Table 10: Nef

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(13-20 LAI)	Nef(13-20) NOTES:	WPTVRERM	HIV-1 infection	human(B8)	[Goulder97c]
	• Unusual	Unusual epitope for HLA-B8, but compatible with crystal structure predictions	h crystal structure prediction	ons	
Nef(61-80)	Nef(60-79) NOTES:	EEEEVGFPVTPQVPLRPMTY	HIV infection	human	[Lieberman95]
	HIV-spec	HIV-specific CTL lines developed by ex vivo stimulation with peptide	ulation with peptide		
Nef(61-80 SF2)	Nef(60-79) NOTES:	EEEEVGFPVTPQVPLRPMTY	HIV infection	human	[Lieberman97]
	Of 25 pat12 subjecTwo of thThe response	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	aan 1 HIV-1 protein a expressed LAI Nef 8, B35, and HLA not deter	mined	
Nef(61-80 SF2)	Nef(60-79) NOTES:	EEEEVGFVTPQVPLRPMTY	HIV-1 infection	human	[Lieberman97b]
	 CTL exp; 	CTL expanded ex vivo were later infused into HIV-1 infected patients	V-1 infected patients		
Nef(66-80 BRU)	Nef(64-78) NOTES:	VGFPVTPQVPLRMT	HIV-1 infection	human(A1,B8)	[Hadida92]
	• HIV-1 sp	 HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients 	of HIV-1 infected patients	32	
Nef(68-77 LAI)	Nef(66-75) NOTES:	FPVTPQVPLR	HIV-1 infection	human(B7)	[Haas96]
	• There wa specific C	There was a high degree of variation in three CTL epitopes in Nef in four slow specific CTLs arose over time to eliminate variants, indicating immune selection	TL epitopes in Nef in four is, indicating immune selection	slow and non-progressors, and variant	s, and variant
Nef(72-80 SF2)	Nef(66-74) NOTES: • Binds HI	66-74) FPVRPQVPL FES: Binds HLA-B*3501	HIV-1 infection	human(B35)	[Shiga96]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(72-80 SF2)	Nef(66-74) NOTES:	FPVRPQVPL	HIV-1 infection	human(B*3501)	[Tomiyama97]
	 A CTL cl 3/7 B35 I An R to 7 	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	ained se to this epitope pecific lysis, but not bindi	ng to B*3501	
Nef(75-85 SF2)	Nef(69-79) RPQVPI NOTES: • Binds HLA-B*3501	RPQVPLRPMTY A-B*3501	HIV-1 infection	human(B35)	[Shiga96]
Nef(75-85 SF2)	Nef(69-79) NOTES:	RPQVPLRPMTY	HIV-1 infection	human(B*3501)	[Tomiyama97]
	• A CTL cl • 4/7 B35 I • An R to I • An R to I	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	ained response to this epitope response to this epitope pecific lysis, but not bindir reactivity	ng to B*3501	
Nef(71-90 SF2)	Nef(70-89) NOTES:	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human	[Lieberman97]
	• Of 25 pat • 11 subjec • Three of • The respo	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, B5.	than 1 HIV-1 protein nia expressed LAI Nef tide 51, B62; HLA-A11, A24,	B8, B53	
Nef(71-90 SF2)	Nef(70-89) NOTES:	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human	[Lieberman97b]
	 CTL exp; 	 CTL expanded ex vivo were later infused into HIV-1 infected patients 	IIV-1 infected patients		
Nef(73-82 LAI)	Nef(71-80) NOTES:	QVPLRPMTYK		human(B27)	[CulmannPerCom]
	Optimal or	Optimal epitope mapped by peptide titration			

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali98]
	and 1 AC and 1 AC to differe Pol react Gag reac Nef react Env react	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 Env Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env One of the nations was shown to react to this enitone: OVPI RPMTYK	nining the CTL activity in otype infection from a per- 8 to B subtype, and HIV-2 gag, 3/8 with HIV-2 Gag gy, 3/8 with B subtype, none with B subtype, none with	seven patients from Bangu son living in France origin 2 Pol was not tested with HIV-2 Nef HIV-2 Env	ii, (6 A subtype, ally from Togo,
Nef(73-82 NL43)	Nef(71-80) NOTES: • Tyr is cri	ef(71-80) QVPLRPMTYK Tyr is critical for binding to A3.1	HIV-1 infection	human(A3.1)	[Koenig90]
Nef(73-82 BRU)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3,A11, B35)	[Culmann91]
	NOTES: • Nef CTL	OTES: Nef CTL clones from HIV+ donors			
Nef(73-82 LAI)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV-1 infection	human(A2?)	[Robertson93]
	Developr[Hunzike it did – a	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]	generate autologous CTI fact present this epitope, i	n spite of the suggestion in	n this study that
Nef(73-82 LAI)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin94, Goulder97e]
	Mutation[Goulder	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	uls with appropriate HLA t summarizes this study	ypes can result in evasion c	of CTL response
Nef(73-82 LAI)	Nef(71-80) NOTES: • Mutation	QVPLRPMTYK s found in this epitope in HLA-A11 po	HIV-1 infection sitive and negative donors	human(A11) were characterized	[Couillin95]
Nef(73-82 LAI)	Nef(71-80) NOTES: • Mutation	QVPLRPMTYK s found in this epitope in HLA-A	.11 po	HIV-1 infection 11 positive and negative donors	lonors we

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82 LAI)	Nef(71-80) NOTES: • Identical 1	(71-80) QVPLRPMTYK HIV-1 infection human(A3) TES: Identical twin hemophiliac brothers were both infected with the same batch of factor VIII	HIV-1 infection th infected with the same ba	human(A3) tch of factor VIII	[Goulder97, Goulder97e]
	IdenticalBoth had[Goulders	Identical twin hemophiliac brothers were both infected with the same to Both had a response to this epitope [Goulder97e] is a review of immune escape that summarizes this study	hat summarizes this study	tch of factor VIII	
Nef(73-82)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki97]
	 82 HIV-1. A sustaine a polyclou An A3+ s at two tim 	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	erm non-progressors were is bserved, and clones were rese epitope, with 10/11 CTL cl	plated and analyzed for braining the HLA eprinced by multiple HLA eprines being specific for this	l analyzed for breadth of response multiple HLA epitopes, indicating specific for this epitope, isolated
Nef(73-82)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV infection	human	[Garcia97]
	 The anti-1 First: Ca² Second: (Findings i CTL med 	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	itope is able to kill target ce Vef-specific lysis it apoptosis that could also lee not mutually exclusive in ay play a role in pathogenes	Ils via two mechanisms ill non-specific targets human CTL, as they are in is	1 mice
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig95]
	NOTES: Alanine substitutioNef CTL clones (load/patient health	TES: 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	[80A significantly decrease an HIV-1 infected volunto	l immunogenicity of pepti er to evaluate effects of	de infusion on viral
Nef(73-82)	Nef(72-80) NOTES:	VPLRPMTYK	no CTL shown	human(A11)	[Zhang93]

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 c	TES: Review of HIV CTL epitopes – defined by B35 motif found within a larger peptide	notif found within a large	r peptide	
Nef(73-82 LAI)	Nef(72-79)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[RowlandJones95]
	NOTES: • VPLRPN	OTES: • VPLRPMTY also recognized by CTL from HIV-2 seropositives, epitope is conserved	·2 seropositives, epitope i	conserved	
Nef	Nef(72-79) NOTES:	VPLRPMTY	HIV-1 exposure	human(B35)	[RowlandJones98]
	A CTL r epitopes and confiThe A an	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	nfected prostitutes from N clades – such cross-reac ypes are circulating he B clade epitope	Vairobi using previously defined B clade ivity could protect against both A and D	lefined B clade t both A and D
Nef(75-82)	Nef(72-79) NOTES:	VPLRPMTY	none	human(B35)	[Lalvani97]
	 A peptide importation could be This pepting activity under the period 	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	nulation of CTLp using c primary response, only se I tetramers eptides used in control ex seronegative donors	ptimized peptide and IL-7 condary – peptide-specifi periments showing that the	concentrations c CTLp counts s assay gave no
Nef(75-82)	Nef(72-79) NOTES:	VPLRPMTY	no CTL shown	human(B*3501)	[Smith96]
	 Crystal st 	 Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex 	HLA-B*3501 complex		
Nef(74-82)	Nef(72-79) NOTES:	VPLRPMTY		human(A3)	[Carreno92]
	• Included	Included in HLA-A3 binding peptide competition study	n study		

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(75-82 LAI)	Nef(73-80) NOTES: • Review o	ef(73-80) PLRPMTYK OTES: • Review of HIV CTL epitopes	HIV-1 infection	human(A11)	[McMichael94]
Nef(77-85 LAI)	Nef(75-83) NOTES:	f(75-83) RPMTYKAAL Structural constraints on the Nef protein may prevent escape	HIV-1 infection	human(B7)	[Bauer97]
Nef(81-100 SF2)	Nef(80-99) NOTES: Of 25 pat It subject Three of the response.	(80-99) KAAVDLSHFLKEKGGLEGLI HIV-1 infection hu **TIES:* 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, R8, B14: HLA-A11, A24, B8, B53	HIV-1 infection han 1 HIV-1 protein ia expressed LAI Nef de B14: HI_A-A11_ A24_B:	human	[Lieberman97]
Nef(83-94 BRU)	Nef(81-92) NOTES: • Epitope d	ef(81-92) AAVDLSHFLKEK HIV-1 infection human(. OTES: Epitope defined by boundaries of overlapping peptides that stimulate Nef CTL clones	HIV-1 infection ptides that stimulate Nef	human(A11) CTL clones	[Culmann91]
Nef(84-92 LAI)	Nef(82-90) NOTES: • Review o	ef(82-90) AVDLSHFLK OTES: • Review of HIV CTL epitopes	HIV-1 infection	human(A11)	[McMichael94]
Nef(84-92 LAI)	Nef(82-90) NOTES: • Mutation. • [Goulder	f(82-90) AVDLSHFLK HIV-1 infection huma NTES: Mutational variation in HIV epitopes in individuals with appropriate HLA types can [Goulder97e] is a review of immune escape that summarizes this study	HIV-1 infection ls with appropriate HLA t summarizes this study	human(A11) [Couillin94, ypes can result in evasion of CTL response	[Couillin94, Goulder97e] of CTL response
Nef(84-92 LAI)	Nef(82-90) NOTES: • Mutation	(82-90) AVDLSHFLK HIV-1 infection human(A11) TES: Mutations found in this epitope in HLA-A11 positive and negative donors were characterized	HIV-1 infection itive and negative donors	human(A11) were characterized	[Couillin95]

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) NOTES:	ef(84-98) DLSHFLKEKGGLEGL HIV-1 infection OTES: Development of a retroviral vector (nNeoNef) to generate autologous targets	HIV-1 infection	human(A2)	[Robertson93]
Nef(84-92 LAI)	Nef(84-92) NOTES: • Review o	(84-92) DLSHFLKEK TES: Review of HIV CTL epitopes	HIV-1 infection	human(A3.1)	[McMichael94]
Nef(89-97 LAI)	Nef(88-95) NOTES:	FLKEKGGL	HIV-1 infection	human(B8)	[Price97]
	CTL escaMost variFLKE(ENDouble m[Goulder	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	B8 HIV-1+ individual, pridue idue iency and recognition I FLKGNGGL) completel summarizes this study in 1	oviding evidence for immune escape secaped recognition the context of CTL escape to fixation	une escape to fixation
Nef	Nef(88-95) NOTES:	FLKEKGGL	Multi-epitope gene in VVA	human(B8)	[Hanke98c, Hanke98b]
	• This epitocells with	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	esented to appropriate CT 20 HIV-1 epitopes recogn	L clones upon infection cuized by humans	of human target
Nef(88-95)	Nef(88-95) NOTES: Natural v Substituti Substituti	(188-95) FLKEKGGL HIV-1 infection TIES: 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	HIV-1 infection ved in several donors on 5 are not well recognized	human(B8)	[Goulder97c]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(93-106 BRU)	Nef(91-104) NOTES:	EKGGLEGLIHSQRR	HIV-1 infection	human(A1,B8)	[Hadida92]
	• HIV-1 spec	HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients	of HIV-1 infected patient	s	
Nef(102-115 LAI)	Nef(100-113) NOTES: • Identical tw	f(100-113) HSQRRQDILDLWIY HIV-1 infection human(B7) TES: Identical twin hemophiliac brothers were both infected with the same batch of factor VIII	HIV-1 infection setted with the same batch	human(B7) of factor VIII	[Goulder97, Goulder97e]
	 Identical tw One had a s [Goulder97	Identical twin hemophiliac brothers were both infected with the same become had a strong response to this peptide, the other did not [Goulder97e] is a review of immune escape that summarizes this study	ected with the same batch or did not immarizes this study	of factor VIII	
Nef(101-120 SF2)	Nef(100-119) NOTES:	HSQRRQDILDLQIYHTQGYF	HIV-1 infection	human	[Lieberman97]
	 Of 25 patien 11 subjects Two of thes The response	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	an 1 HIV-1 protein t expressed LAI Nef 862 and HLA-A2, B21		
Nef(103-127 PV22)	Nef(101-125)	SQRRQDILDLWIYHTQG- YFPDWQNY	HIV-1 infection	human(B13)	[Jassoy93]
	NOTES: • HIV-1 spec:	TES: HIV-1 specific CTLs release γ -IFN, and α - and β -TNF	TNF		
Nef(105-114 LAI)	Nef(103-112) NOTES:	RRQDILDLWI	HIV-1 infection	human(B*2705)	[Goulder97d]
	Defined asHLA-B*27/The HLA-F	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	ptide HSQRRQDILDLW progression ition 2, and L in the C-ter	TYHTQGYF [Nef(102-12) m position	21 LAD]
Nef(111-132)	Nef(110-131)	LWIYHTQGYFPDWQNYT- PGPGV	HIV infection	human	[Lieberman95]
	NOTES: • HIV-specifi	TES: HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide	ulation with peptide		

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(111-132 SF2)	Nef(110-131)	LWIYHTQGYFPDWQNYT- PGPGV	HIV infection	human	[Lieberman97]
	NOTES: Of 25 patie 11 subjects Four of the: The respon	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	1 HIV-1 protein expressed LAI Nef A1, A3, B7, B15; HLA-	A2, A26, B7, B38	
Nef(111-132 SF2)	Nef(110-131) NOTES:	(110-131) LWIYHTQGYFPDWQNYT- HIV-1 infection PGPGV TES: CTI expanded as vivo were later infused into HIV-1 infected patients	HIV-1 infection	human	[Lieberman97b]
Nef(113-128	Nef(111-126)	WIYHTQGYFPDWQNYT	HIV-1 infection	human(A1)	[Hadida92]
DAC)	NOTES: • HIV-1 spec	OTES: HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients	f HIV-1 infected patients	·	
Nef(113-125	Nef(111-123)	WIYHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann89]
DAYO)	NOTES: • Nef CTL cl	OTES: • Nef CTL clones from HIV+ donors			
Nef(115-125	Nef(113-123)	YHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann91]
BRO)	NOTES: • Nef CTL cl	OTES: • Nef CTL clones from HIV+ donors			
Nef(116-125	Nef(114-123)	HTQGYFPDWQ	HIV-1 infection	human(B57)	[Culmann91]
DNO)	NOTES: • Nef CTL cl	TES: Nef CTL clones from HIV+ donors, optimal peptide mapped	mapped		
Nef(117-128	Nef(115-126)	TQGYFPDWQNYT	HIV-1 infection	human(B17,B37)	[Culmann91]
DRO)	NOTES: • Nef CTL cl	OTES: Nef CTL clones from HIV+ donors			

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(117-127 LAI)	Nef(115-125) NOTES: • Optimal per	ef(115-125) TQGYFPDWQNY OTES: Optimal peptide defined by titration, B. Culmann, per. comm.	HIV-1 infection per. comm.	human(Bw62)	[CulmannPerCom]
Nef(118-127 LAI)	Nef(116-125) NOTES: • Review of I	f(116-125) QGYFPDWQNY YTES: Review of HIV CTL epitopes		human(Bw62)	[McMichael94]
Nef(120-128 IIIB)	Nef(118-126) NOTES: • Epitope def study • FFPDWKN	FFFDWKNYT, a naturally occurring variant, was found in mother and infant and was recognized [Walkerperk HIV-1 infection human [Walkerperk FFPDWKNYT], a naturally occurring variant, was found in mother and infant and was recognized	HIV-1 infection DS Foundation ARIEL Pr found in mother and infar	human ject, a mother-infant HIV and was recognized	[Walkerpercom96] transmission
1 (/100 100 1 11)	N 6/110 10/2				
	NOTES: • Nef CTL cl	OTES: Nef CTL clones from HIV+ donors – optimum peptide mapped by titration	ptide mapped by titration		
Nef(120-144 SF2)	Nef(118-142) NOTES:	YFPDWQNYTPGPGIRYP- LTFGWCYK	HIV-1 infection	human(A24)	[Jassoy92]
Nef(121-140 SF2)	Nef(120-139)	(120-139) PDWQNYTPGPGVRYPLTFGW	HIV-1 infection	human	[Lieberman97]
	• Of 25 patien • Il subjects • Three of the • The respon	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	an 1 HIV-1 protein a expressed LAI Nef le A-A3, A24, B7, B38		

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(123-137 IIIB)	Nef(121-135) NOTES:	QWQNYTPGPGVRYPL	HIV-1 infection		[Walkerpercom96]
	Epitope de studyFFPDYTP	Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, study FFPDYTPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants,	S Foundation ARIEL F , naturally occurring va	roject, a mother-infant HIV transmission uriants, were found in mother and are not	IIV transmission other and are not
	recognized • LFPDYKP recognized	recognized LFPDYKPGPGTRFPL and FFPDYKPGPGTRFPL, naturally occurring variants, were found in infant and are not recognized	L, naturally occurring v	ariants, were found in ir	ıfant and are not
Nef(126-138 BRU)	Nef(124-136)	NYTPGPGVRYPLT	HIV-1 infection	human(B7)	[Culmann91]
,	NOTES: • Nef CTL c	• Nef CTL clones from HIV+ donors			
Nef(128-137 LAI)	Nef(126-135) NOTES:	TPGPGVRYPL	HIV-1 infection	human(B7)	[Haas96, Haas97]
	There was specific CTThe epitop	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]	epitopes in Nef in for indicating immune sel	ar slow and non-progress ection	sors, and variant
Nef	Nef(126-135) NOTES:	TPGPGVRYPL	HIV-1 exposure	human(B7)	[RowlandJones98]
	 A CTL res epitopes th and confer The D subt The A subt 	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	ected prostitutes from Nades – such cross-reactives are circulating epitope	Vairobi using previously defined B clade ivity could protect against both A and D	defined B clade st both A and D
Nef(130-143 LAI)	Nef(128-141) NOTES:	GPGVRYPLTFGWCY	HIV-1 infection	human(B*57)	[Goulder96]
	CTL respoPeptide der	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	rm survivors stif, yet not cross-restric	ted except at high conce	ntrations

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(132-147 BRII)	Nef(130-145)	GVRYPLTFGWCYKLVP	HIV-1 infection	human(A1,B8)	[Hadida92]
bico)	NOTES: • HIV-1 spec	OTES: HIV-1 specific CTLs detected in lymphoid organs			
Nef(132-147	Nef(130-145)	GVRYPLTFGWCYKLVP	HIV-1 infection	human(B18)	[Culmann91]
	NOTES: • Nef CTL cl	OTES: • Nef CTL clones from HIV+ donors			
Nef(133-148 LAI)	Nef(131-146) VRYPLTH NOTES: • P. Goulder, pers. comm	VRYPLTFGWCYKLVPV pers. comm.		human(B57)	[Brander96]
Nef(134-144 LAI)	Nef(132-142) NOTES: • Mutational	f(132-142) RYPLTFGWCYK HIV-1 infection hun TES: Mutational variation in HIV epitopes in individuals with appropriate HLA types can	HIV-1 infection	human(B18) [Couillin94, bes can result in evasion of CTL response	[Couillin94, Goulder97e] CTL response
Nef(138-147 SF2)	• [Goulder97]	[Goulder97e] is a review of immune escape that summarizes this study 132-141) RYPLTEGWCF HIV-1 infection	nmarizes this study HIV-1 infection	human (A*2402)	[[kedaMoore97]
Nef(138-147 SF2)	Nef(132-141) NOTES: • Defined usi anchors in I • This peptide • RYPLTFGV specific CT	F(132-141) RYPLTFGWCF HIV-1 infection human(A*2402) [IkedaMoor MTES: 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 IIe 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	HIV-1 infection *2402 binding peptides Ile at the C term) – 53 o sted ope can be processed in:	human(A*2402) [Ike were predicted by searching for the 59 peptides bound A*2402 a vaccinia construct and present	[IkedaMoore97] ng for A*2402 .*2402 resented – two
Nef(134-141 LAI)	Nef(132-139) NOTES: • Optimal per	ef(132-139) RYPLTFGW OTES: Optimal peptide defined by titration		human(B27)	[CulmannPerCom]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(139-147 SF2)	Nef(133-141) YPLTI NOTES: • Binds HLA-B*3501	YPLTFGWCF -B*3501	HIV-1 infection	human(B35)	[Shiga96]
Nef	Nef(133-141) NOTES: • A CTL respectors that and confer pand confer pand confer of the A subty • The D subty	TES: A CTL response was found in exposed but uninfected prostitutes from Nairobi epitopes that tended to be conserved in A and D clades – such cross-reactivity co 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	HIV-1 exposure exted prostitutes from N lades – such cross-react ses are circulating epitope	human(B49) [RowlandJoairobi using previously defined B clade vity could protect against both A and D	[RowlandJones98] defined B clade st both A and D
Nef(135-143)	Nef(133-141) NOTES: • Nef CTL cl	ef(133-141) YPLTFGWCY OTES: Nef CTL clones from HIV+ donors	HIV-1 exposure	human(B18)	[Culmann91, CulmannPenci- olelli94]
Nef(136-145)	Nef(134-143) NOTES: • Cross-clade and 1 AG reto different to different eactivi • Pol reactivi • Gag reactivi • Nef reactivi • Env reactivi • Patient B18	PITES: 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	HIV-1 infection ing the CTL activity in s pe infection from a pers to B subtype, and HIV-2 g, 3/8 with HIV-2 Gag with B subtype, none w h B subtype, none with l of response, and recogni	human(A2) [Durali98] even patients from Bangui, (6 A subtype, on living in France originally from Togo, Pol was not tested ith HIV-2 Nef HIV-2 Env zed Gag SLYNTVATL and Nef PLTFG-	[Durali98] ui, (6 A subtype, nally from Togo, and Nef PLTFG-
Nef(161-180)	Nef(160-179) NOTES: • HIV-specifi	ef(160-179) TSLLHPVSLHGMDDPEREVL HIV infection OTES: • HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide	HIV infection	human	[Lieberman95]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(161-180 SF2)	Nef(160-179) NOTES:	TSLLHPVSLHGMDDPEREVL	HIV infection	human	[Lieberman97]
	 Of 25 patie 11 subjects One of thes	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	n 1 HIV-1 protein expressed LAI Nef		
Nef(101-120 SF2)	Nef(160-179) NOTES: • CTL expan	f(160-179) TSLLHPVSLHGMDDPEREVL HIV-1 infection YTES: CTL expanded ex vivo were later infused into HIV-1 infected patients	HIV-1 infection 1 infected patients	human	[Lieberman97b]
Nef(161-180 SF2)	Nef(160-179)	TSLLHPVSLHGMDDPEREVL	HIV infection	human	[Lieberman97]
	 Of 25 patie 11 subjects One of thes	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	n 1 HIV-1 protein expressed LAI Nef		
Nef(171-190 SF2)	Nef(170-189) NOTES:	GMDDPEREVLEWRFDSRLAF	HIV-1 infection	human	[Lieberman97]
	 Of 25 patie 11 subjects One of thes The respon	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	n 1 HIV-1 protein expressed LAI Nef		
Nef(180-189 LAI)	Nef(178-187) NOTES:	VLEWRFDSRL	HIV-1 infection	human(A2)	[Haas96, Haas97]
	• There was specific CT	There was a high degree of variation in three CTL epitopes in Nef in four slow specific CTLs arose over time to eliminate variants, indicating immune selection	epitopes in Nef in fou indicating immune sele	r slow and non-progressors, and variant extion	rs, and variant
Nef(182-198 BRU)	Nef(180-196)	EWRFDSRLAFHHVAREL	HIV-1 infection	human(A1,B8)	[Hadida92]
	NOTES: • HIV-1 spec	TES: HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients	of HIV-1 infected patien	83	

Nef(182-198 LAI) Nef(180-196) **NOTES: ** Macaca n ** Balb/c mi strong CT
Nef(191-205 SF2) Nef(180-199) NOTES: Of 25 pat 11 subjec One of th
Nef(186-193 LAI) Nef(184-191) NOTES: • The C-ter
Nef(186-194 Nef(184-192) BRU) NOTES: • Resulted

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LOCALIOII	WEAU	Sequence	пинатовен	Species(HLA)	Neterences
Nef(188-196 LAI)	Nef(186-194) NOTES:	ef(186-194) RLAFHHVAR HIV-1 infection human(B52) OTES: The C-terminal region of Nef (182-205) contains multiple CTI enitones with 5 distinct HI A restrictions	HIV-1 infection	human(B52)	[Hadida95]
Nef(190-198 LAI)	Nef(188-196) NOTES:	AFHHVAREL	HIV-1 exposure	human(A2)	[RowlandJones98]
	 CTL recogn [Hunziker9) assembly [One of the content of	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	B52 and A2.1, A2.2 and A fact present this epitope, fected prostitutes from Niclades – such cross-reacting spes are circulating	and notes that it does no airobi using previously de vity could protect against	t promote A2 fined B clade both A and D
	in its A clac both seropo	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.)	and A*0202, and it is one from Nairobi (Rupert Kau	of the most common resp 1, per. comm.)	onses seen in
Nef(190-198 LAI)	Nef(188-196) NOTES:	ef(188-196) AFHHVAREK HIV-1 infection human(A3) OTES: Naturally occurring I to K anchor substitution abrogates A2 binding but permits HI A-A3 binding	HIV-1 infection	human(A3)	[Hadida95]
Nef(192-206 BRU)	Nef(190-204)	HHVARELHPEYFKNC	HIV-1 infection	human(A1)	[Hadida92]
	NOTES: • HIV-1 speci	OTES: - HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients	s of HIV-1 infected patient	S	
Nef(Nef LAI)	Nef(190-204) NOTES:	Nef	HIV infection	human	[Legrand97]
	 17 recently An early res Nef Farly response 	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% Nef Nef Farly responses to Pol Rev. Vif and Tat were rare	response to HIV proteins was noted in 87% of the s	Env, Gag, Pol, Rev, Nef, Vif and Tat ubjects to Gag, 75% to Env, and 50% to	7if and Tat v, and 50% to

WEAU Sequence Immunogen Species(HLA) References 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 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
HIV infection human Env, Gag, Nef and RT were tested at various phases of disease progression – 10 as had CTL responses to all proteins, 10 ARC patients responded well to all proteins exceed few responses to any proteins HIV-1 infection human HIV-1 infection human HIV-1 can exhibit down regulation of T-cell fundationativated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one prought HIV-1 specific CTL activity to detectable levels
HIV infection human [Zerhouni97] d at various phases of disease progression – 10 asymptomatic 10 ARC patients responded well to all proteins except Nef, and HIV-1 infection human [DeMaria97] or (NKR+) can exhibit down regulation of T-cell function function and increased HIV-1 specific CTL activity in e presence of IL-2 from 3/5 patients, and in one other case to detectable levels
human [Zerhouni97] disease progression – 10 asymptomatic anded well to all proteins except Nef, and human [DeMaria97] human [DeMaria97] down regulation of T-cell function and HIV-1 specific CTL activity in man 3/5 patients, and in one other case
References [Zerhouni97]) asymptomatic except Nef, and [DeMaria97] [Inunction [L activity in one other case
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