2)	[Haas96, Haas97]
	NOTES: • There was a high degree of variation in three CTL epitopes in Nef in four slow and non-progressors, and variant specific CTLs arose over time to eliminate variants, indicating immune selection				
Nef(182-198 BRU)	Nef(180-196)	EWRFDSRLAFHHVAREL	HIV-1 infection	human(A1,B8)	[Hadida92]
	NOTES: • HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(182-198 BRU)	Nef(180-196)	EWRFDSRLAFHHVAREL	HIV-1 infection	human(A25)	[Cheynier92]
	NOTES: • CTL isolated in children born to HIV-1 positive mothers				
Nef(182-198 LAI)	Nef(180-196)	EWRFDSRLAFHHVAREL	HIV-1 infection	human(B35)	[Hadida95]
	NOTES: • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(182-198 LAI)	Nef(180-196)	EWRFDSRLAFHHVAREL	HIV-1 infection	human(A1,A25(10))	[Hadida95]
	NOTES: • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(182-198 LAI)	Nef(180-196)	EWRFDSRLAFHHVAREL	Rec Mengo virus-HIV 1 Nef 65-206	murine(H-2^d)	[VanderRyst98]
	NOTES: • Macaca mulatta did not have a detectable response to this vaccine • Balb/c mice had a weak response to this epitope in the Mengo virus construct – in contrast, HIV-1 Nef induces a strong CTL response in mice when presented in a vaccinia background				
Nef(191-205 SF2)	Nef(180-199)	EWRFDSRLAFHHVARELHPE	HIV-1 infection	human	[Lieberman97]
	NOTES: • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could recognize vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, B21				
Nef(186-193 LAI)	Nef(184-191)	DSRLAFHH	HIV-1 infection	human(B35)	[Hadida95]
	NOTES: • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(186-194 BRU)	Nef(184-192)	DSRLAFHHV		human(B51)	[Connan94]
	NOTES: • Resulted in the assembly of HLA-B51				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(188-196 LAI)	Nef(186-194)	RLAFHHVAR	HIV-1 infection	human(B52)	[Hadida95]
	NOTES: • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(190-198 LAI)	Nef(188-196)	AFHHVAREL	HIV-1 exposure	human(A2)	[RowlandJones98]
	NOTES: • CTL recognition reported in the context of HLA-B52 and A2.1, A2.2 and A2.4 • [Hunziker98] suggests that HLA-A2 does not in fact present this epitope, and notes that it does not promote A2 assembly [Connan94] – also see [Brander98b] • 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 ALKHRAYEL • The D subtype consensus is AfEHKAREm • [Hunziker98] maintains that HLA-A2 does not present this epitope contrary to an earlier report [Hadida95], (also see [Brander98]) – despite the position of Hunziker et al., Rowland-Jones and colleagues are confident that this epitope in its A clade form is presented by HLA-A*0201 and A*0202, and it is one of the most common responses seen in both seropositive and exposed-uninfected donors from Nairobi (Rupert Kaul, per. comm.)			
Nef(190-198 LAI)	Nef(188-196)	AFHHVAREK	HIV-1 infection	human(A3)	[Hadida95]
	NOTES: • Naturally occurring L to K anchor substitution abrogates A2 binding, but permits HLA-A3 binding				
Nef(192-206 BRU)	Nef(190-204)	HHVARELHPEYFKNC	HIV-1 infection	human(A1)	[Hadida92]
	NOTES: • HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(Nef LAI)	Nef(190-204)	Nef	HIV infection	human	[Legrand97]
	NOTES: • 17 recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef • Early responses to Pol, Rev, Vif and Tat were rare				

HIV CTL Epitopes

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(Nef LAI)	Nef(190-204)	Nef	HIV infection	human	[Zerhouni97]
	NOTES: • CTL responses to Env, Gag, Nef and RT were tested at various phases of disease progression – 10 asymptomatic patients generally had CTL responses to all proteins, 10 ARC patients responded well to all proteins except Nef, and AIDS patients had few responses to any proteins				
Nef			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				