Table 10: Nef

Location	WEAU	Sequence	lmmunogen	Species(HLA)	References
Nef(13-20 LAI)	Nef(13-20)	WPTVRERM	HIV-1 infection	human(B8)	[Goulder97c]
	² Unusual 6	Unusual epitope for HLA-B8, but compatible with crystal structure predictions	th crystal structure predi	ictions	
Nef(61-80)	Nef(60-79) NOTES:	EEEEVGFPVTPQVPLRPMTY	HIV infection	human	[Lieberman95]
	² HIV-speci	HIV-specibc CTL lines developed by vivostimulation with peptide	lation with peptide		
Nef(61-80 SF2)	Nef(60-79)	EEEEVGFPVTPQVPLRPMTY	HIV infection	human	[Lieberman97]
	_	Of 25 patients, most had CTL specibc for more than 1 HIV-1 protein 12 subjects had CTL that could recognize vaccinia expressed LAI Nef	than 1 HIV-1 protein inia expressed LAI Nef		
	² The respo	The responding subjects were HLA-A11, A24, B8, B35, and HLA not determined	38, B35, and HLA not de	etermined	
Nef(61-80 SF2)	Nef(60-79)	EEEEVGFVTPQVPLRPMTY	HIV-1 infection	human	[Lieberman97b]
	² CTL expa	CTL expande@x vivowere later infused into HIV-1 infected patients	-1 infected patients		
Nef(66-80 BRU)	Nef(64-78) NOTES:	VGFPVTPQVPLRMT	HIV-1 infection	human(A1,B8)	[Hadida92]
	² HIV-1 spe	² HIV-1 specibc CTLs detected in lymphoid organs of HIV-1 infected patients	ns of HIV-1 infected pati	ents	
Nef(68-77 LAI)	Nef(66-75) NOTES:	FPVTPQVPLR	HIV-1 infection	human(B7)	[Haas96]
	² There wa specibc C	There was a high degree of variation in three CTL epitopes in Nef in four slow specibc CTLs arose over time to eliminate variants, indicating immune selection	CTL epitopes in Nef in tants, indicating immune	four slow and non-pro selection	slow and non-progressors, and variant ction
Nef(72-80 SF2)	Nef(66-74) NOTES:	FPVRPQVPL	HIV-1 infection	human(B35)	[Shiga96]
	² Binds HLA-B*3501	A-B*3501			

	Immunogen	Species(HLA)	References
FPVRPQVPL	HIV-1 infection	human(B*3501)	[Tomiyama97]
ne responsive to this epitope was obtainsitive individuals had a CTL response substitution at position 4 abrogates spe	ned to this epitope sciÞc lysis, but not bindin	ng to B*3501	
Nef(69-79) RPQVPLRPMTY OTES: ² Binds HLA-B*3501	HIV-1 infection	human(B35)	[Shiga96]
RPQVPLRPMTY The responsive to this epitope was obtainstive individuals had a strong CTL resubstitution at position 1 abrogates specific to the strong of the strong care.	HIV-1 infection ned ponse to this epitope sciectlysis, but not bindin	uman(B*3501) to B*3501	[Tomiyama97]
PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human [[Lieberman97]
ents, most had CTL specibc for more the shad CTL that could recognize vaccininese 11 had CTL response to this peption of subjects were HLA-A3, A32, B51	nan 1 HIV-1 protein ia expressed LAI Nef ide I, B62; HLA-A11, A24, B	88, B53	
PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human	[Lieberman97b]
ndeex vivowere later infused into HIV-1	1 infected patients		
(71-80) QVPLRPMTYK TES: Optimal epitope mapped by peptide titration	h		[CulmannPerCom]
	FPVRPQVPL responsive to this epitope was obtaine responsive to this epitope was obtained individuals had a CTL response substitution at position 4 abrogates specification at position 4 abrogates specification at position 4 abrogates specification individuals had a strong CTL responsive to this epitope was obtained individuals had a strong CTL responsition 1 abrogates specification at position 1 abrogates specification individuals had a strong CTL responsition 1 abrogates specification individuals had a strong CTL responsition individuals had a strong CTL responsition individuals had a strong CTL responsition individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had CTL response to this peption individuals had CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong CTL response to this peption individuals had a strong	PQVPL HIV-1 infection nsive to this epitope was obtained dividuals had a CTL response to this epitope ion at position 4 abrogates speciPc lysis, but not bindiful PLRPMTY HIV-1 infection HIV-1 infection HIV-1 infection FLRPMTY HIV-1 infection FLRPMTY HIV-1 infection To this epitope was obtained dividuals had a strong CTL response to this epitope ion at position 1 abrogates speciPc lysis, but not bindiful tion at position 7 did not alter reactivity LRMTYKAAVDLSHFL HIV-1 infection St had CTL response to this peptide bjects were HLA-A3, A32, B51, B62; HLA-A11, A24, Infection LRPMTYKAAVDLSHFL HIV-1 infected patients RPMTYK Apped by peptide titration	human(B*3501) himan(B*3501) human(B*3501) human(B*3501) human human human human human human human human

HIV CTL Epitopes

Location	WEAU	Sequence	lmmunogen	Species(HLA)	References
Nef(73-82)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali98]
	² Cross-cla and 1 AG to different Pol 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	termining the CTL activi subtype infection from a 7/8 to B subtype, and F	ty in seven patients from person living in France IV-2 Pol was not tested	seven patients from Bangui, (6 A subtype, on living in France originally from Togo, Pol was not tested
	2 Gag react2 Nef react2 Env react2 One of th	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	e gag, 3/8 with HIV-2 G d 5/8 with B subtype, no 3 with B subtype, none v s epitope: QVPLRPMTY		
Nef(73-82 NL43)	Nef(71-80) NOTES: ² Tyr is crit	Nef(71-80) QVPLRPMTYK IOTES: ² 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: ² Nef CTL	OTES: Nef CTL clones from HIV+ donors			
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A2?)	[Robertson93]
	² Developr ² [Hunzike it did Đ a	Development of a retroviral vector (pNeoNef) to generate autologous CTL [Hunziker98] suggests that HLA-A2 does not in fact present this epitope, in the did D also see [Brander98b]	to generate autologous in fact present this epitc	CTL targets pe, in spite of the sugge	targets n spite of the suggestion in 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	als with appropriate HL/ nat summarizes this stu	\ types can result in eva: dy	sion of CTL response
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin95]
	² Mutation	Mutations found in this epitope in HLA-A11 positive and negative donors w	ositive and negative dor	ors were characterized	

Location	WEAU	Sequence	Immunogen	Species(HLA)	References
Nef(73-82 LAI)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder97, Goulder97e]
	IdenticalBoth had[Goulder	Identical twin hemophiliac brothers were both infected with the same batch Both had a response to this epitope [Goulder97e] is a review of immune escape that summarizes this study	th infected with the same that summarizes this stu	batch of factor VIII dy	
Nef(73-82)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki97]
	² 82 HIV-1- ² A sustain a polyclou a NA3+s at two tim	82 HIV-1-specibc 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 specibc for this epitope, isolated at two time points, 1 year apart	rm non-progressors were observed, and clones were sepitope, with 10/11 CTL	isolated and analyzed e restricted by multiple h clones being specibc f	for breadth of response HLA epitopes, indicating or this epitope, isolated
Nef(73-82)	Nef(71-80) NOTES:	QVPLRPMTYK	HIV infection	human	[Garcia97]
	2 The anti-l 2 First: C& 2 Second: 2 Findings 2 CTL med	The anti-Nef CTL line P1 specibc for this epitope is able to kill target cells via two mechanisms First: Ca²+ -dependent, perforin-dependent Nef-specibc lysis Second: Ca²+ -independent, CD95-dependent apoptosis that could also kill non-specibc 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 Nef-specibc lysis It apoptosis that could als are not mutually exclusive may play a role in pathogo	cells via two mechanisn to kill non-specibc targe in human CTL, as they anesis	ns ets eare in mice
Nef(73-82 LAI)	Nef(71-80)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig95]
	NOTES: ² Alanine s ² Nef CTL load/patic	LES: Alanine substitutions L76A, R77A, M79A, T80A signibcantly decreased immunogenicity of peptide Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of inf load/patient health	80A signibcantly decreas an HIV-1 infected volun	ed immunogenicity of p teer to evaluate effects	nunogenicity of peptide evaluate effects of infusion on viral
	² Infusion l	Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression	hich resulted in higher vii	al load/accelerated disc	ease progression
Nef(73-82)	Nef(72-80) NOTES:	(72-80) VPLRPMTYK TES: Exploration of A11 binding motif	no CTL shown	human(A11)	[Zhang93]

HIV CTL Epitopes

Location	WEAU	Sequence	lmmunogen	Species(HLA)	References
Nef(73-82 LAI)	Nef(72-79)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael94]
	NOTES: ² Review o	TES: Review of HIV CTL epitopes Đ deÞned by B35 motif found within a larger	5 motif found within a lar	ger peptide	
Nef(73-82 LAI)	Nef(72-79)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[RowlandJones95]
	NOTES: 2 VPLRPN	OTES: 2 VPLRPMTY also recognized by CTL from HIV-2 seropositives, epitope is	/-2 seropositives, epitopo	is conserved	
Nef	Nef(72-79)	VPLRPMTY	HIV-1 exposure	human(B35)	[RowlandJones98]
	² A CTL re epitopes and confo	A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously debned B clade epitopes that tended to be conserved in A and D clades D 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	ininfected prostitutes frod D clades D such cross by such cross subtypes are circulating to the B clade epitope	m Nairobi using previc s-reactivity could protec	ນusly deÞned B clade ਖ਼ against both A and D
Nef(75-82)	Nef(72-79) NOTES:	VPLRPMTY	none	human(B35)	[Lalvani97]
	² A peptide D imports	A peptide based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations b importantly this protocol does not stimulate a primary response, only secondary b peptide-specibc CTLp counts	stimulation of CTLp usin a primary response, on	g optimized peptide an ly secondary Đ peptide	d IL-7 concentrations -specibc CTLp counts
	2 This pept activity u	could be obtained via staining with peptide-Class I tetramers This peptide was one of the B35 presented test peptides used in control electivity using lymphocytes from 21 healthy B35 seronegative donors	ass I terramers st peptides used in conti	ol experiments showing	xperiments showing that the assay gave no
Nef(75-82)	Nef(72-79)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith96]
	² Crystal s	Ores. Crystal structure of VPLRPMTY-class B allele HLA-B*3501 complex	HLA-B*3501 complex		
Nef(74-82)	Nef(72-79)	VPLRPMTY		human(A3)	[Carreno92]
	² Included	Included in HLA-A3 binding peptide competition study	on study		