

Table 9: Nef

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(13-20 LAI)	Nef(13-20)	WPTVRRER <ul style="list-style-type: none"> Unusal epitope for HLA-B8, but compatible with crystal structure predictions 	HIV-1 infection	human(B8)	[Goulder et al.(1997e)]
Nef(61-80)	Nef(60-79)	EEEEVGFPVTPQVPL- RPMTY <ul style="list-style-type: none"> HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide 	HIV infection	human(unk)	[Lieberman et al.(1995)]
Nef(61-80 SF2)	Nef(60-79)	EEEEVGFPVTPQVPL- RPMTY <ul style="list-style-type: none"> Of 25 patients, most had CTL specific for more than 1 HIV-1 protein 12 subjects had CTL that could lyse 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 	HIV infection	human(unk)	[Lieberman et al.(1997)]
Nef(66-80 BRU)	Nef(64-78)	VGFPVTPQVPLRMT <ul style="list-style-type: none"> HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients 	HIV-1 infection	human(A1,B8)	[Hadida et al.(1992)]
Nef(68-77 LAI)	Nef(66-75)	FPVTPQVPLR <ul style="list-style-type: none"> Also pers. comm. B. Maier and B. Autran 	HIV-1 infection	human(B7)	[Haas et al.(1996)]
Nef(72-80 SF2)	Nef(66-74)	FPVRRPQVPL <ul style="list-style-type: none"> Binds HLA-B*3501 	HIV-1 infection	human(B35)	[Shiga et al.(1996)]
Nef(72-80 SF2)	Nef(66-74)	FPVRRPQVPL <ul style="list-style-type: none"> 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 	HIV-1 infection	human(B*3501)	[Tomiyama et al.(1997)]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(75-85 SF2)	Nef(69-79)	RPQVPLRPMTY • Binds HLA-B*3501	HIV-1 infection	human(B35)	[Shiga et al.(1996)]
Nef(75-85 SF2)	Nef(69-79)	RPQVPLRPMTY • 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	HIV-1 infection	human(B*3501)	[Tomiyama et al.(1997)]
Nef(71-90 SF2)	Nef(70-89)	PQVPLRMITYKAAVDL- SHFL • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse 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; and HLA-A1, A3, B7, B35	HIV-1 infection	human(unk)	[Lieberman et al.(1997)]
Nef(73-82 NL432)	Nef(71-80)	QVPLRPMTYK • Tyr is critical for binding to A3.1	HIV-1 infection	human(A3.1)	[Koenig et al.(1990)]
Nef(73-82 BRU)	Nef(71-80)	QVPLRPMTYK • Nef CTL clones from HIV+ donors	HIV-1 infection	human(A3,A11,B35)	[Culmann et al.(1991)]
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK • Development of a retroviral vector (pNeoNef) to generate autologous CTL targets	HIV-1 infection	human(A2)	[Robertson et al.(1993)]
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response	HIV-1 infection	human(A11)	[Couillin et al.(1994)]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Coullin et al.(1995)]
					<ul style="list-style-type: none"> • Mutations found in this epitope in HLA-A11 positive and negative donors were characterized
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder et al.(1997a)]
					<ul style="list-style-type: none"> • Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • Both had a response to this epitope
Nef(73-82)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki et al.(1997)]
					<ul style="list-style-type: none"> • 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()	[Garcia et al.(1997)]
					<ul style="list-style-type: none"> • 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)	Nef(72-80)	VPLRPMTYK	no CTL shown	human(A11)	[Zhang et al.(1993)]
					<ul style="list-style-type: none"> • Exploration of A11 binding motif
Nef(73-82 LAI)	Nef(72-79)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael & Walker(1994)]
					<ul style="list-style-type: none"> • 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)	[Rowland-Jones et al.(1995)]
					<ul style="list-style-type: none"> • VPLRPMTY also recognized by CTL from HIV-2 seropositives, epitope is conserved

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(75-82)	Nef(72-79)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith et al.(1996)]
		• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex			
Nef(74-82)	Nef(72-79)	VPLRPMTY	Included in HLA-A3 binding peptide competition study	human(A3)	[Carreno et al.(1992)]
Nef(75-82 LAI)	Nef(73-80)	PLRPMTYK	HIV-1 infection	human(A11)	[McMichael & Walker(1994)]
		• Review of HIV CTL epitopes; defined by HLA-A11 motif found within a larger peptide			
Nef(77-85 LAI)	Nef(75-83)	RPMTYKAAL	HIV-1 infection	human(B7)	[Bauer et al.(1997)]
		• Structural constraints on the Nef protein may prevent escape			
Nef(81-100 SF2)	Nef(80-99)	KAAVDLSHFLEKGG-LEGLI	HIV-1 infection	human(unk)	[Lieberman et al.(1997)]
		• Of 25 patients, most had CTL specific for more than 1 HIV-1 protein			
		• 11 subjects had CTL that could lyse 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; and HLA-A1, A11, B8, B27			
Nef(83-94 BRU)	Nef(81-92)	AAVDLSHFLEK	HIV-1 infection	human(A11)	[Culmann et al.(1991)]
		• 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)	[McMichael & Walker(1994)]
		• Review of HIV CTL epitopes; defined by A11 motif found within a larger peptide			
Nef(84-92 LAI)	Nef(82-90)	AVDLSHFLK	HIV-1 infection	human(A11)	[Couillin et al.(1994)]
		• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response			

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(84-92 LAI)	Nef(82-90)	AVDLSHFLK	HIV-1 infection	human(A11)	[Coullin et al.(1995)]
					• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized
Nef(86-100 LAI)	Nef(84-98)	DLSHFLKEKGGLEGL	HIV-1 infection	human(B35)	[Buseyne et al.(1993)]
Nef(86-100 LAI)	Nef(84-98)	DLSHFLKEKGGLEGL	HIV-1 infection	human(A2)	[Robertson et al.(1993)]
					• Development of a retroviral vector (pNeoNef) to generate autologous targets
Nef(84-92 LAI)	Nef(84-92)	DLSHFLKEK	HIV-1 infection	human(A3.1)	[McMichael & Walker(1994)]
					• Review of HIV CTL epitopes; defined by A3.1 motif found within a larger peptide
Nef(89-97 LAI)	Nef(88-95)	FLKEKGGGL	HIV-1 infection	human(B8)	[Price et al.(1997)]
					• 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 FLKNGGGL) completely escaped recognition
Nef(88-95)	Nef(88-95)	FLKEKGGGL	HIV-1 infection	human(B8)	[Goulder et al.(1997e)]
					• 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
Nef(93-106 BRU)	Nef(91-104)	EKGGLEGLHSQRR	HIV-1 infection	human(A1,B8)	[Hadida et al.(1992)]
					• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(102-115 LAI)	Nef(100-113)	HSQRRQDILDWLY	HIV-1 infection	human(B7)	[Goulder et al.(1997a)]
	<ul style="list-style-type: none"> • 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 				
Nef(101-120 SF2)	Nef(100-119)	HSQRRQDILDQYH-TQGYF	HIV-1 infection	human(tunk)	[Lieberman et al.(1997)]
	<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse 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)	SQRRQDILDWYHT-QGYFPDWQNY	HIV-1 infection	human(B13)	[Jasoy et al.(1993)]
	<ul style="list-style-type: none"> • HIV-1 specific CTLs release γ-IFN, and α- and β-TNF 				
Nef(105-114 LAI)	Nef(103-112)	RRQDILDWLI	HIV-1 infection	human(HLA-B*2705)	[Goulder et al.(1997c)]
	<ul style="list-style-type: none"> • Defined as optimal epitope from within reactive peptide HSQRRQDILDWYHTQGYF [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)	LWYHTQGYFPDWQN-YTPGPGV	HIV infection	human(tunk)	[Lieberman et al.(1995)]
	<ul style="list-style-type: none"> • HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide 				

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(111-132 SF2)	Nef(110-131)	LWYHTQGYFPDWQN- YTPGPGV	HIV infection	human(unk)	[Lieberman et al.(1997)]
		<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse 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; and HLA-A1, A2, B51, B57 			
Nef(113-128 BRU)	Nef(111-126)	WYHTQGYFPDWQNY- T	HIV-1 infection	human(A1)	[Hadida et al.(1992)]
		<ul style="list-style-type: none"> • HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients 			
Nef(113-125 BRU)	Nef(111-123)	WYHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann et al.(1989)]
		<ul style="list-style-type: none"> • Nef CTL clones from HIV + donors 			
Nef(115-125 BRU)	Nef(113-123)	YHTQGYFPQWQ	HIV-1 infection	human(B17)	[Culmann et al.(1991)]
		<ul style="list-style-type: none"> • Nef CTL clones from HIV + donors 			
Nef(117-128 BRU)	Nef(115-126)	TQGYFPDWQNYT	HIV-1 infection	human(B17,B37)	[Culmann et al.(1991)]
		<ul style="list-style-type: none"> • Nef CTL clones from HIV + donors 			
Nef(118-127 LAI)	Nef(116-125)	QGYFPDWQNY	?	human(Bw62)	[McMichael & Walker(1994)]
		<ul style="list-style-type: none"> • Review of HIV CTL epitopes; defined by Bw62 motif found within a larger peptide 			

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(120-128 IIIB)	Nef(118-126)	YFPDWQNYT <ul style="list-style-type: none"> • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL project 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 	HIV-1 infection	human(unk)	[Wilkes et al.(1996)]
Nef(120-144 SF2)	Nef(118-142)	YFPDWQNYTPGPGIR- YPLTFGWCYK <ul style="list-style-type: none"> • Epitope recognized by CTL clone derived from CSF 	HIV-1 infection	human(A24)	[Jassey et al.(1992)]
Nef(121-140 SF2)	Nef(120-139)	PDWQNYTPGPGVRYP- LTFGW <ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse 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; and HLA-A2, A26, B7, B38 	HIV-1 infection	human(unk)	[Lieberman et al.(1997)]
Nef(123-137 IIIB)	Nef(121-135)	QWQNYTPGPGVRYPL <ul style="list-style-type: none"> • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL project 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 	HIV-1 infection	human(unk)	[Wilkes et al.(1996)]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(126-138 BRU)	Nef(124-136)	NYTPGPGVRYPLT • Nef CTL clones from HIV+ donors	HIV-1 infection	human(B7)	[Culmann et al.(1991)]
Nef(136-145 LAI)	Nef(126-135)	TPGPGVRYPL • Also: pers. comm. B. Maier and B. Autran	HIV-1 infection	human(B7)	[Haas et al.(1996)]
Nef(130-143 LAI)	Nef(128-141)	GPGVRYPLTFGWYCY • 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	HIV-1 infection	human(B*57)	[Goulder et al.(1996b)]
Nef(132-147 BRU)	Nef(130-145)	GVRYP ^P LTFGWYKLV- • HIV-1 specific CTLs detected in lymphoid organs	HIV-1 infection	human(A1,B8)	[Hadida et al.(1992)]
Nef(132-147 BRU)	Nef(130-145)	GVRYP ^P LTFGWYKLV- • Nef CTL clones from HIV+ donors	HIV-1 infection	human(B18)	[Culmann et al.(1991)]
Nef(133-148 LAI)	Nef(131-146)	VRYPL ^V TFGWYKLV ^P - • P. Goulder, pers. comm.	?	human(B57)	[Brander & Walker(1997a)]
Nef(134-144 LAI)	Nef(132-142)	RYPLTFGWYCYK • Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response	HIV-1 infection	human(B18)	[Couillin et al.(1994)]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(139-147 SF2)	Nef(133-141) • Binds HLA-B*3501	YPLTFGWCF	HIV-1 infection	human(B35)	[Shiga et al.(1996)]
Nef(161-180)	Nef(160-179) • HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide	TSLLHPVSLHGMDDP- EREVL	HIV infection	human(unk)	[Lieberman et al.(1995)]
Nef(161-180 SF2)	Nef(160-179) • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide	TSLLHPVSLHGMDDP- EREVL	HIV infection	human(unk)	[Lieberman et al.(1997)]
Nef(161-180 SF2)	Nef(160-179) • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide	TSLLHPVSLHGMDDP- EREVL	HIV infection	human(unk)	[Lieberman et al.(1997)]
Nef(171-190 SF2)	Nef(170-189) • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse vaccinia expressed LAI Nef • One of these 11 had CTL response to this peptide • The responding subject was HLA-A2, B21	GMDDPEREVEWRFD- SRLAF	HIV-1 infection	human(unk)	[Lieberman et al.(1997)]
Nef(180-189 LAI)	Nef(178-187) • Also: pers. comm. B. Maier and B. Autran	VLEWRFDSRL	HIV-1 infection	human(A2)	[Haas et al.(1996)]

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(182-198 BRU)	Nef(180-196)	EWRFD ^{EL} SRLAFHHVAR-	HIV-1 infection	human(A1,B8)	[Hadida et al.(1992)]
		<ul style="list-style-type: none"> • HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients 			
Nef(182-198 BRU)	Nef(180-196)	EWRFD ^{EL} SRLAFHHVAR-	HIV-1 infection	human(A25)	[Cheynier et al.(1992)]
		<ul style="list-style-type: none"> • CTL isolated in children born to HIV-1 positive mothers 			
Nef(182-198 LAI)	Nef(180-196)	EWRFD ^{EL} SRLAFHHVAR-	HIV-1 infection	human(B35)	[Hadida et al.(1995)]
		<ul style="list-style-type: none"> • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions 			
Nef(182-198 LAI)	Nef(180-196)	EWRFD ^{EL} SRLAFHHVAR-	HIV-1 infection	human(A1,A25(10))	[Hadida et al.(1995)]
		<ul style="list-style-type: none"> • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions 			
Nef(191-205 SF2)	Nef(180-199)	EWRFD ^{ELHPE} SRLAFHHVAR-	HIV-1 infection	human(unk)	[Lieberman et al.(1997)]
		<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than 1 HIV-1 protein • 11 subjects had CTL that could lyse 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)	[Hadida et al.(1995)]
		<ul style="list-style-type: none"> • The C-terminal region of Nef (182-205) contains multiple CTL epitopes with 5 distinct HLA restrictions 			

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(186-194 BRU)	Nef(184-192)	DSRLAFHHV	?	human(B51)	[Coman et al.(1994)]
		<ul style="list-style-type: none"> Resulted in the assembly of HLA-B51; anchor residues: V (position 9) and L (position 4) 			
Nef(188-196 LAI)	Nef(186-194)	RLAFHHVAR	HIV-1 infection	human(B52)	[Hadida et al.(1995)]
		<ul style="list-style-type: none"> 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 infection	human(B52,A2)	[Hadida et al.(1995)]
		<ul style="list-style-type: none"> CTL recognition in the context of HLA-B52 and A2.1, A2.2 and A2.4; high effector cell frequency 			
Nef(190-198 LAI)	Nef(188-196)	AFHHVAREK	HIV-1 infection	human(A3)	[Hadida et al.(1995)]
		<ul style="list-style-type: none"> 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)	[Hadida et al.(1992)]
		<ul style="list-style-type: none"> HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients 			