Table 19: **Nef**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(13–20)	Nef(13–20 LAI)	WPTVRERM	HIV-1 infection	human(B*0801)	[Goulder (1997g), Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
Nef(13–20)	Nef(13–20 LAI)	WPTVRERM	HIV-1 infection	human(B8)	[Goulder (1997g)]
	• Unusual epitope for HLA-B8, but compatible with crystal structure predictions				
Nef(13–20)	Nef(13–20)	WPTVRERM	HIV-1 infection	human(B8)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the HLA A2+ was HLA A*0201, A31, B8, B51 and responded to this epitope as well as seven others				
Nef(62–81)	Nef(61–80)	EEEEVGFPVTPQVPLRPMTY	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
Nef(62–81)	Nef(61–80 SF2)	EEEEVGFPVTPQVPLRPMTY	HIV infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Twelve 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(62–81)	Nef(61–80 SF2)	EEEEVGFVTPQVPLRPMTY	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(66–80)	Nef(66–80 BRU)	VGFPVTPQVPLRMT	HIV-1 infection	human(A1, B8)	[Hadida (1992)]
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(66–97)	Nef(66–97 LAI)	VGFPVTPQVPLRPMTYK-AAVDLSHFLKEKGGL	Lipopeptide vaccine	human( )	[Gahery-Segard (2000)]
	• Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual • 5/12 tested had an IgG response to this peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(68–76)	Nef(72–80 SF2)	FPVRPQVPL	HIV-1 infection	human(B*3501)	[Tomiyama (1997)]
	• 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(68–76)	Nef(72–80 SF2)	FPVRPQVPL	HIV-1 infection	human(B35)	[Shiga (1996)]
	• Binds HLA-B*3501				
Nef(68–76)	( )	FPVRPQVPL	HIV-1 infection	human(B35)	[Kawana (1999)]
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation				
Nef(68–76)	Nef(68–76)	FPVTPQVPL	*in vitro* stimulation	human(B7)	[Wilson (1999b)]
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN α enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within • B7 and A2 Nef epitopes were studied – FPVTPQVPL has a high affinity for B7				
Nef(68–77)	Nef(68–77 LAI)	FPVTPQVPLR	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(68–77)	Nef(68–77 LAI)	FPVTPQVPLR	HIV-1 infection	human(B7)	[Haas (1996)]
	• 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(68–84)	Nef( )	FPVRPQVPLRPMTYK-GA		human( )	[Jubier-Maurin (1999)]
	• 41 new HIV-1 strains describing Envelope subtypes of HIV-1 A-H were genetically characterized in the Nef region – 34 subtypes were classified in the same subtype in Nef and Env and 7 of the 41 strains were recombinants • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(69–79)	( )	RPQVPLRPMTY	HIV-1 infection	human(B35)	[Kawana (1999)]
	• HLA B35 is associated with rapid disease progression • The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals • 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation • ----------F was found in 9/10 of the B35+ individuals, none of the B35- individuals – the Y ⟶ F substituted peptide had a similar binding affinity with B35 and was recognized by a CTL clone equally with wildtype				
Nef(71–79)	Nef(71–79 LAI)	TPQVPLRPM	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(71–81)	Nef(75–85 SF2)	RPQVPLRPMTY	HIV-1 infection	human(B*3501)	[Tomiyama (1997)]
	• 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(71–81)	Nef(75–85 SF2)	RPQVPLRPMTY	HIV-1 infection	human(B35)	[Shiga (1996)]
	• Binds HLA-B*3501				
Nef(72–79)	Nef( )	VPLRPMTY	HIV-1 exposed seronegative	human(B35)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(72–79)	Nef( )	VPLRPMTY	HIV-1 infection	human(B35)	[Wilson (2000)]
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderately strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(72–91)	Nef(71–90 SF2)	PQVPLRMTYKAAVDL-SHFL	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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(72–91)	Nef(71–90 SF2)	PQVPLRPMTYKAAVD-LSHFL	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV infection	human( )	[Garcia (1997)]
	• 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(73–82 NL43)	QVPLRPMTYK	HIV-1 infection	human(A*0301)	[Koenig (1990)]
	• 81 Tyr is critical for binding to A3.1 • C. Brander notes that this is an A*0301 epitope in the 1999 database				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Le Borgne (2000)]
	• Soluble factors in supernatant from both an HIV-specific cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Robertson (1993)]
	• Development of a retroviral vector (pNeoNef) to generate autologous CTL targets • [Hunziker (1998)] suggests that HLA-A2 does not in fact present this epitope • The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, Pers. Comm., 2000)				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1994), Goulder (1997a)]
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1995)]
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				
Nef(73–82)	( )	QVPLRPMTYK		(A11)	[Brander & Goulder(2001), Buseyne(1999)]
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-infection	human(A3)	[Chassin (1999)]
	• Mutations in Nef that flank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali (1998)]
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infection) 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				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder (1997b), Goulder (1997a)]
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • Both had a response to this epitope • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki (1997)]
	• Eighty two 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(73–82 BRU)	QVPLRPMTYK	HIV-1 infection	human(A3, A11, B35)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig (1995)]
	• 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(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(B*0301)	[Wilson (2000)]
	• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderately strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(B27)	[Culmann(1998)]
	• Optimal epitope mapped by peptide titration				
Nef(73–82)	Nef(73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human(B35 or C4)	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef(74–81)	Nef(74–82)	VPLRPMTY		human(A3)	[Carreno (1992)]
	• Included in HLA-A3 binding peptide competition study				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith (1996)]
	• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael & Walker(1994), Culmann (1991)]
	• Review of HIV CTL epitopes – defined by B35 motif found within a larger peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[Rowland-Jones (1995)]
	• VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved				
Nef(74–81)	Nef( )	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998a)]
	• 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(74–81)	Nef(75–82)	VPLRPMTY	none	human(B35)	[Lalvani (1997)]
	• 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(74–81)	Nef( )	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998b)]
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90–95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B, and D clade viruses				
Nef(74–81)	Nef( )	VPLRPMTY		human(B35)	[Rowland-Jones (1999)]
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]				
Nef(74–82)	Nef(73–82)	VPLRPMTYK	no CTL shown	human(A11)	[Zhang (1993)]
	• Exploration of A11 binding motif				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*1101 epitope				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Bauer (1997)]
	• Structural constraints on the Nef protein may prevent escape • Noted in Brander 1999, this database, to be B*0702				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802)	[Nixon (1999)]
	• A patient who made a mono-specific CTL response to this Nef specific epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous • Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped • The patient went from having an activated effector population (detected by CTLp and clone specific RNA) to a non-activated quiescent population (detected by the CTL-clone specific DNA)				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802(Cw8))	[Brander & Goulder(2001)]
	• C. Brander notes this is a C*0802(Cw8) epitope				
Nef(82–101)	Nef(81–100 SF2)	KAAVDLSHFLKEKGG-LEGLI	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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)	Nef(83–94 BRU)	AAVDLSHFLKEK	HIV-1 infection	human(A11)	[Culmann (1991)]
	• Epitope defined by boundaries of overlapping peptides that stimulate Nef CTL clones				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(84–91)	Nef(84–91 LAI)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Culmann-Penciolelli (1994)]
Nef(84–91)	Nef(84–91)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope				
Nef(84–92)	Nef(84–92 LAI)	AVDLSHFLK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*1101 epitope				
Nef(84–92)	Nef(84–92 LAI)	AVDLSHFLK	HIV-1 infection	human(A11)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef(84–92)	Nef(84–92)	AVDLSHFLK	HIV-1 infection	human(A11)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that didn't respond to SLYNTVATL reacted with seven other epitopes including this epitope				
Nef(84–92)	Nef(84–92 LAI)	AVDLSHFLK	HIV-1 infection	human(A11)	[Couillin (1994), Goulder (1997a)]
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(84–92)	Nef(84–92 LAI)	AVDLSHFLK	HIV-1 infection	human(A11)	[Couillin (1995)]
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				
Nef(86–94)	Nef(84–92 LAI)	DLSHFLKEK	HIV-1 infection	human(A3.1)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes				
Nef(86–100)	Nef(86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human(A2)	[Robertson (1993)]
	• Development of a retroviral vector (pNeoNef) to generate autologous targets				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(86–100)	Nef(86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human(B35)	[Buseyne (1993b)]
Nef(86–100)	Nef(86–100 LAI)	DLSHFLKEKGGLEGL	HIV-1 infection	human(B35 or C4)	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef(87–102)	Nef( )	FSHFLKEKGGLEGLIY		human( )	[Jubier-Maurin (1999)]
	• 41 new HIV-1 strains describing Envelope subtypes of HIV-1 A-H were genetically characterized in the Nef region – 34 subtypes were classified in the same subtype in Nef and Env and 7 of the 41 strains were recombinants • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes				
Nef(90–97)	Nef(89–97)	FLKEKGGL	HIV-1 infection	human( )	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that responded to SLYNTVATL reacted with seven other epitopes including this epitope previously described as presented by B8				
Nef(90–97)	Nef(89–97 LAI)	FLKEKGGL	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
Nef(90–97)	Nef(89–97 LAI)	FLKEKGGL	HIV-1 infection	human(B8)	[Price (1997)]
	• CTL escape variants appeared over time in HLA-B8 HIV-1+ individual, providing evidence of immune escape • Most variants appear at position 5, an anchor residue • FLKE(E,N or Q)GGL showed reduced binding efficiency and recognition • Double mutants (FIKENGGL, FLEENGGL, and FLKGNGGL) completely escaped recognition • [Goulder (1997a)] is a review of immune escape that summarizes this study in the context of CTL escape to fixation				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(90–97)	Nef(90–97 IIIB)	FLKEKGGL	HIV-1 infection	human(B8)	[Spiegel (1999)]
	• Study examines the effect of highly active antiretroviral therapy (HAART) on HIV-1 plasma viral load, CTLp and CTLe frequencies in 8 infected children • CTLp (precursors) were measured by stimulating in culture and assaying using 51Cr release, against vaccina expressed IIIB Env, Gag, Pol, Nef • B7-FLKEKGGL tetramer complex was used for one of the children that was HLA-B7, and this infant showed a vigorous response (> 4% of CD8+ T cells) at 9 months of age • HIV-1 specific CTL responses initially increased in children with complete viral suppression, but then decreased, suggesting viral replication is needed to maintain CTL responses				
Nef(90–97)	Nef( )	FLKEKGGL	Polyepitope encoding DNA in VVA	human(B8)	[Hanke (1998b), Hanke (1998a)]
	• 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(90–97)	Nef(88–95)	FLKEKGGL	HIV-1 infection	human(B8)	[Goulder (1997g)]
	• 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(90–97)	Nef(90–97)	FLKEKGGL	HIV-1 infection	human(B8)	[Dyer (1999)]
	• CTL-specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
Nef(92–100)	( )	KEKGGLEGL		human(B*4001)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*4001,B60 epitope				
Nef(93–106)	Nef(93–106 BRU)	EKGGLEGLIHSQRR	HIV-1 infection	human(A1, B8)	[Hadida (1992)]
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(102–115)	Nef(102–115 LAI)	HSQRRQDILDLWIY	HIV-1 infection	human(B7)	[Goulder (1997b), Goulder (1997a)]
	• 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 • [Goulder (1997a)] is a review of immune escape that summarizes this study				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(102–121)	Nef(101–120 SF2)	HSQRRQDILDLQIYHT-QGYF	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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)	Nef(103–127 PV22)	SQRRQDILDLWIYHTQ-GYFPDWQNY	HIV-1 infection	human(B13)	[Jassoy (1993)]
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
Nef(105–114)	Nef(105–114 LAI)	RRQDILDLWI	HIV-1 infection	human(B*2705)	[Goulder (1997d)]
	• 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(105–114)	Nef(105–114 LAI)	RRQDILDLWI	HIV-1 infection	human(B*2705)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*2705 epitope				
Nef(106–115)	( )	RQDILDLWIY		(B7)	[Brander & Goulder(2001), Goulder(1999)]
Nef(112–133)	Nef(111–132)	LWIYHTQGYFPDWQN-YTPGPGV	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
Nef(112–133)	Nef(111–132 SF2)	LWIYHTQGYFPDWQN-YTPGPGV	HIV infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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(112–133)	Nef(111–132 SF2)	LWIYHTQGYFPDWQN-YTPGPGV	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(113–125)	Nef(113–125 BRU)	WIYHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann (1989)]
	• Nef CTL clones from HIV+ donors				
Nef(113–126)	Nef( )	VYHTQGYFPDWQNY	HIV-1 infection	human( )	[Jubier-Maurin (1999)]
Nef(113–128)	Nef(113–128 BRU)	WIYHTQGYFPDWQNY-T	HIV-1 infection	human(A1)	[Hadida (1992)]
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(115–125)	Nef(115–125 BRU)	YHTQGYFPDWQ	HIV-1 infection	human(B17)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(116–125)	Nef(116–125 BRU)	HTQGYFPDWQ	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5701 epitope • Subtype of B57 not determined				
Nef(116–125)	Nef(116–125)	HTQGYFPDWQ	HIV-1 infection	human(B57)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • One of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others				
Nef(116–125)	Nef(116–125 BRU)	HTQGYFPDWQ	HIV-1 infection	human(B57)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors, optimal peptide mapped				
Nef(117–127)	Nef(117–127)	TQGYFPDWQNY	HIV-1 infection	human( )	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA Bw62 epitope TQGYFPDWQNY, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one				
Nef(117–127)	Nef(117–127 LAI)	TQGYFPDWQNY	HIV-1 infection	human(B*1501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*1501 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(117–127)	Nef(117–127 LAI)	TQGYFPDWQNY	HIV-1 infection	human(Bw62)	[Culmann(1998)]
	• Optimal peptide defined by titration				
Nef(117–128)	Nef(117–128 BRU)	TQGYFPDWQNYT	HIV-1 infection	human(B17, B37)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(117–147)	Nef(117–147 LAI)	TQGYFPDWQNYTPGP-GVRYPLTFGWCYKLVP	Lipopeptide vaccine	human( )	[Gahery-Segard (2000)]
	• Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual • 10/12 tested had an IgG response to this peptide				
Nef(118–127)	Nef(118–127 LAI)	QGYFPDWQNY		human(Bw62)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes				
Nef(120–128)	Nef(120–128)	YFPDWQNYT	HIV-1 infection	human( )	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty five optimally defined peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0205/A*0208, A30, B27, B44 but responded to HLA B37 epitope IYKRWIILGL, and one of the other individuals that was A2+, but otherwise of unknown HLA type, reacted with seven epitopes including this one				
Nef(120–128)	Nef(120–128 LAI)	YFPDWQNYT	HIV-1 infection	human(B*3701)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3701 and B*5701 epitope				
Nef(120–128)	Nef(120–128 LAI)	YFPDWQNYT	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5701 epitope • Subtype of B57 not determined				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(120–128)	Nef(120–128 IIIB)	FFPDWKNYT	HIV-1 infection	human(B15)	[Wilson (1999a)]
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • LFPDWKNYT is an escape mutant				
Nef(120–128)	Nef(120–128 LAI)	YFPDWQNYT	HIV-1 infection	human(B37,B57)	[Culmann(1998)]
	• Nef CTL clones from HIV+ donors – optimum peptide mapped by titration				
Nef(120–144)	Nef(120–144 SF2)	YFPDWQNYTPGPGIR-YPLTFGWCYK	HIV-1 infection	human(A24)	[Jassoy (1992)]
	• Epitope recognized by CTL clone derived from CSF				
Nef(122–141)	Nef(121–140 SF2)	PDWQNYTPGPGVRYP-LTFGW	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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				
Nef(123–137)	Nef(123–137 IIIB)	QWQNYTPGPGVRYPL	HIV-1 infection	human( )	[Wilson (1996)]
	• 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)	Nef(126–138 BRU)	NYTPGPGVRYPLT	HIV-1 infection	human(B7)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(128–137)	Nef(128–137 LAI)	TPGPGVRYPL	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(128–137)	Nef(128–137 LAI)	TPGPGVRYPL		human(B*4201)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*4201 epitope				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(128–137)	( )	TPGPGVRYPL	HIV-1 infection	human(B7)	[Wilson (2000)]
• Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-specific T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderately strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(128–137)	Nef(128–137 LAI)	TPGPGVRYPL	HIV-1 infection	human(B7)	[Haas (1996), Haas (1997)]
• 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 [Haas (1997)]					
Nef(128–137)	Nef( )	TPGPGVRYPL	HIV-1 exposure	human(B7)	[Rowland-Jones (1998a)]
• 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(128–137)	Nef( )	TPGPGVRYPL	HIV-1 exposure	human(B7)	[Rowland-Jones (1998b)]
• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90–95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among B and D clade viruses • The Clade A version of the epitope: TPGPGIRYPL					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(128–137)	Nef(128–137)	TPGPGVRYPL	*in vitro* stimulation	human(B7)	[Wilson (1999b)]
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN α enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within • CTL from a B7 donor displayed no reactivity to this epitope, although it had been immunodominant in another study [Haas (1996)]				
Nef(128–137)	Nef( )	TPGPGVRYPL	HIV-1 exposure	human(B7(*8101))	[Rowland-Jones (1998b)]
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90–95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • Clade A version of the epitope: TPGPGIRYPL, clade D version: TPGPGIRYPL				
Nef(128–137)	Nef(128–137 Clade B)	TPGPGVRYPL	HIV-1 exposed seronegative	human(B7,B*8101)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Nef(130–143)	Nef(130–143 LAI)	GPGVRYPLTFGWCY	HIV-1 infection	human(B*57)	[Goulder (1996b)]
	• 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				
Nef(131–143)	Nef( )	GIRYPLTFGWCFK		human( )	[Jubier-Maurin (1999)]
	• 41 new HIV-1 strains describing Envelope subtypes of HIV-1 A-H were genetically characterized in the Nef region – 34 subtypes were classified in the same subtype in Nef and Env and 7 of the 41 strains were recombinants • This region was defined as a CTL epitope region that is conserved among HIV-1 M group subtypes				
Nef(132–147)	Nef(132–147 BRU)	GVRYPLTFGWCYKLVP	HIV-1 infection	human(A1, B8)	[Hadida (1992)]
	• HIV-1 specific CTLs detected in lymphoid organs				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(132–147)	Nef(132–147 BRU)	GVRYPLTFGWCYKLVP	HIV-1 infection	human(B18)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(133–148)	Nef(133–148 LAI)	VRYPLTFGWCYKLVPV		human(B57)	[Brander & Walker(1996)]
	• P. Goulder, pers. comm.				
Nef(134–141)	Nef(138–147 LAI)	RYPLTFGW	HIV-1 infection	human(A*2402)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*2402 epitope				
Nef(134–141)	Nef(134–141 LAI)	RYPLTFGW		human(B27)	[Culmann(1998)]
	• Optimal peptide defined by titration				
Nef(134–143)	Nef(138–147 SF2)	RYPLTFGWCF	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
	• 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(134–144)	Nef(134–144 LAI)	RYPLTFGWCYK	HIV-1 infection	human(B18)	[Couillin (1994), Goulder (1997a)]
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(135–143)	Nef(135–143 LAI)	YPLTFGWCY	HIV-1 exposure	human(B*1801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*1801 epitope				
Nef(135–143)	Nef( )	YPLTFGWCF	HIV-1 exposed seronegative	human(B18)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(135–143)	Nef(135–143 LAI)	YPLTFGWCY	HIV-1 exposure	human(B18)	[Culmann (1991), Culmann-Penciolelli (1994)]
	• Nef CTL clones from HIV+ donors				
Nef(135–143)	Nef(139–147 SF2)	YPLTFGWCF	HIV-1 infection	human(B35)	[Shiga (1996)]
	• Binds HLA-B*3501				
Nef(135–143)	Nef( )	YPLTFGWCY	HIV-1 exposure	human(B49)	[Rowland-Jones (1998a)]
	• 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( )	YLPTFGWCY	HIV-1 exposure	human(B49)	[Rowland-Jones (1998b)]
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90–95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A and B clade viruses • The Clade D version of the epitope, YPLTFGWCF, was preferentially recognized by CTL				
Nef(136–145)	Nef(136–145)	PLTFGWCYKL	*in vitro* stimulation	human(A*0201)	[Wilson (1999b)]
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN α enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL • Noted in Brander *et al.*, 1999 this database, to be A*0201				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(136–145)	Nef(136–145 LAI)	PLTFGWCYKL	Nef(180–189)	human(A*0201)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0201 epitope				
Nef(136–145)	Nef(136–145)	PLTFGWCFKL	HIV-1 infection	human(A2)	[Durali (1998)]
	• 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 PLTFGWCFKL				
Nef(136–145)	Nef(157–166)	PLTFGWCFKL	HIV-1 infection (human) or HIV A2-Polyepitope (Polytope) DNA vaccine with vaccinia boost (rVV.HIV.pt) (mouse)	human(A2)	[Woodberry (1999)]
	• A Polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2 • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^{d} – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77–85) SLYNTVATL, Pol (476–484) ILKEPVHGV, gp120 (120–128) KLTPLCVTL, and Nef (190–198) AFHHVAREL were observed in HIV Polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157–166 (PLTFGWCYKL), Pol 346–354 (VIYQYMDDL), and Nef 180–189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the Polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • PLTFGWCFKL was recognized by 1 of the HLA-A2 patients				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(162–181)	Nef(161–180)	TSLLHPVSLHGMDDP-EREVL	HIV infection	human( )	[Lieberman (1995)]
	• HIV-specific CTL lines developed by *ex vivo* stimulation with peptide				
Nef(162–181)	Nef(161–180 SF2)	TSLLHPVSLHGMDDP-EREVL	HIV infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • One of these 11 had CTL response to this peptide				
Nef(162–181)	Nef(101–120 SF2)	TSLLHPVSLHGMDDP-EREVL	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(162–181)	Nef(161–180 SF2)	TSLLHPVSLHGMDDP-EREVL	HIV infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • One of these 11 had CTL response to this peptide				
Nef(172–191)	Nef(171–190 SF2)	GMDDPEREVLEWRFD-SRLAF	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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(175–184)	Nef(175–184)	DPEKEVLQWK	HIV-1 infection	human(B7)	[Jin (2000)]
	• This a B7 epitope, a subdominant CTL response, was defined by an un-conventional approach used to predict epitopes in an HLA B7+ long-term non-progressor • Three additional sub-dominant HLA B7 epitopes were defined using EpiMatrix, a non-anchor based strategy for defining potential epitopes, which highlighted 2078 possible epitopes in the autologous HIV-1 derived from the study subject, followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes				
Nef(180–189)	Nef(180–189 LAI)	VLEWRFDSRL	HIV-1 infection	human(A*0201)	[Haas (1996), Haas (1997)]
	• 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 • Noted in Brander *et al.*, 1999 this database, to be A*0201				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(180–189)	Nef(180–189 LAI)	VLEWRFDSRL	Nef(180–189)	human(A*0201)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0201 epitope				
Nef(180–189)	Nef(180–189)	VLEWRFDSRL	*in vitro* stimulation	human(A2)	[Wilson (1999b)]
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN α enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL				
Nef(180–189)	Nef(180–189)	VLEWRFDSRL	HIV-1 infection (human) or HIV A2-Polyepitope (Polytope) DNA vaccine with vaccinia boost (rVV.HIV.pt) (mouse)	human(A2)	[Woodberry (1999)]
	• A Polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2 • HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice • CTL responses to Gag (77–85) SLYNTVATL, Pol (476–484) ILKEPVHGV, gp120 (120–128) KLTPLCVTL, and Nef (190–198) AFHHVAREL were observed in HIV Polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost • No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157–166 (PLTFGWCYKL), Pol 346–354 (VIYQYMDDL), and Nef 180–189 (VLEWRFDSRL) • Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the Polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested • VLEWRFDSRL was recognized by 2 of the HLA-A2 patients				
Nef(182–198)	Nef(182–198 BRU)	EWRFDSRLAFHHVARELHIV-1 infection		human(A1, B8)	[Hadida (1992)]
	• HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients				
Nef(182–198)	Nef(182–198 LAI)	EWRFDSRLAFHHVARELHIV-1 infection		human(A2, A25(10))	[Hadida (1995)]
	• The C-terminal region of Nef (182–205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(182–198)	Nef(182–198 BRU)	EWRFDSRLAFHHVARELHIV-1 infection		human(A25)	[Cheynier (1992)]
	• CTL isolated in children born to HIV-1 positive mothers				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(182–198)	Nef(182–198 LAI)	EWRFDSRLAFHHVAR-EL	HIV-1 infection	human(B35)	[Hadida (1995)]
	• The C-terminal region of Nef (182–205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(182–198)	Nef(182–198 LAI)	EWRFDSRLAFHHVAR-EL	Rec Mengo virus HIV-1 Nef 65–206	murine(H-2^d)	[Van der Ryst (1998)]
	• *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(182–201)	Nef(191–205 SF2)	EWRFDSRLAFHHVAR-ELHPE	HIV-1 infection	human( )	[Lieberman (1997a)]
	• Of 25 patients, most had CTL-specific for more than 1 HIV-1 protein • Eleven 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(182–205)	Nef(182–205 LAI)	EWRFDSRLAFHHVAR-ELHPEYFKN	Lipopeptide vaccine	human( )	[Gahery-Segard (2000)]
	• Anti-HIV lipopeptide vaccine consisting of six long amino acid peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial • A CD4+ T cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide • 9/12 tested mounted a CTL response to at least one of the six peptides; each of the six peptides elicited a CTL response in at least one individual • None of the 12 tested had an IgG response to this peptide				
Nef(186–193)	Nef(186–193 LAI)	DSRLAFHH	HIV-1 infection	human(B35)	[Hadida (1995)]
	• The C-terminal region of Nef (182–205) contains multiple CTL epitopes with 5 distinct HLA restrictions				
Nef(186–194)	Nef(186–194 BRU)	DSRLAFHHV		human(B51)	[Connan (1994)]
	• Resulted in the assembly of HLA-B51				
Nef(188–196)	Nef(188–196 LAI)	RLAFHHVAR	HIV-1 infection	human(B52)	[Hadida (1995)]
	• The C-terminal region of Nef (182–205) contains multiple CTL epitopes with 5 distinct HLA restrictions				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(188–201)	Nef(188–201 LAI)	RLAFHHVARELHPE	HIV-1 infection	human(B35 or C4)	[Buseyne (1993a)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef(190–198)	Nef(190–198 LAI)	AFHHVAREL	HIV-1 exposure	human(A2)	[Rowland-Jones (1998a)]
	• CTL recognition reported in the context of HLA-B52 and A2.1, A2.2 and A2.4 • 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 • [Hunziker (1998)] suggests that HLA-A2 does not in fact present this epitope, and notes that it does not promote A2 assembly [Connan (1994)] – also see [Brander (1998b)] • [Hunziker (1998)] maintains that HLA-A2 does not present this epitope contrary to an earlier report [Hadida (1995)], (also see [Brander (1998a)]) – 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, Pers. Comm.)				
Nef(190–198)	Nef(190–198)	AFHHVAREL	*in vitro* stimulation	human(A2)	[Wilson (1999b)]
	• Dendritic cells are the most potent for priming T cell responses – DCs can stimulate autologous CTL responses from T cells cultured from HIV negative donors • Th1-biasing cytokines IL-12 or IFN α enhance CTL responses *in vitro* whether the epitope is delivered by pulsing from peptide, or expressed from within • B7 and A2 Nef epitopes were studied and the relative binding affinity of A2 epitopes for A2 was: PLTFGWCYKL greater than VLEWRFDSRL which was much greater than AFHHVAREL				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(190–198)	Nef(190–198)	AFHHVAREL	HIV A2-Polyepitope (Polytope) DNA vaccine with vaccinia boost (rVV.HIV.pt)	human(A2)	[Woodberry (1999)]

- A Polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice
- CTL responses to Gag (77–85) SLYNTVATL, Pol (476–484) ILKEPVHGV, gp120 (120–128) KLTPLCVTL, and Nef (190–198) AFHHVAREL were observed in HIV Polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157–166 (PLTFGWCYKL), Pol 346–354 (VIYQYMDDL), and Nef 180–189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the Polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested
- AFHHVAREL was recognized by 2 of the patients

Nef(190–198)	Nef( )	AFHHVAREL	HIV-1 exposure	human(A2, A*0202, A*0201)	[Rowland-Jones (1998b)]

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection
- Seroprevalence in this cohort is 90–95% and their HIV-1 exposure is among the highest in the world
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes
- Clade A version of the epitope: ALKHRAYEL, Clade D epitope: AFEHKAREM
- This epitope was recognized by two different exposed and uninfected prostitutes

Nef(190–198)	Nef(190–198 LAI)	AFHHVAREK	HIV-1 infection	human(A3)	[Hadida (1995)]

- Naturally occurring L to K anchor substitution abrogates A2 binding, but permits HLA-A3 binding

Nef(192–206)	Nef(192–206 BRU)	HHVARELHPEYFKNC	HIV-1 infection	human(A1)	[Hadida (1992)]

- HIV-1 specific CTLs detected in lymphoid organs of HIV-1 infected patients

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef( )	Nef( )		HIV-1 infection	human( )	[Wasik (2000)]
• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of β-chemokines and IL-2 relative to other HIV+ infants • No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs					
Nef( )	Nef( )		HIV-1 infection	human( )	[De Maria (1997)]
• 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					
Nef( )	Nef( )		HIV-infection	human( )	[Lubaki (1999)]
• Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20) • A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20					
Nef( )	Nef( )		rec canarypox vaccine expressing HIV-1 Env, Gag, Pol, Nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120	human( )	[Gorse (1999)]
• *In vitro* inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity					
Nef( )	Nef( )		HIV-1 infection	human( )	[Gamberg (1999)]
• 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens • Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCRβV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef( )	Nef( )		DNA constructs encoding HIV-1 genes Nef, Rev or Tat	human( )	[Calarota (1999)]
	• 9/9 HIV-1+ subjects were given one of three DNA vaccinations for Nef, Rev or Tat, and novel proliferative and CTL responses were generated • The Nef DNA immunization induced the highest and most consistent CTLp activity, IFN-γ production, and IL-6 and IgG responses • Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination				
Nef( )	Nef( )		HIV-1 infection	human( )	[Buseyne (1998a)]
	• This study showed a correlation between strong CTL memory and breadth of response in 7–12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load				
Nef( )	Nef( )		HIV-1 infection	human( )	[Buseyne (1998b)]
	• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes				
Nef( )	Nef( )		canarypox HIV vaccine	human( )	[Evans (1999)]
	• A canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3–6 months after the last vaccination				
Nef( )	Nef( )		HIV-1 infection	human( )	[da Silva & Hughes(1998)]
	• CTL dense regions of Nef tend to lie in conserved domains with low non-synonymous substitution per site – authors consider that this may be due to a host adaptation to infection that focuses the CTL response to be directed against conserved functional domains [da Silva & Hughes(1998)]				
Nef( )	Nef( )		HIV infection	human( )	[Legrand (1997)]
	• Seventeen 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				
Nef( )	Nef( )		HIV-1 infection	human( )	[Aladdin (1999)]
	• *In vitro* measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef( )	Nef( )		HIV infection	human( )	[Zerhouni (1997)]
• 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( )	Nef( )		HIV-1 infection	( )	[Kuiken (1999)]
• A correlation between conserved regions of Nef and CTL epitope density was also noted in [Kuiken (1999)]. The authors suggest that this may be due to biological reasons such as the one described above [da Silva & Hughes(1998)], or due to epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents • Both p17 and Nef show a correlation between epitope density and conserved regions in the protein – in contrast, p24 is a more conserved protein and known epitopes are evenly distributed across p24					
Nef( )	Nef( )		HIV-1 infection	human(A*0201 and Cw*08)	[Shacklett (2000)]
• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples					
Nef( )	Nef( )		DNA vaccination of HIV-1 Nef expression vectors pBN-CMV-NEF and pBN-RSV-NEF (self-replicating), pCGE2-NEF (non-replicating)	murine(H-2D^d)	[Collings (1999)]
• CTL immune responses were detected using all three expression vectors, while a humoral immune response to Nef was only observed in the self-replicating expression vectors; possibly antibody responses require higher levels of protein expression					
Nef( )	Nef( )	SIV Nef and Env CTL epitopes	SIV-infection	Rhesus macaques(Mamu-A*11, -B*03, -B*04, and -B*17)	[Dzuris (2000)]
• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here					