

Table 3: **p24**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(8–17)	p24(140–149) • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety five optimally defined peptides from this database were used to screen for γ interferon responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others	GQMVHQAIISP	HIV-1 infection	human(B57)	[Betts (2000)]
p24(8–20)	p24(140–152 IIIB) • Fine specificity of human Cw3 restricted Gag CTL epitope	GQMVHQAIISPRTL	HIV-1 infection	human(Cw3)	[Littau (1991)]
p24(8–27)	p24(140–159) • CTL specific for this epitope were found in the peripheral blood but not in the cervical mucosa of one donor	GQMVHQAIISPRTLNA- WVKVV	HIV-1 infection	human(B14)	[Musey (1997)]
p24(9–18)	Gag(173–182) • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)	QMVHQAIISPR	HIV-1 infection	human(A3 supertype)	[Propato (2001)]
p24(10–18)	Gag(174–182) • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)	MVHQAIISPR	HIV-1 infection	human(A3 supertype)	[Propato (2001)]
p24(11–24)	p24() • The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A34/68 B57/71 Cw3/7 – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses	VQHAIISPRTLNAWV	HIV-1 infection	human()	[Goulder (2000a)]

			<ul style="list-style-type: none"> Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 		
p24(11–32)	p24(143–164 BH10)	VHQAI SPRTLNAWVK-VVEEKAF	HIV-1 infection	human(Bw57)	[Johnson (1991)]
			<ul style="list-style-type: none"> Gag CTL response studied in three individuals 		
p24(12–20)	Gag(146–154)	HQAI SPRTL	HIV-1 infection	chimpanzee(Patr-B*02)	[Balla-Jhagjhoorsingh (1999b)]
			<ul style="list-style-type: none"> Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57 Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they responded to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57 The human HLA protein which presents this Patr-B*02 epitope is HLA-B*5701 but the amino acid sequences in the binding pockets of HLA-B*5701 and Patr-B*02 are distinctive 		
p24(13–20)	p24(145–152)	QAISPRTL	HIV-1 exposed seronegative, HIV-1 infection	human(Cw3)	[Kaul (2001a)]
			<ul style="list-style-type: none"> ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers 		
p24(13–23)	p24(145–155)	QAISPRTLNAW	HIV-1 infection	human()	[Betts (2000)]
			<ul style="list-style-type: none"> Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant Ninety five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to QAISPRTLNAW noted previously to be A25 		
p24(13–23)	p24(145–155 LAI)	QAISPRTLNAW		human(A*2501)	[Brander & Goulder(2001)]
			<ul style="list-style-type: none"> C. Brander notes that this is an A*2501 (Pers. Comm. I. Kurane and K. West) 		
p24(13–23)	p24(145–155 SF2)	QAISPRTLNAV	HIV-1 infection	human(A25)	[Altfeld (2001c)]
			<ul style="list-style-type: none"> Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef Previously described and newly-defined optimal epitopes were tested for CTL response Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3 		

HIV CTL Epitopes

p24(13–23)	p24(145–155 LAI)	QAISPRTLNAW		human(A5)	[Kurane & West(1998)]
p24(15–23)	()	LSPRTLNAW	HIV-1 infection	human()	[Kaul (2001b)]
					<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • ISPRTLNAW was consistently recognized by one of 22 HEPS sex worker controls (ML1250), and LSPRTLNAW was recognized by two additional HEPS sexworker control (ML1693 and ML1589)
p24(15–23)	p24(147–155 IIIB)	ISPRTLNAW	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5701 epitope
p24(15–23)	Gag(147–155 LAI)	ISPRTLNAW	HIV-1 infection	human(B*5701 B*5801)	[Klein (1998)]
					<ul style="list-style-type: none"> • B57 has been associated with long-term non-progression in the Amsterdam cohort • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag
p24(15–23)	p24(147–155)	ISPRTLNAW	HIV-1 infection	human(B57)	[Betts (2000)]
					<ul style="list-style-type: none"> • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others, but not SLYNTVATLjt
p24(15–23)	Gag()	ISPRTLNAW	HIV-1 infection	human(B57)	[Goulder (2001b)]
					<ul style="list-style-type: none"> • Epitope name: IW9. This epitope elicited the second strongest CTL response in patient PI004 during acute infection, and maintained the response • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGGL were detectable at 5 months post-infection and beyond
p24(15–23)	p24(147–155)	ISPRTLNAW	HIV-1 infection	human(B57)	[Oxenius (2000)]
					<ul style="list-style-type: none"> • Epitope name: ISP. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+
p24(15–23)	p24(15–23)	ISPRTLNAW	HIV-1 infection	human(B57)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

p24(15–23)	p24(147–155 SF2)	ISPRTLNAW	HIV-1 infection	human(B57)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3 				
p24(15–23)	p24(147–155 IIIB)	ISPRTLNAW	HIV-1 infection	human(B57,B*5801)	[Goulder (1996b)]
	<ul style="list-style-type: none"> • Five slow progressors made a response to this epitope, and in two it was the dominant response • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations 				
p24(15–23)	p24()	LSPRTLNAW	HIV-1 exposed seronegative	human(B57,B58)	[Kaul (2000)]
	<ul style="list-style-type: none"> • 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+ T-cell epitopes DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women 				
p24(15–23)	p24(147–155)	LSPRTLNAW	HIV-1 exposed seronegative, HIV-1 infection	human(B57,B58)	[Kaul (2001a)]
	<ul style="list-style-type: none"> • Variants (L/I)SPRTLNAW are specific for the A/B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B57/B58 women, 4/6 HEPS and 14/17 HIV-1-infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 14/17 responsive HIV-1-infected women 				
p24(16–24)	p24()	SPRTLNAWV	HIV-1 infection	chimpanzee()	[Santra (1999)]
	<ul style="list-style-type: none"> • 3/4 animals displayed HIV-1 Gag-specific CTL activity • Effector cells from two chimpanzees were able to recognize epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14) 				

HIV CTL Epitopes

- No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWIILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14

p24(16–24)	p24(148–156)	SPRTLNAWV		human(B*0702)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*0702 epitope • Optimal peptide mapped by titration, Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker
p24(16–24)	p24(148–156)	SPRTLNAWV		human(B7)	[Brander & Walker(1997)]
					<ul style="list-style-type: none"> • Optimal peptide mapped by titration, Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker
p24(16–24)	p24(148–156)	SPRTLNAWV	HIV-1 infection	human(B7)	[Brodie (2000)]
					<ul style="list-style-type: none"> • Study tracks and quantifies <i>in vivo</i> migration of neo-marked CD8+ HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, colocalizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL <i>in vivo</i>
p24(16–24)	p24(148–156)	SPRTLNAWV	HIV-1 exposed seronegative, HIV-1 infection	human(B7)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Subject ML 1203 started with CTL responses to A*6802 DTVLEDINL and to B7 FPVTPQVPLR prior to seroconversion, and upon seroconversion acquired additional responses to A*6802 ETAYFILKL which became dominant, B7 TPGPGV/IRYPL, B7 IPRRIRQGL, and B7 SPRTLNAWV
p24(16–24)	p24(16–24)	SPRTLNAWV	HIV-1 infection	human(B7)	[Day (2001)]
					<ul style="list-style-type: none"> • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconverter homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconverter failed to recognize any of the 11 B7-restricted epitopes tested

- The B7-restricted CTL response was highly variable and there was no clearly dominant epitope

p24(16–24)	p24()	SPRTLNAWV	HIV-1 exposed seronegative	human(B7,B*8101)	[Kaul (2000)]
					<ul style="list-style-type: none"> • 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+ T-cell epitopes DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women
p24(16–24)	Gag()	SPRTLNAWV	HIV-1 exposed seronegative	human(B7,B*8101)	[Rowland-Jones (1998b)]
					<ul style="list-style-type: none"> • 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
p24(19–27)	p24(151–159)	TLNAWVKVV	HIV-1 infection	human(A*02)	[Huang (2000)]
					<ul style="list-style-type: none"> • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in γ interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT • In 3/3 HLA-A*02 B*27 subjects the immunodominant epitope was against HLA B*27 Gag p24 epitope KRWILGL, not A2 Gag epitopes
p24(19–27)	p24(151–159)	TLNAWVKVV	HIV-1 infection	human(A*02)	[Rinaldo (2000)]
					<ul style="list-style-type: none"> • Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that can persist after therapy and long periods of virus being below the level of detection
p24(19–27)	p24(151–159)	TLNAWVKVV	HIV-1 infection	human(A2)	[Parker (1992), Parker (1994)]
					<ul style="list-style-type: none"> • Study of sequence motifs preferred for peptide binding to class I HLA-A2
p24(19–27)	p24(19–27)	TLNAWVKVV	HIV-1 infection	human(A2)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(19–27)	p24(150–159)	TLNAWVKVI	HIV-1 exposed seronegative, HIV-1 infection	human(A2)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • Variants TLNAWVKV(I/V) are A/B clade specific • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

HIV CTL Epitopes

p24(19–27)	p24()	TLNAWVKVV	HIV-1 exposed seronegative	human(A2, A*0202)	[Rowland-Jones (1998b)]
					<ul style="list-style-type: none"> • 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
p24(21–40)	p24(153–172 SF2)	NAWVKVVEEKAFSPE- VIPMF	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, B21
p24(21–40)	p24(153–172 SF2)	NAWVKVVEEKAFSPE- VIPMF	Vaccine	Rhesus macaque()	[Wagner (1998b)]
					<p>Vaccine: <i>Vector/type:</i> virus-like particle <i>HIV component:</i> gag, gp120, V3, CD4BS</p> <ul style="list-style-type: none"> • A VLP is a non-infectious virus-like particle self-assembled from HIV Pr55 gag – macaques were immunized with VLPs bound to either gp120 or V3+CD4 linear domains Gag and Env specific CTL were stimulated in each case, and Ab response to gag and gp120 was elicited, but the gp120 neutralizing response occurred only with whole gp120, not V3+CD4 – despite the CTL and Ab response, immunized macaques were infected by intervenous challenge with SHIV chimeric challenge stock [Wagner (1998b)] • CTL specific for this epitope could be found both before and after SHIV challenge
p24(21–40)	Gag(153–172)	NAWVKVVEEKAFSPE- VIPMF	HIV-1 infection	human(B57)	[Brodie (1999)]
					<ul style="list-style-type: none"> • The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL <i>in vitro</i>, and adoptively transferring them • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T-cells, showing that CTL move to appropriate target sites and mediate anti-viral effects
p24(21–40)	p24(153–172)	NAWVKVVEEKAFSPE- VIPMF	HIV-1 infection	human(B57)	[Brodie (2000)]
					<ul style="list-style-type: none"> • Study tracks and quantifies <i>in vivo</i> migration of neo-marked CD8+ HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, co-localizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL <i>in vivo</i>

p24(21–42)	p24(153–174 BH10)	NAWVKVVEEKAFSPE- VIPMFSA	HIV-1 infection	human(Bw57)	[Johnson (1991)]
					<ul style="list-style-type: none"> • Gag CTL response studied in three individuals
p24(28–47)	p24(160–179)	EKAFSPEVIPMFSALS- EGA	HIV-1 infection	human(B27)	[Musey (1997)]
					<ul style="list-style-type: none"> • Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope
p24(30–37)	p24(162–170 LAI)	KAFSPEVI	HIV-1 infection	human(B*5703)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5703 epitope
p24(30–37)	p24(30–37)	KAFSPEVI	HIV-1 infection	human(B57)	[Goulder (2000c)]
					<ul style="list-style-type: none"> • Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11 • Improved stabilization of the B57-peptide complex was demonstrated by the 11 mer which fits the B57 binding motif, relative to the 8 mer, which does not • B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection
p24(30–39)	p24()	KAFSPEVIPMF	HIV-1 infection	human()	[Kaul (2001b)]
					<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized by 1/22 HEPS sex worker controls, ML1250
p24(30–40)	p24()	KAFSPEVIPMF	HIV-1 infection	human(B*57)	[Spiegel (1999)]
					<ul style="list-style-type: none"> • 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 III B Env, Gag, Pol, Nef, and CTLe were measured by ELISPOT • CTL against B*57-KAFSPEVIPMF was a de novo response observed in one of the children when viral load increased as a result of stopping therapy • 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
p24(30–40)	p24(162–172 LAI)	KAFSPEVIPMF	HIV-1 infection	human(B*5701)	[Goulder (1996b)]
					<ul style="list-style-type: none"> • This peptide was recognized by CTL from five slow progressors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations • This epitope is highly conserved

HIV CTL Epitopes

p24(30–40)	p24(162–172 LAI) • C. Brander notes this is a B*5701 epitope	KAFSPEVIPMF	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
p24(30–40)	p24(162–172 LAI) • C. Brander notes this is a B*5703 epitope	KAFSPEVIPMF	HIV-1 infection	human(B*5703)	[Brander & Goulder(2001)]
p24(30–40)	p24(30–40) • Two strong clonal CTL responses were generated in donor 026-BMC (HLA A3/-, B42/B57, Cw7/17) against different optimal versions of this epitope, one 8 amino acids long, one 11 • Improved stabilization of the B57-peptide complex was demonstrated by the 11mer which fits the B57 binding motif, relative to the 8 mer, which does not • B57 tolerates marked difference in optimal peptide length – and B57 is associated with non-progressive infection	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Goulder (2000c)]
p24(30–40)	p24(162–172) • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes • 1/11 of the A2+ individuals was HLA A*0201, A1, B57 and responded to four B57 epitopes and two others	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Betts (2000)]
p24(30–40)	p24() • The CTL-dominant response was focused on this epitope in an HIV+ Caucasian living in Boston – this epitope is not among the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Goulder (2000a)]
p24(30–40)	Gag() • Epitope name: KF11. Three CTL responses in patient PI004, to epitopes TSTLQEIQGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Goulder (2001b)]
p24(30–40)	p24(162–172) • Epitope name: KAF. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Oxenius (2000)]

p24(30–40)	p24()	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Kostense (2001)]
					<ul style="list-style-type: none"> • HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load • Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional • In 15 of the patients, the proportion of IFNγ producing tetramer cells correlated with AIDS-free survival
p24(30–40)	p24(162–172 SF2)	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Altfeld (2001c)]
					<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 2/2 group 3
p24(30–40)	p24(163–174)	KAFSPEVIPMF	HIV-1 infection	human(B57)	[Appay (2000)]
					<ul style="list-style-type: none"> • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T-cells specific for HIV and CMV • HIV-specific CD8+ T-cells expressed lower levels of perforin than CMV-specific CD8+ T-cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T-cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α
p24(30–40)	p24(153–164)	KAFSPEVIPMF	HIV-1 exposed seronegative, HIV-1 infection	human(B57,B58)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B57/B58 women, 4/6 HEPS and 12/17 HIV-1-infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 2 of the 4/6 HEPS cases and in 7 of the 12/17 HIV-1-infected women
p24(30–40)	p24(30–40)	KAFSPEVIPMF	HIV-1 infection	human(B58)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

HIV CTL Epitopes

p24(31–50)	p24(163–182)	AFSPEVIPMFSALSEG-ATPQ	HIV-1 infection	human()	[Lieberman (1995)]
					<ul style="list-style-type: none"> • HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide
p24(31–50)	p24(163–182 SF2)	AFSPEVIPMFSALSEG-ATPQ	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, B21
p24(31–50)	p24(163–182 SF2)	AFSPEVIPMFSALSEG-ATPQ	HIV-1 infection	human()	[Lieberman (1997b)]
					<ul style="list-style-type: none"> • CTL expanded <i>ex vivo</i> were later infused into HIV-1 infected patients
p24(31–50)	p24()	AFSPEVIPMFSALSEG-ATPQ	HIV-1 infection	human()	[Altfeld (2000)]
					<ul style="list-style-type: none"> • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual • The response to the peptide was CD4 dependent, but the HLA presenting molecule and optimal epitope were not determined
p24(35–43)	p24(167–175 LAI)	EVIPMFSAL		human(A*2601)	[Goulder (1996a)]
					<ul style="list-style-type: none"> • Identified as optimal epitope within Gag sequence AFSPEVIPMFSALSEGATPQ • Relatively conserved epitope within B clade and in other clades • Suspected binding motif for HLA-A26 includes T or V anchor at position 2, negative charge at position 1 • C. Brander notes that this is an A*2601 epitope in the 1999 database
p24(35–43)	p24(167–175 LAI)	EVIPMFSAL		human(A*2601)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes that this is an A*2601
p24(35–43)	p24(167–175)	EVIPMFSAL	HIV-1 infection	human(A26)	[Betts (2000)]
					<ul style="list-style-type: none"> • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ 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
p24(36–43)	p24(168–175 LAI)	VIPMFSAL		human(C*0102(Cw1))	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a C*0102(Cw1) epitope
p24(36–43)	p24(168–175 LAI)	VIPMFSAL		human(Cw*0102,Cw1)	[Goulder (1997b)]

p24(36–43)	p24(168–175)	VIPMFSAAL	HIV-1 infection	human(Cw01,02)	[Betts (2000)]
	<ul style="list-style-type: none"> • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ 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 				
p24(37–52)	Gag(169–184 LAI)	IPMFSAALSEGATPQDL	HIV-1 infection	human(B12)	[Buseyne (1993a)]
	<ul style="list-style-type: none"> • 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 EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag 				
p24(37–52)	p24(169–184 LAI)	IPMFSAALSEGATPQDL	HIV-1 infection	human(B12(44))	[Buseyne (1993b)]
	<ul style="list-style-type: none"> • Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people 				
p24(37–52)	p24(37–52)	IPMFSAALSEGATPDQL	HIV-1 infection	human(B44)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(41–60)	p24(173–192 SF2)	SALSEGATPQDLNTML- NTVG	HIV-1 infection	human()	[Lieberman (1997a)]
	<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • Three of these 12 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B7, B14; and HLA-A2, A3, B14, B44 				
p24(41–60)	p24(173–192 SF2)	SALSEGATPQDLNTML- NTVG	HIV-1 infection	human()	[Lieberman (1997b)]
	<ul style="list-style-type: none"> • CTL expanded <i>ex vivo</i> were later infused into HIV-1 infected patients 				
p24(41–60)	p24()	SALSEGATPQDLNTML- NTVG	HIV-1 infection	human()	[Altfeld (2000)]
	<ul style="list-style-type: none"> • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual • The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined 				
p24(41–60)	p24(179–188 clade A)	SALSEGATPQDLNMM- LNIVG	HIV-1 infection	human(B*8101)	[Dorrell (1999)]
	<ul style="list-style-type: none"> • CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa 				

HIV CTL Epitopes

- This CTL epitope is presented by B*8101 in one of the patients with an A subtype infection – B*8101 is a newly discovered HLA allele found in Africans, and the epitope has yet to be mapped precisely
- This epitope is distinct in subtype A relative to subtypes B, C, and D which share the dominant sequence: SALSEGATPQDLNTML-NTVG

p24(41–62)	p24(173–194 BH10)	SALSEGATPQDLNTML-NTVGGH	HIV-1 infection	human(B14)	[Johnson (1991)]
			<ul style="list-style-type: none"> • Gag CTL response studied in three individuals 		
p24(43–52)	p24()	LSEGATPQDL	HIV-1 infection	human(B42,B44)	[Cao (2000)]
			<ul style="list-style-type: none"> • HIV-1 subtypes A and D dominate the Ugandan epidemic, and a vaccine trial using B clade antigen is underway – this study addresses relative levels of cross-reactive CTL responses in Ugandans to A, D, and B clade recombinant vaccinia viruses expressing Gag, Env, Pol, RT or Nef from HIV-1 clades A, B, and D • Proteins corresponding to the subtype of the infecting strains tended to trigger higher levels of CTL response measured by percent specific lysis, but there was extensive inter-subtype cross-reactivity with B clade proteins and the co-circulating subtype • This optimal epitope sequence, recognized by CTL derived from a Ugandan with an A subtype infection (patient SP 511), is cross-reactive with subtypes A, B and D peptides 		
p24(44–52)	p24(176–184)	SEGATPQDL		human(B*4001)	[Brander & Goulder(2001)]
			<ul style="list-style-type: none"> • C. Brander notes this is a B*4001, B60 epitope (Pers. Comm. A. Trocha and S. Kalams) 		
p24(44–52)	p24()	SEGATPQDL	HIV-1 infection	human(B60(B*4001)	[Altfeld (2000)]
			<ul style="list-style-type: none"> • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes • B60 is present in 10-20% of the Caucasoid and very common in Asian populations 		
p24(44–52)	p24(44–52)	SEGATPQDL	HIV-1 infection	human(B60/B61)	[Day (2001)]
			<ul style="list-style-type: none"> • No immunodominant responses were detected to five B61-restricted epitopes tested • All five B60-restricted epitopes were reactive in another subject, the strongest CTL response directed against the B60-epitope p24 SEGATPQDL, and the B60-restricted responses together contributed over one-third of the total CTL response 		
p24(46–59)	p24()	GATPQDLNTMLNTV	HIV-1 infection	human()	[Goulder (2000a)]
			<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ African American living in Boston with HLA A*3002/68 B14/*5802 Cw6/8 – this epitope fell within the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 		

p24(47–55)	p24(47–55)	ATPQDLNTM	HIV-1 infection	human(B7)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(47–56)	p24()	ATPQDLNMML	HIV-1 exposed seronegative	human(B53)	[Kaul (2000)]
	<ul style="list-style-type: none"> • 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+ T-cell epitopes DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women 				
p24(47–58)	p24(181–192)	CTPYDINQMLNC	HIV-2 infection	human(B58)	[Bertoletti(1998)]
	<ul style="list-style-type: none"> • HIV-2 epitope defined from an infection in Gambia, Bertoletti, Pers. Comm. 				
p24(48–56)	Gag()	TPQDLNTML		human(A*4201,B*8101)	[Novitsky (2001)]
	<ul style="list-style-type: none"> • Epitope name: G180-TL9. This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 19/46 (41.3%) had CTL responses to one or more peptides within the first immunodominant region of Gag (peptides TL-NAWVKVIEEKAFSPEVIP, EKAFSPEVIPMFTALSEGAT, and MFTALSEGATPQDLNTMLNT), with magnitudes of response with ELISPOT results median and range 495 (103 to 1,447) SFC/10⁶ PBMC • 7/11 HLA-A*4201+ subjects (64%) responded to peptide MFTALSEGATPQDLNTMLNT • TPQDLNTML is an A*4201 epitope within TLNAWVKVIEEKAFSPEVIP 				
p24(48–56)	p24(180–188 IIIB)	TPQDLNTML	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*0702 epitope 				
p24(48–56)	p24(179–187 LAI)	TPQDLNTML		human(B*4201)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*4201 epitope 				
p24(48–56)	Gag(173–181 HIV-2)	TPYDINQML	HIV-2 infection	human(B*5301)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*5301 epitope 				
p24(48–56)	p24(180–188 LAI)	TPQDLNTML	HIV-1 infection	human(B*8101)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*8101 epitope 				
p24(48–56)	Gag(180–188 HXB2)	TPQDLNTML	HIV-1 infection	human(B*8101)	[Mulligan (2001)]
	<ul style="list-style-type: none"> • Epitope G18 from Patient 02110 with HLA genotypes A*3402, A*7401, B*5301, B*8101, Cw*0401, Cw*0802 				
p24(48–56)	p24()	TPQDLNTML	HIV-1 infection	human(B42)	[Goulder (2000a)]
	<ul style="list-style-type: none"> • B42 and B81 are very similar, and both can present this epitope to B42-positive effector cells – this epitope is almost certainly optimal for B81 as well – B42 and or B81 are expressed in 40-45% of Zulu and Xhosa infected individuals in South Africa, and in 14/18 B42 or B81+ individuals, the dominant gag response was to TPQDLNTML 				

HIV CTL Epitopes

- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNNTMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects.

p24(48–56)	Gag()	TPQDLNNTML	HIV-1 infection	human(B42)	[Goulder (2000b)]
					<ul style="list-style-type: none"> • Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection
p24(48–56)	p24()	TPQDLNQML		human(B53)	[Rowland-Jones (1999)]
					<ul style="list-style-type: none"> • 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, and the B35 allele seems to be protective • HIV-2 sequence: TPYDINQML, no cross-reactivity, [Gotch (1993)]
p24(48–56)	Gag(173–181 HIV-2)	TPYDINQML	HIV-2 infection	human(B53)	[Gotch (1993)]
p24(48–56)	Gag(180–188 subtype A)	TPQDLNMML	HIV-1 infection, <i>in vitro</i> stimulation	human(B53)	[Dorrell (2001)]
					<ul style="list-style-type: none"> • In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins
p24(48–56)	p24(180–188 subtype A consensus)	TPQDLNMML	HIV-1 infection	human(B53)	[Dorrell (2001)]
					<ul style="list-style-type: none"> • In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays • This optimal epitope was identified within the 20 mer reactive peptide that carried it by homology with a B53 epitope from HIV-2, a B subtype B7 peptide that corresponds to it, as B53 is part of the B7 superfamily, and by the proline in the anchor at position 2 • TPQDLNMML was recognized in 6/7 HLA-B53 subjects and was immunodominant in most subjects • TPQDLNMML was A subtype-specific with no cross-recognition of the subtype B, C, and D variant, TPQDLNNTML, although the B/C/D variant bound more efficiently to B53 • Position 7 showed great positional variation in crystal structures of two HLA-B53 complexes, suggesting variation here might significantly alter the position of the peptide in the binding groove and thus affect TCR interactions • Only one subject might have had a cross-reactive response with the HIV-2 and Mamu-A*01 variant CTPYDINQML, and this subject might have been dual infected with HIV-2

p24(48–56)	p24(180–188 IIIB)	TPQDLNTML	HIV-1 infection	human(B7)	[Wilson (1999a)]
					<ul style="list-style-type: none"> • 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 • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope
p24(48–56)	p24(180–188)	TPQDLNTML	HIV-1 infection	human(B7)	[Jin (2000b)]
					<ul style="list-style-type: none"> • This is the optimal epitope for the immunodominant response defined using a conventional approach 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 – this was followed by B7 anchor residue prediction which narrowed the set to 55 peptides, three of which could serve as functional CTL epitopes
p24(48–56)	p24()	TPQDLNTML	HIV-1 infection	human(B7)	[Goulder (2001b)]
					<ul style="list-style-type: none"> • Epitope name: TL9. Recognized by patient 9354 during chronic infection, used as a positive control in a study of the SLYNTVATL epitope
p24(48–56)	p24(48–56)	TPQDLNTML	HIV-1 infection	human(B7)	[Day (2001)]
					<ul style="list-style-type: none"> • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconverter homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconverter failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope
p24(48–56)	p24(180–188 LAI)	TPQDLNTML	HIV-1 infection	human(C*0802(Cw8))	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a C*0802(Cw8) epitope
p24(48–57)	Gag()	TPQDLNMLN		human(B7)	[De Groot (2001)]
					<ul style="list-style-type: none"> • The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • TPQDLNMLN was newly-defined as an HLA-B7 epitope in this study, although it was previously published as a B*8101 epitope • TPQDLNMLN was shown to stimulate an ELISPOT response, but could not be shown to bind to HLA-B7 • The variant TPQDLNTMLN was cross-reactive, had previously been identified as a HLA-B14 epitope, and could bind to HLA-B7

HIV CTL Epitopes

p24(49–57)	p24(181–189 LAI)	PQDLNTMLN	HIV-1 infection	human(B14, Cw8)	[Lubaki (1997)]
					<ul style="list-style-type: none"> • 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 • Despite this being a well defined conserved epitope, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 RAEQASQEV • Christian Brander notes that B14 and Cw8 are in linkage disequilibrium, and that this epitope may be Cw8
p24(51–59)	p24()	DLNTMLNTV	HIV-1 infection	chimpanzee()	[Santra (1999)]
					<ul style="list-style-type: none"> • 3/4 animals displayed HIV-1 Gag-specific CTL activity • Effector cells from two chimpanzees were able to recognize two epitopes also recognized by human HIV-1 Gag-specific CTL (SPRTLNAWV, HLA-B7, and DLNTMLNTV, HLA-B14) • No chimpanzee CTL were detected to the following human HIV-1 specific Gag epitopes, although they were embedded within 20mer peptides that contained a reactive epitope: ISPRTLNAW, HLA-B57; KRWILGLNK, HLA-B27; and DRFYKTLRA, HLA-B14
p24(51–59)	p24()	DLNMMLNIV	HIV-1 exposed seronegative	human(B14)	[Kaul (2000)]
					<ul style="list-style-type: none"> • 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+ T-cell epitopes DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women
p24(51–59)	p24()	DLNMMLNIV	HIV-1 infection	human(B14)	[Kaul (2001b)]
					<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML1792
p24(51–59)	p24(183–191 LAI)	DLNTMLNTV	HIV-1 infection	human(B14)	[Mollet (2000)]
					<ul style="list-style-type: none"> • Epitope name: G5. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change
p24(51–59)	p24(183–191)	DLNMMLNIV	HIV-1 exposed seronegative, HIV-1 infection	human(B14)	[Kaul (2001a)]

- Variants DLNMMLNIV/DLNTMLNVV are specific for clades A/B
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-B14 women, 4/4 HEPS and 3/7 HIV-1-infected women recognized this epitope, likelihood ratio 4.8, p value 0.1, and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA
- The dominant response to this HLA allele was to this epitope for all 4/4 HEPS cases and in only one of the 3/7 HIV-1-infected women
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort
- Four epitopes were considered to be “resistant epitopes”, as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILKD/EPVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLNM/TLNI/VV in p24 and B18 FRDYVDRFY/FK also in p24

p24(51–59)	p24(183–191 LAI)	DLNTMLNTV	HIV-1 infection	human(B14, Cw8)	[Johnson (1992), Nixon (1988)]
					<ul style="list-style-type: none"> • Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)
p24(51–59)	p24()	DLNTMLNTV	HIV-1 exposed seronegative	human(B14, Cw8)	[Rowland-Jones (1998a)]
					<ul style="list-style-type: none"> • 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 dLNmMLNiV • Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)
p24(51–59)	p24(183–191 LAI)	DLNTMLNTV	HIV-1 infection	human(C*0802)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a C*0802 epitope
p24(51–59)	p24(183–191 LAI)	DLNTMLNTV	HIV-1 infection	human(Cw8)	[McMichael & Walker(1994)]
					<ul style="list-style-type: none"> • Review of HIV CTL epitopes – defined by B14 motif found within a larger peptide • Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)

CTL

HIV CTL Epitopes

p24(51–59)	p24()	DLNTMLNTV	HIV-1 exposed seronegative	human(Cw8, B*1402)	[Rowland-Jones (1998b)]
					<ul style="list-style-type: none"> • 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, DLNNMLNIV, was preferentially recognized by CTL • Recent evidence indicates this is a Cw8 epitope; B14 and Cw8 are in linkage disequilibrium and the HLA presenting molecule is hard to distinguish (P. Goulder, personal communication)
p24(51–70)	p24(183–202 SF2)	DLNTMLNTVGGHQAA- MQMLK	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A26, A30, B38
p24(51–82)	Gag(183–214 LAI)	DLNTMLNTVGGHQAA- MQMLKETINEEAAEWD- R	Vaccine	human()	[Gahery-Segard (2000)]
					<p>Vaccine: <i>Vector/type:</i> lipopeptide <i>HIV component:</i> six peptides</p> <ul style="list-style-type: none"> • 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 – 2/10 reacted to this 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
p24(61–69)	p24(193–201 LAI)	GHQAAMQML		human(B*3901)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*3901 epitope
p24(61–69)	p24(193–201 LAI)	GHQAAMQML		human(B39)	[Kurane & West(1998)]
					<ul style="list-style-type: none"> • Optimal peptide defined by titration
p24(61–71)	p24(193–203 BRU)	GHQAAMQMLKE	HIV-1 infection	human(A2)	[Claverie (1988)]
					<ul style="list-style-type: none"> • One of four epitopes first predicted, then shown to stimulate HLA-A2 restricted CTL line

p24(61–80)	p24(193–212 SF2)	GHQAAMQMKETINEE- AAEW	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A26, A30, B38
p24(61–82)	p24(193–214 BH10)	GHQAAMQMLKETINE- EAAEWDR	HIV-1 infection	human(Bw52)	[Johnson (1991)]
					<ul style="list-style-type: none"> • Gag CTL response studied in three individuals
p24(62–70)	p24(194–202 LAI)	HQAAMQMLK		human(B52)	[Brander & Walker(1996)]
					<ul style="list-style-type: none"> • P. Goulder, pers. comm.
p24(65–73)	p24(199–207 SF2)	AMQMLKETI	Vaccine	murine(H-2K ^d)	[Doe & Walker(1997)]
					<p>Vaccine: <i>Vector/type:</i> vaccinia <i>HIV component:</i> Gag, Pol</p> <ul style="list-style-type: none"> • Immunodominant murine CTL response to this peptide observed after immunization with vaccine VVgagpol • Optimal peptide was defined
p24(65–73)	Gag(197–205)	AMQMLKETI	Vaccine	murine(H-2K ^d)	[Rayevskaya & Frankel(2001)]
					<p>Vaccine: <i>Vector/type:</i> Listeria monocytogenes <i>HIV component:</i> gag</p> <ul style="list-style-type: none"> • BALB/c mice were immunized with a highly attenuated recombinant Listeria monocytogenes, Lmdaldat, that can grow only when supplemented with D-alanine, and that expresses HIV-1 HXB2 Gag • Parenteral immunization provided protection against systemic and mucosal challenges with a recombinant vaccinia virus expressing HIV-1 gag, and a long lasting memory CTL response against Gag in spleen, mesenteric lymph nodes, and Peyer’s patches directed against the gag protein • Oral immunization gave protection only against mucosal virus challenge and was associated with a transient CTL response in the three lymphoid tissues examined • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways
p24(65–73)	Gag(197–205 SF2)	AMQMLKETI	Vaccine	murine(H-2K ^d)	[Mata (1998)]
					<p>Vaccine: <i>Vector/type:</i> Listeria monocytogenes <i>Strain:</i> HXB2 <i>HIV component:</i> Gag</p> <ul style="list-style-type: none"> • BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways • This is the immunodominant CTL epitope in Gag in BALB/c mice

CTL

HIV CTL Epitopes

- AMQMLKETI does not contain established Kd anchoring residue in position 2, tyrosine or phenylalanine, thus deviating from the typical Kd anchoring motif – the lack of the aromatic anchor residue is compensated for by interaction of the glutamine at P3 with pocket D of Kd

p24(65–73)	Gag(199–207 HXB2)	AMQMLKETI	Vaccine	murine(H-2 ^d)	[Qiu (1999)]
Vaccine: <i>Vector/type:</i> DNA <i>Strain:</i> HXB2 <i>HIV component:</i> gag					
<ul style="list-style-type: none"> • Different expression vectors were tested to increase Gag expression in cell lines and create suitable vectors for DNA vaccines • Stable Gag expression was achieved in murine p815 cells, using a Gag gene that had mutated silent base positions that disrupt inhibitory RNA sequences which promote RNA degradation • Silent mutations were more effective than introduction of the D retrovirus cis-acting posttranscriptional control element (CTE) for enhancing Gag expression • The gag vector with silent mutations given as a vaccine to BALB/c mice gave CTL responses in splenic mononuclear cells, using peptide pulsed cells as targets 					
p24(65–73)	p24(199–207 SF2)	AMQMLKETI	Vaccine	murine(H-2 ^d)	[Neidleman (2000)]
Vaccine: <i>Vector/type:</i> protein, vaccinia <i>Strain:</i> SF2 <i>HIV component:</i> soluble Gag, or GagPol expressing vaccinia <i>Stimulatory Agents:</i> heat-labile enterotoxin (LT) from E. coli					
<ul style="list-style-type: none"> • Epitope name: p7g. Intranasal immunization of CB6F1 (H2bxd) mice with soluble gag p55 with LT ADP-ribosyltransferase mutants (LTK63 and LTK73) from Escherichia coli as adjuvants was tested • Intranasal and intramucosal immunization of p55 gag protein with LTK63 or LTK72 adjuvant induced a CTL response comparable to intramuscular immunization responses • Oral co-administration of LTR72, with residual ADP-ribosyltransferase activity, induced systemic CTL responses, but LTK63 with no ADP-ribosyltransferase activity did not 					
p24(69–86)	Gag(201–218 LAI)	LKETINEEAAEWDRVP- V	HIV-1 infection	human()	[Buseyne (1993a)]
<ul style="list-style-type: none"> • 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 EM28 (CDC P2A) had a CTL response to four epitopes in Gag 					
p24(70–78)	Gag(202–210 HXB2)	KETINEEAA	HIV-1 infection	human(B*4002)	[Mulligan (2001)]
<ul style="list-style-type: none"> • Epitope G20 from Patient 12129 with HLA genotypes A*0207, A*0217, B*0801, B*4002, Cw*0303, Cw*07(01, 06) 					
p24(71–80)	p24(203–212)	ETINEEAAEW	HIV-1 infection	human(A*2501)	[Klenerman (1996)]
<ul style="list-style-type: none"> • The epitope was defined through direct stimulation of PBMC with 20-mer peptides • This epitope is in a conserved region and is found in most B, D, and E subtype isolates • DTINEEAAEW is found in A and some D subtype sequences 					

p24(71–80)	p24(203–212) • C. Brander notes this is an A*2501 epitope	ETINEEAAEW	HIV-1 infection	human(A*2501)	[Brander & Goulder(2001)]
p24(71–80)	p24(203–212) • Conserved between B and D subtypes, variable in other clades; a consensus of clades A,C, F, G, and H and a peptide of HIV-2ROD over this region were not recognized by CTL recognizing the index peptide • C. Brander notes that this is an A*2501 epitope in the 1999 database	ETINEEAAEW	HIV-1 infection	human(A*2501)	[van Baalen (1996)]
p24(71–80)	p24() • 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, and the B35 allele seems to be protective • HIV-2 sequence: EIINEEAAEW, no cross-reactivity [van Baalen (1996)]	ETINEEAAEW		human(A25)	[Rowland-Jones (1999)]
p24(71–80)	p24(203–212 SF2) • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-A25+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/2 group 2, and 1/3 group 3	ETINEEAAEW	HIV-1 infection	human(A25)	[Altfeld (2001c)]
p24(71–80)	p24(203–212) • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B53 women, 0/2 HEPS and 7/9 HIV-1-infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in 4 of the 7/9 responsive HIV-1-infected women	DTINEEAAEW	HIV-1 exposed seronegative, HIV-1 infection	human(B53)	[Kaul (2001a)]
p24(71–80)	p24(203–212 subtype A consensus) • In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays	DTINEEAAEW	HIV-1 infection	human(B53)	[Dorrell (2001)]

CTL

HIV CTL Epitopes

- Two of the new epitopes lacked the predicted by P2 anchors, DTINEEAAEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35
- Two overlapping 20 mer peptides carry this complete epitope, but only one stimulates recognition, which could be due to different peptide processing
- DTINEEAAEW was recognized in only 2/7 HLA-B53 subjects
- DTINEEAAEW was not A subtype specific and there was cross-recognition although diminished, of the subtype B, C, and D variant, ETINEEAAEW
- In one of the two subjects there was cross-recognition of the HIV-2 version of the epitope, EIINEEAADW

p24(71–90)	p24(203–222 SF2)	ETINEEAAEWDRVHP- VVHAGP	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A2, B21
p24(78–86)	Gag(210–218 HXB2)	AEWDRVHPV	HIV-1 infection	human(B*4002)	[Mulligan (2001)]
					<ul style="list-style-type: none"> • Epitope G21,G22 from Patient 07118 with HLA genotypes A*0209, A*3201, B*4002, B*5301, Cw*0202, Cw*0401 • Epitope G21,G22 Patient 07118 has 4 more optimal peptides P55, PIQKETWETW with HLA A*3201; N10, KEKGGLEGL with HLA B*4002; G31, QASQEVKNW with HLA B*5301;G43, TERQANFL with HLA B*4002
p24(83–92)	p24(215–223 IIIB)	VHPVHAGPIA	HIV-1 infection	human(B55)	[Sipsas (1997)]
					<ul style="list-style-type: none"> • HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • LHPVHAGPVA, a variant found in HIV-1 PH136, was also recognized • LHPVHAGPIA, a variant found in HIV-1 RF, was also recognized • LHPVHAGPIT, a variant found in HIV-1 MN, was also recognized • LHPAQAGPIA, a variant found in HIV-1 JH3, was recognized at high peptide concentrations
p24(87–101)	Gag(219–233 LAI)	HAGPIAPGQMREPRG	HIV-1 infection	human()	[Buseyne (1993a)]
					<ul style="list-style-type: none"> • 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 EM28 (CDC P2A) had a CTL response to four epitopes in Gag
p24(87–101)	p24(219–233 BRU)	HAGPIAPGQMREPRG	HIV-1 infection	human(A2)	[Claverie (1988)]
					<ul style="list-style-type: none"> • One of four epitopes predicted then shown to stimulate HLA-A2 restricted CTL line
p24(91–110)	p24(223–242 SF2)	IAPGQMREPRGSDIAG- TTST	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein

- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag
- One of these 12 had CTL response to this peptide
- The responding subject was HLA-A2, A24, B13, B35

p24(101–120)	p24(233–252 SF2)	GSDIAGTTSTLQEQIG- WMTN	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A26, A30, B38
p24(107–114)	Gag(239–247 SF2)	TTSTLQEQI	Vaccine	murine(H-2K ^d)	[Mata (1998)]
	<i>Vaccine:</i>	<i>Vector/type:</i> Listeria monocytogenes	<i>Strain:</i> HXB2	<i>HIV component:</i> Gag	
					<ul style="list-style-type: none"> • BALB/c mice were immunized with recombinant Listeria monocytogenes (Lm-Gag) expressing HIV-1 HXB2 Gag • L. monocytogenes is a gram-positive bacteria that enters the macrophage on phagocytosis and lives in the cytoplasm – secreted L. monocytogenes antigens are processed and presented by both class I and class II pathways
p24(108–117)	()	TSTLQRQIGW	HIV-1 infection	human()	[Kaul (2001b)]
					<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls (ML1250)
p24(108–117)	p24(240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human(B*57,B*5801)	[Goulder (1996b)]
					<ul style="list-style-type: none"> • Response to this epitope was found in 4 slow progressing HLA-B*57 individuals, in 2 it was dominant or very strong • For one donor (from Zimbabwe) this was defined as the optimal peptide • This epitope can be presented in the context of the closely related HLA molecules B*5801 and B*57
p24(108–117)	p24(241–250 LAI)	TSTVEEQIWF	HIV-2 infection	human(B*5801)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5801 epitope
p24(108–117)	P24(240–249 LAI)	TSTLQEQIGW	HIV-1 infection	human(B*5801)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5801 epitope
p24(108–117)	p24(233–252)	TSTLQEQIGW	HIV-1 infection	human(B57)	[Bernard (1998)]
					<ul style="list-style-type: none"> • This study focuses on six rare HIV-infected long-term survivors who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population

HIV CTL Epitopes

- No direct CTL were found in any of the six INHIs, but above background CTL_p activity was founded in 3/6 INHIs
- Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XSXXXXXXXXW is a B57 binding motif, and CTL activity against TSTLQEQIGW has been found in two other B57 long-term non-progressors

p24(108–117)	Gag()	TSTLQEQIGW	HIV-1 infection	human(B57)	[Goulder (2001b)]
					<ul style="list-style-type: none"> • Epitope name: TW10. Dominant epitope in acute infection in patient PI004, who did not receive any antiviral therapy • 1-2 months post seroconversion, subject PI004 displayed a significant decrease in TW10 peptide recognition, followed by an increased CTL response against epitope SL9, SLYNTVATL and other epitopes • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond
p24(108–117)	p24(108–117)	TSTLQEQIGW	HIV-1 infection	human(B57)	[Oxenius (2000)]
					<ul style="list-style-type: none"> • Epitope name: TST. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B57+
p24(108–117)	p24(108–117)	TSTLQEQIGW	HIV-1 infection	human(B57)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(108–117)	p24(235–243)	TSTLQEQIGW	HIV-1 exposed seronegative, HIV-1 infection	human(B57,B58)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • TSTLQEQIGW cross reacts with both for the A and B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
p24(108–117)	p24(241–250)	TSTVEEQIQW	HIV-2 infection	human(B58)	[Bertoletti(1998)]
					<ul style="list-style-type: none"> • HIV-2 epitope defined from an infection in Gambia, Bertoletti, Pers. Comm. • All HIV-2 sequences from the database are TSTVEEQIQW in this region, not TSTVEEQQW as in the paper
p24(108–117)	p24()	TSTLQEQIGW	HIV-1 exposed seronegative	human(B58)	[Rowland-Jones (1999)]
					<ul style="list-style-type: none"> • CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 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, and the B35 allele seems to be protective • HIV-2 sequence: TSTVEEQIQW, CTL are cross-reactive, [Bertoletti (1998)]

p24(108–117)	p24(240–249)	TSTLQEQIGW	HIV-2 infection	human(B58)	[Bertoletti (1998)]
					<ul style="list-style-type: none"> • CTL responses in HLA-B*5801 positive HIV-2 infected individuals have a dominant response to Gag and tolerate extensive substitution, thus HLA-B*5801+ individuals may have an enhanced potential for cross-protection between HIV-1 and HIV-2 • This can be an immunodominant epitope in HLA-B57 and B*5801 infected individuals, and is associated with long-term non-progression [Goulder (1996b)] • HIV-2 sequence: HIV-2 ROD has the epitope sequence TSTVEEQIQW, and the CTL from a person infected with HIV-2 was cross-reactive with HIV-1 epitopes • The epitope is TSTLQEQIGW in HIV-1 B clade, and TSTVEEQIQW in HIV-2 ROD • HLA B*5801 and B35 may preferentially select HIV-1 and HIV-2 cross-reactive epitopes
p24(108–117)	p24(240–249 SF2)	TSTLQEQIGW	HIV-1 infection	human(B58)	[Altfeld (2001c)]
					<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B58+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3
p24(108–117)	p24(108–117)	TSTLQEQIGW	HIV-1 infection	human(B58)	[Goulder (2001d)]
					<ul style="list-style-type: none"> • Epitope name: TW10. Responses to this dominant A3-restricted Gag epitope are present during the time of decreasing viral load in acute infection • Mutations in this epitope were observed in autologous clones of subjects who were B58-positive with a higher frequency than those who were B58-negative (P = 0.02) • These mutations are being sexually transmitted in adult infections
p24(108–118)	p24(240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5701 epitope
p24(109–117)	Gag(241–249 LAI)	STLQEQIGW	HIV-1 infection	human(B*5701 B*5801)	[Klein (1998)]
					<ul style="list-style-type: none"> • B57 has been associated with long-term non-progression in the Amsterdam cohort • The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag
p24(118–126)	Gag(282–290)	MTNNPIPV	HIV-1 infection	human(A2 supertype)	[Propato (2001)]
					<ul style="list-style-type: none"> • Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs

HIV CTL Epitopes

- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)

p24(121–135)	p24(253–267)	NPPIPVGEIYKRWII	HIV-1 infection	human(B8)	[Gotch (1990)]
					<ul style="list-style-type: none"> • High frequency of memory and effector Gag-specific CTL
p24(121–135)	p24(255–274 SF2)	NPPIPVGEIYKRWII	HIV-1 infection	human(B8)	[Goulder (1997a), Phillips (1991)]
					<ul style="list-style-type: none"> • Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time • [Goulder (1997a)] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients
p24(121–135)	p24(121–135)	NPPIPVGEIYKRWII	HIV-1 infection	human(B8)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(121–140)	p24(253–272)	NPPIPVGEIYKRWIILG-LNK	HIV-1 infection	human()	[Lieberman (1995)]
					<ul style="list-style-type: none"> • HIV-specific CTL lines developed by <i>ex vivo</i> stimulation with peptide
p24(121–140)	p24(253–272 SF2)	NPPIPVGEIYKRWIILG-LNK	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • Two of these 12 had CTL response to this peptide • The responding subjects were HLA-A2, A3, B8, B62, and HLA-A1, B8, B18
p24(121–140)	p24(253–272 SF2)	NPPIPGEIKRWIILGNIK	HIV-1 infection	human()	[Lieberman (1997b)]
					<ul style="list-style-type: none"> • CTL expanded <i>ex vivo</i> were later infused into HIV-1 infected patients
p24(121–140)	p24(255–274 SF2)	NPPIPVGEIYKRWIILG-LNK	HIV-1 infection	human()	[van Baalen (1993)]
					<ul style="list-style-type: none"> • Gag CTL epitope precursor frequencies were estimated and peptide mapping was performed
p24(121–142)	p24(253–274 BH10)	NPPIPVGEIYKRWIILG-LNKIV	HIV-1 infection	human(B8)	[Johnson (1991)]
					<ul style="list-style-type: none"> • Gag CTL response studied in three individuals

p24(121–152)	Gag(183–214 LAI)	NPPIPVGGEIYKRWILG- LNKIVRMYSPTSILD	Vaccine	human()	[Gahery-Segard (2000)]
<p>Vaccine: <i>Vector/type:</i> lipopeptide <i>HIV component:</i> six peptides</p> <ul style="list-style-type: none"> • 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 – 9/10 reacted to this 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 – this peptide was particularly immunogenic, eliciting a CTL response in four vaccinees • All of the 12 tested had an IgG response to this peptide 					
p24(121–152)	Gag()	NPPIPVGGEIYKRWILG- LNKIVRMYSPTSILD	HIV-1 infection, Vaccine	human(A*0201)	[Seth (2000)]
<p>Vaccine: <i>Vector/type:</i> lipopeptide <i>HIV component:</i> gag peptide</p> <ul style="list-style-type: none"> • Immunization of 2/4 HIV seropositive HLA selected individuals with a 32 amino acid Gag lipopeptide that contains CTL epitopes restricted by HLA A33, B8, B27, B35, and Bw62 gave a transient increase in peptide-specific bulk CTL response, but they did not decrease plasma viral • Placebo and HLA mis-matched controls showed no change in CTL • The responders carried HLA Bw62 and B35 – the two that did not respond carried B35 and B8 					
p24(122–130)	p24()	PPIPVGDIH	HIV-1 infection	human()	[Kaul (2001b)]
<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML887 					
p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	HIV-1 or HIV-2 infection	human(B*3501)	[Brander & Goulder(2001)]
<ul style="list-style-type: none"> • C. Brander notes this is a B*3501 epitope 					
p24(122–130)	p24(245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human(B*3501)	[Rowland-Jones (1995)]
p24(122–130)	p24(245–253 HIV-2)	NPVPVGNIY	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]
<ul style="list-style-type: none"> • C. Brander notes this is a B*3501 epitope 					
p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	HIV-1 or HIV-2 infection	human(B35)	[Rowland-Jones (1995)]
<ul style="list-style-type: none"> • Defined as minimal peptide by titration curve, PPIPVGGEIY and HIV-2 form NPVPVGNIY are also recognized 					

HIV CTL Epitopes

p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	<i>in vitro</i> stimulation	human(B35)	[Lalvani (1997)]
					<ul style="list-style-type: none"> • 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
p24(122–130)	p24(260–268 LAI)	PPIPVGDIY	HIV-1 infection	human(B35)	[McMichael & Walker(1994)]
					<ul style="list-style-type: none"> • Review of HIV CTL epitopes
p24(122–130)	p24()	PPIPVGDIY	HIV-1 exposed seronegative	human(B35)	[Rowland-Jones (1998b)]
					<ul style="list-style-type: none"> • 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, PPIPVGDIY, was preferentially recognized by CTL
p24(122–130)	()	PPIPVGDIY	HIV-1 infection	human(B35)	[Wilson (2000)]
					<ul style="list-style-type: none"> • 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 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 was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWILGGLNK • 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-PPIPVGDIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL
p24(122–130)	p24()	PPIPVGDIY		human(B35)	[Rowland-Jones (1999)]
					<ul style="list-style-type: none"> • 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, and the B35 allele seems to be protective

- HIV-2 version of this epitope is not conserved: NPVPVGNIY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]

p24(122–130)	p24(260–268)	PPIPVGDIY	HIV-1 infection	human(B35)	[Oxenius (2000)]
	<ul style="list-style-type: none"> • Epitope name: PPI. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • One of two HLA B35+ among the eight study subjects recognized this epitope • Patient SC15 (HLA A1/68, B8/35, Bw4/6, Cw4/0704) was given acute and sustained therapy and recognized epitopes PPIPVGDIY and VPLRPMTY during 331 days of HAART treatment 				
p24(122–130)	p24(122–130)	PPIPVGDIY	HIV-1 infection	human(B35)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(122–130)	p24(254–262 SF2)	PPIPVGDIY	HIV-1 infection	human(B35)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 0/2 group 2, and 1/1 group 3 				
p24(122–130)	p24(260–268)	PPIPVGDIY	HIV-1 exposed seronegative, HIV-1 infection	human(B35)	[Kaul (2001a)]
	<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B35 women, 1/3 HEPS and 3/4 HIV-1-infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in the 1/3 HEPS cases and in all the 3/4 responsive HIV-1-infected women • Subject ML 857 shifted from an A*6802 DTVLEDINL and B35 H/NPDIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion 				

HIV CTL Epitopes

p24(124–138)	p24(256–270 LAI)	IPVGEIYKRWIILGL	HIV-1 infection	human(B8)	[Buseyne (1993b)]
			<ul style="list-style-type: none"> • Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people 		
p24(124–138)	Gag(256–270 LAI)	IPVEGEIYKRWIILGL	HIV-1 infection	human(B8)	[Buseyne (1993a)]
			<ul style="list-style-type: none"> • 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 • Two children, EM16 (CDC P2A+D2) and EM18 (CDC P2A), had a CTL response to this epitope, and it was shown to be presented by B8 in EM18 		
p24(127–135)	p24(259–267 SF2)	GDIYKRWII	HIV-1 infection	human(B*0801)	[McAdam (1998)]
			<ul style="list-style-type: none"> • GDIYKRWII specific CTL clone also recognized GEIYKRWII 		
p24(127–135)	p24(261–269)	GEIYKRWII	HIV-1 infection	human(B8)	[Sutton (1993)]
			<ul style="list-style-type: none"> • Predicted epitope based on B8-binding motifs, from larger peptide NPIPVGGEIYKRWII 		
p24(127–135)	p24(259–267)	GEIYKRWII	<i>in vitro</i> stimulation	human(B8)	[Zarling (1999)]
			<ul style="list-style-type: none"> • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL 		
p24(127–135)	p24(259–267 LAI)	GEIYKRWII	HIV-1 infection	human(B8)	[Klenerman (1994)]
			<ul style="list-style-type: none"> • Naturally-occurring variant GDIYKRWII may act as antagonist 		
p24(127–135)	p24(259–267)	GEIYKRWII	HIV-1 infection	human(B8)	[Betts (2000)]
			<ul style="list-style-type: none"> • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ 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 		
p24(127–135)	p24(259–267)	GEIYKRWII	HIV-1 infection	human(B8)	[Nowak (1995)]
			<ul style="list-style-type: none"> • Longitudinal study of CTL response and study of immune escape – GDIYKRWII could also stimulate CTL, reactivity fluctuated 		
p24(127–135)	p24(259–267)	GEIYKRWII	HIV-1 infection	human(B8)	[McAdam (1995)]
			<ul style="list-style-type: none"> • Equivalent sequence GDIYKRWII also recognized by CTL from some donors 		

p24(127–135)	p24(259–267)	GEIYKRWII	HIV-1 infection	human(B8)	[Oxenius (2000)]
	<ul style="list-style-type: none"> • Epitope name: GEI. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Six of the 7/8 study subjects that were HLA B8 recognized this epitope • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responses against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones • Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDWYHTQGYFPDWQNY, and GEIYKRWII and all responses declined during therapy initiated at day 390 but were restored when therapy became intermittent • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKRWII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197 • Patient SC10(HLA A1/3, B8/35, DR1/8, DQ 4/5) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL and a response to GEIYKRWII through day 1088 • Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640, and had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy 				
p24(127–135)	p24(259–267 SF2)	GEIYKRWII	HIV-1 infection	human(B8)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 2/3 group 1, 2/3 group 2, and 2/2 group 3 				
p24(127–136)	Gag(259–268 HXB2)	GEIYKRWIIL	HIV-1 infection	human(B*0801)	[Mulligan (2001)]
	<ul style="list-style-type: none"> • Epitope G26 from Patient 07111 with HLA genotypes A*0101, A*0301, B*0801, B*5802, Cw*0602, Cw*07(01, 06) 				
p24(128–135)	p24(260–267 LAI)	EIYKRWII		human(B*0801)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*0801 epitope 				

HIV CTL Epitopes

p24(128–135)	p24(260–267 LAI)	EIYKRWII		human(B8)	[Goulder (1997g)]
	<ul style="list-style-type: none"> Defined in a study of the B8 binding motif 				
p24(128–135)	p24()	EIYKRWII	HIV-1 infection	human(B8)	[Goulder (2000a)]
	<ul style="list-style-type: none"> The CTL-dominant response was focused on this epitope in an HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 				
p24(128–135)	p24()	DIYKRWII	HIV-1 infection	human(B8)	[Goulder (2000a)]
	<ul style="list-style-type: none"> The CTL-dominant response was focused on this epitope in an HIV+ South African – this epitope did not fall within the five most recognized peptides in the study Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 				
p24(128–135)	p24()	EIYKRWII	HIV-1 infection	human(B8)	[Goulder (2001b)]
	<ul style="list-style-type: none"> Epitope name: EI8. This peptide elicited a weak CTL response during acute HIV-1 infection in patient PI004 Three CTL responses to epitopes, TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGGL were detectable at 5 months post-infection and beyond 				
p24(128–135)	p24()	EIYKRWII	HIV-1 infection	human(B8)	[Kostense (2001)]
	<ul style="list-style-type: none"> HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional In 15 of the patients, the proportion of IFNγ producing tetramer cells correlated with AIDS-free survival 4/13 patients that reacted with EIYKRWII displayed epitope mutations in a minority of sequences, which did not seem to influence disease progression or viral load – these mutations were: Patient 156 (KIYKRWMI), Patient 36 (EIYKRRII), Patient 656 (KIYKRWII, EIYERWMI), and Patient 159 (EIYKRWVI) Stimulation with HLA-B8 p24 and Nef epitopes significantly increased Nef-specific T-cell numbers in 2 patients (748 and 1113) There were more functional IFN-γ producing Nef-specific T-cells within the T-cell population than there were active p24 Gag-specific T-cells 				

p24(128–135)	p24(259–267)	DIYKRWII	HIV-1 infection	human(B8)	[Appay (2000)]
					<ul style="list-style-type: none"> • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T-cells specific for HIV and CMV • HIV-specific CD8+ T-cells expressed lower levels of perforin than CMV-specific CD8+ T-cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T-cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α
p24(128–135)	p24(128–135)	EIYKRWII	HIV-1 infection	human(B8)	[Day (2001)]
					<ul style="list-style-type: none"> • B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual
p24(128–135)	Gag()	EIYKRWII	HIV-1 infection	human(B8)	[Goulder (2000b)]
					<ul style="list-style-type: none"> • Tetramer assays were compared with three functional assays in 42 people with chronic HIV infection: ELISPOT, intracellular cytokine staining, and precursor frequency (limiting dilution assay [LDA]) • HIV-specific tetramer staining CTLs appeared to be active, and inert CTL were not found to play a significant role in chronic pediatric or adult HIV infection
p24(129–136)	p24(263–270 SF2)	IYKRWIIL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
					<ul style="list-style-type: none"> • 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 1/4 HIV-1+ people tested • IYKRWIIL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained
p24(129–138)	p24(263–272 SF2)	IYKRWIILGL	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1997)]
					<ul style="list-style-type: none"> • 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 1/4 HIV-1+ people tested • IYKRWIILGL bound to A*2402 with medium strength, the epitope can be processed in a vaccinia construct and presented – two specific CTL clones were obtained
p24(129–138)	p24(263–272)	IYKRWIILGL	HIV-1 infection	human(B27)	[Betts (2000)]
					<ul style="list-style-type: none"> • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes • 1/11 of the A2+ individuals was B27 and responded to IYKRWIILGL
p24(130–148)	p24(265–280 BRU)	YKRWIILGLNKIVRMY-SPT	HIV-1 infection	human(B27)	[Dadaglio (1991)]
					<ul style="list-style-type: none"> • Used as a positive control for HLA specificity

HIV CTL Epitopes

p24(131–139)	p24(263–272)	KRWIILGNK	HIV-1 infection	human(B27)	[Durali (1998)]
	<ul style="list-style-type: none"> • Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: KRWIILGNK 				
p24(131–139)	Gag(265–273)	KRWIILGLN	HIV-1 infection	chimpanzee(Patr-B*03)	[Balla-Jhagjhoorsingh (1999b)]
	<ul style="list-style-type: none"> • Certain HLA-alleles have been associated with long-term survival – among them are HLA-B*27 and HLA-B*57 • Of more than 150 chimpanzees that have been reported to be infected with HIV-1, only one has developed AIDS • CTL responses were studied in two HIV-1 infected chimpanzees that have strong CTL responses, and they responded to highly conserved epitopes that are recognized in humans in the context of HLA-B*27 and HLA-B*57 • The human HLA protein which presents this Patr-B*03 epitope is HLA B*2705, but the amino acid sequences in the binding pockets of HLA-B*2705 and Patr-B*03 are distinctive 				
p24(131–140)	Gag(263–272 LAI)	KRWILLGLNK	HIV-1 infection	human()	[Buseyne (1993a)]
	<ul style="list-style-type: none"> • 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 EM28 (CDC P2A) had a CTL response to four epitopes in Gag 				
p24(131–140)	p24(263–272)	KRWIILLGLNK	HIV-1 infection	human(B*27)	[Huang (2000)]
	<ul style="list-style-type: none"> • The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed • Increases in γ interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT • In 3/3 HLA A*02, B*27 individuals, the dominant response in gag measured by both γ IFN production and T-cell lysis was to the B27 epitope, KRWIILLGLNK, not the A2 SLYNTVATL epitope 				
p24(131–140)	p24(263–272 SF2)	KRWIILGLNK	HIV-1 infection	human(B*27)	[McAdam (1998)]
	<ul style="list-style-type: none"> • Epitope invariant across clades A, B, C, and D 				
p24(131–140)	p24(260–269 HIV-2)	RRWIQLGLQK		human(B*2703)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*2703 epitope 				

p24(131–140)	p24()	KRWIILGGLNK	HIV-1 infection	human(B*2705)	[Wilson (2000)]
	<ul style="list-style-type: none"> • 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 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 • Tetramers with peptide variants KRWIILGGLNK and KRWIIMGGLNK were used – CTL from most B27 donors recognize both variants, although one of the three subjects recognized only KRWIILGGLNK • ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was 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-PIIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL 				
p24(131–140)	p24(263–272 LAI)	KRWIILGGLNK	HIV-1 infection	human(B*2705)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*2705 epitope 				
p24(131–140)	p24(263–272)	KRWIILGGLNK	HIV-1 infection	human(B*2705)	[Kelleher (2001)]
	<ul style="list-style-type: none"> • A mutation in 4/5 B*2705 patients had substitution to lysine (K) at HIV-1 gag residue 264 (R264K), in three the change occurred late in infection – in one patient a substitution of glycine at HIV-1 gag residue 264 (R264G) was detected – these substitutions reduce binding to B27 • The R264K mutations were associated with an L268M mutation that may be compensatory, and R264G occurred in conjunction with E260D • Positions 260, 264, and 268 all lie along one aspect of helix seven of the capsid protein, a region that is important for capsid self-association and assembly • R264G and R264K escape mutation outgrowth occurred in conjunction with high viral loads 				
p24(131–140)	p24(263–272)	KRWIIMGLNK	HIV-1 infection	human(B*2705)	[Appay (2000)]
	<ul style="list-style-type: none"> • Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T-cells specific for HIV and CMV • HIV-specific CD8+ T-cells expressed lower levels of perforin than CMV-specific CD8+ T-cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation • In most donors, between 50% and 95% of the activated virus-specific CD8+ T-cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α 				
p24(131–140)	p24(263–272 LAI)	KRWIILGGLNK	HIV-1 infection	human(B*2705,B27)	[Goulder (1997c), Goulder (1997a)]

HIV CTL Epitopes

- HLA-B*2705 is associated with slow HIV disease progression
- 11/11 HLA-B*2705 donors make a response to this epitope, usually an immunodominant response
- This is a highly conserved epitope
- The HLA-B*2705 binding motif includes R at position 2, and L in the C-term position
- [Goulder (1997a)] is a review on CTL immune escape that discusses this epitope in the context of the difficulty in detection of immune escape – KRWIILGLNK and an R2K change, KKWIILGLNK, show little difference in titration curves, yet the K2 variants fail to bind to targets for more than 1 hour, while the R2 form can sensitize lysis by CTL for over 24 hours – minigene transfection experiments confirmed the importance of this for the CTL response

p24(131–140)	p24(260–269 HIV-2)	RRWIQLGLQK		human(B*2703)	[Brander & Walker(1996)]
					<ul style="list-style-type: none"> • HIV-2, HLA-B*2703, S. Rowland-Jones, Pers. Comm.
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[Fan (1997)]
					<ul style="list-style-type: none"> • The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied
p24(131–140)	Gag(263–272)	KRWIILGLNK	HIV-1 infection	human(B27)	[Zheng (1999)]
					<ul style="list-style-type: none"> • Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone • Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by a classical proteasome pathway • The CTL response to p24 was measured in individuals with a response to B27-KRWIILGLNK
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[Wilson (1998a)]
					<ul style="list-style-type: none"> • HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T-cells was followed <i>in vivo</i> • Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls • Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases
p24(131–140)	p24()	KRWIILGLNK	HIV-1 infection	human(B27)	[Rowland-Jones (1997)]
					<ul style="list-style-type: none"> • Described in this review as the first identified HIV CTL epitope
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[Buseyne (1993b)]
					<ul style="list-style-type: none"> • Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people
p24(131–140)	p24(263–272 LAI)	KRWIILGLNK	HIV-1 infection	human(B27)	[McMichael & Walker(1994)]
					<ul style="list-style-type: none"> • Review of HIV CTL epitopes

HIV CTL Epitopes

p24(131–140)	p24(263–272)	KRWIIMGLNK	HIV-1 infection	human(B27)	[Klenerman (1994), Klenerman (1995)]
					<ul style="list-style-type: none"> • Naturally-occurring variant KRWIILGLNK may act as antagonist
p24(131–140)	p24(265–274)	KRWIILGLNK	HIV-1 infection	human(B27)	[Moss (1995)]
					<ul style="list-style-type: none"> • In one individual, TCR usage changed over time indicating that new populations of CTL can be recruited • TCR usage showed a CTL clonal response to this epitope that persisted over 5 years • CTL clones specific for HIV epitopes may represent between 0.2 and 1% of the total CD8+ population of T-cells
p24(131–140)	p24(265–276)	KRWIILGLNK		human(B27)	[Carreno (1992)]
					<ul style="list-style-type: none"> • Included in HLA-B27 binding peptide competition study
p24(131–140)	p24(265–274 SF2)	KRWIILGLNK	HIV-1 infection	human(B27)	[Goulder (1997a), Phillips (1991)]
					<ul style="list-style-type: none"> • Longitudinal study of CTL escape mutants – little variation was observed in the immunodominant B27 epitope, relative to B8 epitope • [Goulder (1997a)] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients
p24(131–140)	p24(263–272)	KRWIILGLNK	HIV-1 infection	human(B27)	[Goulder (1997a), Nietfeld (1995)]
					<ul style="list-style-type: none"> • Single point mutations were introduced and viral viability and CTL recognition tested – an Arg to Lys change at anchor position P2 abrogates binding to B27, but doesn't change viral viability <i>in vitro</i> • [Goulder (1997a)] is a review of immune escape that summarizes this study
p24(131–140)	p24(263–272)	KRWIIMGNK	HIV-1 infection	human(B27)	[Nowak (1995)]
					<ul style="list-style-type: none"> • Longitudinal study of CTL response and immune escape – the form KRWIILGNK was also found, and both forms stimulate CTL
p24(131–140)	p24(263–272)	KRWIIMGLNK	HIV-1 infection	human(B27)	[Goulder (1997f), Goulder (1997a)]
					<ul style="list-style-type: none"> • Six HLA-B27 donors studied make a strong response to this epitope • In 4/6 cases, this was the immunodominant or only CTL response • Two of the cases had an epitope switch to the form KKWIIMGLNK during a period of rapid decline to AIDS, following their asymptomatic period • The arginine to lysine switch is in an anchor residue, and results in immune escape due to severely diminished binding to the B27 molecule • [Goulder (1997a)] is a review of immune escape that summarizes this study in the context of CTL escape to fixation
p24(131–140)	p24()	KRWIILGLNK		human(B27)	[Rowland-Jones (1999)]
					<ul style="list-style-type: none"> • CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 deletion in CCR5

CTL

HIV CTL Epitopes

- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective
- HIV-2 sequence: RRWIQLGLQK – this B27 epitope was not HIV-1 and HIV-2 cross-reactive

p24(131–140)	Gag()	KRWILGLNK	computer prediction	(B27)	[Schafer (1998)]
	<ul style="list-style-type: none"> • This study uses EpiMatrix for T-cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV • This peptide sequence is not conserved between clades, but is found in most B clade isolates 				
p24(131–140)	p24(263–282)	KRWIILGLNK	HIV-1 infection	human(B27)	[Bernard (1998)]
	<ul style="list-style-type: none"> • This study focuses on six HIV-infected long-term survivors who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs within the peptide – XRXXXXXXXXX is a B*2705 binding motif 				
p24(131–140)	p24(265–274 SF2)	KRWIILGLNK	HIV-1 infection	human(B27)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B27+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/1 group 3 				
p24(131–140)	p24(263–272)	KRWIILGLNK	HIV-1 exposed seronegative, HIV-1 infection	human(B27)	[Kaul (2001a)]
	<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Subject ML 1760 had an A2 response to ILK[D/E]PVHGV prior to seroconversion, and gained responses to epitopes A2 SL[F/Y]NTVATL and B27 KRWII[L/M]GLNK post-seroconversion 				

p24(131–140)	p24(131–140)	KRWIILGLNK	HIV-1 infection	human(B27)	[Day (2001)]
p24(131–140)	p24(260–299)	RRWIQLGLQK	HIV-1 infection	human(B27)	[Day (2001)]
p24(131–140)	p24(131–140)	KRWIILGLNK	HIV-1 infection	human(B27)	[Goulder (2001c)]
					<ul style="list-style-type: none"> • Epitope name: KK10. 85% of B27+ adults have CTL that recognize this epitope, but only 2/6 children did • Responses to this dominant B27-restricted Gag epitope are present during the time of decreasing viral load in acute infection • Three children who shared B27 with their mothers did not respond to this epitope and inherited escape mutations from their mothers • A transmitted R132T anchor residue mutation abrogated binding to B27 • In the three children infected with the non-binding KK10 variants, the dominant CTL specificity was still HLA-B27-restricted, but it was directed against an epitope in p17, IRLRPGGKK, only rarely recognized in adults when KRWIILGLNK is the dominant response • Mutations in this epitope were observed in autologous clones of subjects who were B27-positive with a higher frequency than those who were B27-negative (P = 0.0005) • These mutations are being sexually transmitted in adult infections
p24(131–142)	p24(265–276)	KRWIILGLNKIV	Peptide-HLA interaction	human(B27)	[Jardetzky (1991)]
					<ul style="list-style-type: none"> • Epitope examined in the context of peptide binding to HLA-B27
p24(131–142)	p24(263–274 LAI)	KRWIILGLNKIV	HIV-1 infection	human(B27)	[Fan (1997)]
					<ul style="list-style-type: none"> • The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied
p24(131–142)	p24(131–142)	KRWIILGLNKIV	HIV-1 infection	human(B27)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(131–145)	p24()	KRWIILGLNKIVRMY	HIV-1 infection	human()	[Goulder (2000a)]
					<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ African American living in Boston with unknown HLA – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa
p24(131–145)	p24(263–277 LAI)	KRWIILGLNKIVRMY	HIV-1 infection	human(A33)	[Buseyne (1993b)]
					<ul style="list-style-type: none"> • Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people
p24(131–145)	p24(266–277)	KRWIILGLNKIVRMY	Vaccine	human(B27)	[Nixon (1988)]
					<p>Vaccine: <i>Vector/type:</i> vaccinia <i>HIV component:</i> Gag</p>

HIV CTL Epitopes

- Gag CTL epitope mapped with rec gag-vaccinia and synthetic peptides
- This was the first HIV-1 epitope to be mapped

p24(131–145)	p24(266–277 LAI)	KRWIILGLNKIVMRY	HIV-1 infection	human(B27)	[Meyerhans (1991)]
					<ul style="list-style-type: none"> • Longitudinal study showing persistence of epitope despite CTL activity
p24(131–145)	p24(265–279)	KRWIILGLNKIVRMY	HIV-1 infection	human(B27)	[Nixon (1990), Rowland-Jones (1999)]
					<ul style="list-style-type: none"> • HIV-1 and HIV-2 cross-reactive CTL clone, highly conserved epitope • Reviewed in Rowland-Jones99, notes that it did not appear cross-reactive with HIV-2 in Rowland-Jones98, HIV-2 form: RRWIQL-GLQK
p24(131–146)	p24(265–279)	KRWIILGLNKIVRMYC	HIV-1 infection	human(B27)	[Bouillot (1989)]
					<ul style="list-style-type: none"> • HLA-B27 restricted epitope also binds to HLA-A2 and HLA-B37 in solid phase assay
p24(131–150)	p24(263–282 SF2)	KRWIILGLNKIVRMYS-PTSI	HIV-1 infection	human()	[Lieberman (1997a)]
					<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 A-2 had CTL response to this peptide • The responding subject was HLA-A3, A32, B51, B62
p24(131–150)	p24(265–284 SF2)	KRWIILGLNKIVRMYS-PTSI	HIV-1 infection	human(Bw62?)	[van Baalen (1993)]
					<ul style="list-style-type: none"> • Gag CTL epitope precursor frequencies estimated
p24(131–152)	p24(263–284 BH10)	KRWIILGLNKIVRMYS-PTSILD	HIV-1 infection	human(Bw62)	[Johnson (1991)]
					<ul style="list-style-type: none"> • Gag CTL response studied in three individuals
p24(132–145)	Gag()	KWILGLNKIVRMY	HIV-1 infection	human()	[Weekes (1999a)]
					<ul style="list-style-type: none"> • Peptide 728: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations
p24(132–145)	Gag()	KWILGLNKIVRMY	HIV-1 infection	human(B27)	[Weekes (1999b)]
					<ul style="list-style-type: none"> • Peptide 728: Almost all CD8+ T-cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones specific for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of TCR Vβ responses were studied and was found to be highly focused, with one TCR β-chain sequence tending to dominate the peptide-specific response – clones to this epitope were Vβ22.1

p24(134–143)	p24()	IILGLNKIVR	HIV-1 exposed seronegative	human(A33)	[Rowland-Jones (1998b)]
					<ul style="list-style-type: none"> • 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
p24(136–145)	p24(268–277 LAI)	LGLNKIVRMY	HIV-1 infection	human(Bw62)	[McMichael & Walker(1994)]
					<ul style="list-style-type: none"> • Predicted from larger peptide • Review of HIV CTL epitopes • Also P. Johnson, Pers. Comm.
p24(136–146)	p24(271–281)	LGLNKIVRMYS	HIV-1 infection	human(B62)	[Lubaki (1997)]
					<ul style="list-style-type: none"> • 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 • A subject who was B62+ had CTL that recognized this epitope, and p17 KIRLRPGGKKKYKL, and one additional unknown epitope • The two clones that recognized this epitope used two different Vβ genes, further demonstrating a polyclonal response
p24(136–146)	p24(136–146)	LGLNKIVRMYS	HIV-1 infection	human(B62)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(137–145)	p24()	GLNKIVRMY	HIV-1 infection	human()	[Goulder (2000a)]
					<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ South African living in Durban, HLA A2/- B5802/62 Cw4/6 – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa
p24(137–145)	p24(272–280 LAI)	GLNKIVRMY	HIV-1 infection	human(B*1501)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*1501 epitope
p24(137–145)	p24(272–280 LAI)	GLNKIVRMY	HIV-1 infection	human(B62)	[Goulder (1997a)]
					<ul style="list-style-type: none"> • This paper is a review of CTL and immune evasion, but it presents a study of a shift from an HLA-A*0201 response to SLYNTVATL, to a B62 response to GLNKIVRMY

HIV CTL Epitopes

- As long as a strong CTL response to SLYNTVATL was evident, the epitope variants SLFNTVATL or SLYNTIATL dominated the viral population – eventually the CTL response to the index peptide became undetectable, the CTL response shifted to a focus on GLNKIVRMY, and the index peptide SLYNTVATL once again established itself as the dominant form

p24(137–145)	p24()	GLNKIVRMY	HIV-1 infection	human(B62)	[Goulder (2000a)]
	<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ African American living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 				
p24(137–145)	p24(267–277 SF2)	GLNKIVRMY	HIV-1 infection	human(B62)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B62+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/1 group 2, and 1/1 group 3 				
p24(137–145)	p24(137–145)	GLNKIVRMY	HIV-1 infection	human(B62)	[Day (2001)]
	<ul style="list-style-type: none"> • No immunodominant responses were detected to four B62-restricted epitopes tested 				
p24(143–150)	p24(273–283 IIIB)	RMYSPTSI	HIV-1 infection	human(B*5201)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*5201 epitope 				
p24(143–150)	p24(273–283 IIIB)	RMYSPTSI	HIV-1 infection	human(B52)	[Brander (1999)]
	<ul style="list-style-type: none"> • Epitope name: SL9. Multiple natural variations in the SL9 flanking regions of the immunodominant epitope SLYNTVATL were tested and found not to adversely affect CTL recognition or prevent epitope processing, suggesting that viral escape from the HLA-A*0201-restricted CTL response against SLYNTVATL is probably not linked to variations in the flanking regions of this epitope • The CTL response to RMYSPTSI was used as a control 				
p24(143–150)	p24(273–283 IIIB)	RMYSPTSI	HIV-1 infection	human(B52)	[Wilson (1999a)]
	<ul style="list-style-type: none"> • 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 • No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope 				

p24(143–150)	p24(143–150)	RMYSPTSI	HIV-1 infection	human(B52)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(151–170)	p24(283–302 SF2)	LDIRQGPKEPFRDYVD- RFYK	HIV-1 infection	human()	[McAdam (1998)]
p24(155–177)	p24(287–309)	QGPKEPFRDYVDRFY- KTLRAEQA?	Vaccine	murine()	[Nakamura (1997)]
	<p>Vaccine: <i>Vector/type:</i> peptide <i>HIV component:</i> p24</p> <ul style="list-style-type: none"> • Mice immunized with this synthetic peptide generated specific CTLs, a proliferative response, and antibodies • The CTL epitope was shown to be located in positions 291-300 				
p24(157–178)	p24(290–309)	PKEPFRDYVDRFYKTL- RAEQAS	HIV-1 infection	human(B14)	[Musey (1997)]
	<ul style="list-style-type: none"> • Cervical and peripheral blood derived CTL clones from an HIV-infected woman recognized this epitope 				
p24(159–168)	Gag(291–300)	EPFRDYVDRF	Vaccine	murine(H-2 ^d)	[Billaut-Mulot (2001)]
	<p>Vaccine: <i>Vector/type:</i> DNA with DNA boost, DNA with recombinant protein boost <i>Strain:</i> LAI <i>HIV component:</i> Gag, Tat, Nef <i>Stimulatory Agents:</i> IL-18</p> <ul style="list-style-type: none"> • DNA vaccinated BALB/c mice primed and boosted with the multiepitopic vaccine with IL-18 showed lymphoproliferative responses 7 weeks post immunization • Strong but non-lasting HIV-specific CTL responses were detected by a Cr-release assay and DNA prime/DNA boost was more effective than DNA prime protein boost • Immunization with either the multiepitopic DNA or with the mixed DNA vaccine induced HIV-1 specific Th1 cytokines (IL-2 and IFN-γ) • Co-administration of IL-18 increased T-cell responses but decreased anti-HIV antibody levels 				
p24(159–178)	Gag()	EPFRDYVDRFFKTLRA- EQAT		human(B*44031)	[Novitsky (2001)]
	<ul style="list-style-type: none"> • This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • 16/46 (34.8%) had CTL responses to one or more peptides within the second immunodominant region of Gag (peptides SILDIKQGP-KEPFRDYVDRF, EPFRDYVDRFFKTLRAEQAT, and FKTLRAEQATQEVKNWMTDT) with ELISPOT results median and range 500 (100 to 1,250) SFC/10⁶ PBMC • 3/6 (50%) carriers of HLA-B*44031 showed CTL responses to the peptide EPFRDYVDRFFKTLRAEQAT 				

HIV CTL Epitopes

p24(161–170)	()	FRDYVDRFFK	HIV-1 infection	human()	[Kaul (2001b)]
					<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was recognized in 1/22 HEPS sex worker controls, ML1732
p24(161–170)	p24()	FRDYVDRFYK	HIV-1 infection	human(B*1801)	[Ogg (1998a)]
					<ul style="list-style-type: none"> • Noted in Brander 1999, this database, to be B*1801, FRDYVDRFY
p24(161–170)	p24()	FRDYVDRFYK	HIV-1 infection	human(B*1801)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*1801 epitope
p24(161–170)	p24(161–170)	FRDYVDRFYK	HIV-1 infection	human(B18)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(161–170)	p24(293–302)	FRDYVDRFYK	HIV-1 exposed seronegative, HIV-1 infection	human(B18)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • Variants FRDYVDRF(Y/F)K are specific for the B,D/A,C clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B18 women, 3/4 HEPS and 1/9 HIV-1-infected women recognized this epitope, likelihood ratio 5.3, p value 0.04, and HEPS women tended to respond to FRDYVDRFY/FK, while infected women tended to respond to YPLTFGWCY/F • The dominant response to this HLA allele was to this epitope for all 3/4 HEPS cases and for the single HIV-1 infected woman that responded to this epitope • Four epitopes were considered to be “resistant epitopes”, as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILKD/EPVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLNM/TLNI/VV in p24 and B18 FRDYVDRFY/FK also in p24 • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort
p24(161–180)	p24(293–312 SF2)	FRDYVDRFYKTLRAE- QASQD	HIV-1 infection	human()	[Lieberman (1997a)]

- Of 25 patients, most had CTL specific for more than one HIV-1 protein
- Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag
- One of these 12 had CTL response to this peptide
- The responding subject was HLA-A2, A3, B8, B62

p24(161–180)	p24(293–312 SF2)	FRDYVDRFYKTLRAE- QASQD	HIV-1 infection	human()	[Lieberman (1997b)]
					<ul style="list-style-type: none"> • CTL expanded <i>ex vivo</i> were later infused into HIV-1 infected patients
p24(161–180)	p24(293–312 SF2)	FRDYVDRFYKTLRAE- QASQD	HIV-1 infection	human(B71)	[McAdam (1998)]
p24(162–171)	p24(296–306)	RDYVDRFFKTL	HIV-1 exposed seronegative, HIV-1 infection	human(A24)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-A24 women, 0/4 HEPS and 6/10 HIV-1-infected women recognized this epitope, likelihood ratio 7.2, p value 0.03, and (R)YL(R/K)DQQLL tended to be reactive in HEPS and infected women, RDYVDRFFKTL in infected women only • The dominant response to this HLA allele was to this epitope in all of the 6/10 HIV-1-infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort • Subject ML 1707 started with a CTL response to A*6802 DTVLEDINL prior to seroconversion, and switched to A*6802 ETAYFILKL and A24 RDYVDRFFKTL post-seroconversion
p24(162–172)	p24(296–306 clade A)	RDYVDRFFKTL	HIV-1 infection	human(A*2402)	[Dorrell (1999)]
					<ul style="list-style-type: none"> • CTL responses in three individuals with non-clade B infections were studied, two with subtype A infections, one with subtype C – their infections all originated in East Africa • This epitope is similar to the A24 DYVDRYFKT epitope found for B subtype, but CTL from this A subtype infection required the additional Arg – the B clade sequence change from F to Y diminished CTL reactivity • C. Brander notes that this is an A*2402 epitope in the 1999 database
p24(162–172)	p24(296–306 clade A)	RDYVDRFFKTL	HIV-1 infection	human(A*2402)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is an A*2402 epitope

HIV CTL Epitopes

p24(162–172)	p24(293–312 LAI) • C. Brander notes this is a B*4402 epitope	RDYVDRFYKTL	HIV-1 infection	human(B*4402)	[Brander & Goulder(2001)]
p24(162–172)	p24(162–172) • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles	RDYVDRFYKTL	HIV-1 infection	human(B44)	[Ferrari (2000)]
p24(162–172)	p24(162–172)	RDYVDRFYKTL	HIV-1 infection	human(B44)	[Day (2001)]
p24(162–172)	p24(293–312 LAI)	RDYVDRFYKTL	HIV-1 infection	human(B44, A26 or B70)	[Ogg (1998a)]
p24(163–172)	p24(163–172) • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles	DYVDRFYKTL	HIV-1 infection	human(A24)	[Ferrari (2000)]
p24(164–172)	p24(298–306 clade A) • CTL responses in three individuals with non-clade B infections were studied, two with subtype A infections, one with subtype C – their infections all originated in East Africa • This CTL epitope is conserved in A and C subtype, and B clade sequences tend to have a change from F to Y, YVDRFYKTL – both variants showed strong CTL reactivity • CTL reacted with targets presenting either in the context A26 or B70 – the epitope has the HLA-26 motif of Val at position 2 and Leu at the carboxy terminus, and the B70 anchor residue motif is unknown	YVDRFFKTL	HIV-1 infection	human(A26 or B70)	[Dorrell (1999)]
p24(164–172)	Gag(298–306 subtype A) • In vitro restimulation of CTL specific for dominant epitopes from infected individuals is possible using recombinant modified vaccinia virus Ankara (MVA) carrying A or D subtype HIV-1 Gag proteins	YVDRFFKTL	HIV-1 infection, <i>in vitro</i> stimulation	human(A26 or B70)	[Dorrell (2001)]
p24(164–172)	Gag(296–304 96ZM651.8) • This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort • Four subjects responded to the CTL epitope YVDRFFKTL – all were HLA-B*1510 and also shared HLA-Cw03, suggesting linkage disequilibrium • An HIV-1 B variant of the epitope YVDRFYKTL has been described, and was recognized by CTL from an HIV-1 subtype A-infected patient, and the HLA restriction of the epitope was suggested to be A26 or B70 – HLA-B*1510 is equivalent to the serological specificity HLA B70	YVDRFFKRL		human(B*1510, B70)	[Novitsky (2001)]

p24(164–172)	p24(164–172)	YVDRFYKTL	HIV-1 infection	human(B70)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(166–174)	p24(298–306 LAI)	DRFYKTLRA	HIV-1 infection	human(B*1402)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is a B*1402 epitope 				
p24(166–174)	p24(298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human(B14)	[Wilson (1996)]
	<ul style="list-style-type: none"> • Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • DRFYKILRA, a naturally occurring variant, was found in the mother, and is recognized although less reactive • DQFYKTLRA, a naturally occurring variant, was found in the infant and is not recognized 				
p24(166–174)	p24(298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human(B14)	[Cao (1997)]
	<ul style="list-style-type: none"> • The consensus peptide for clades B and D is DRFYKTLRA • The consensus peptide for clades A and C is DRFFKTLRA and it is equally reactive 				
p24(166–174)	p24(298–306 HXB2)	DRFYKTLRA	HIV-1 infection	human(B14)	[Yang (1997b)]
	<ul style="list-style-type: none"> • A chimeric universal T-cell receptor was created by linking CD4 or an HIV-specific anti-gp41 Ig sequence to the signaling domain of the T-cell receptor chain ζ, and transducing into CD8+ cells • The response using universal-receptor-bearing CD8+ cells to lyse infected cells <i>in vitro</i> was comparable to the natural occurring responses of CTL-clones from HIV+ individuals in terms of kinetics and efficiency • A CTL clone specific for this epitope was used for the comparison 				
p24(166–174)	p24()	DRFWKTLRA	HIV-1 exposed seronegative	human(B14)	[Rowland-Jones (1998a)]
	<ul style="list-style-type: none"> • 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 drFfKtLRA 				
p24(166–174)	p24(298–306 LAI)	DRFYKTLRA	HIV-1 infection	human(B14)	[Harrer (1996b)]
p24(166–174)	p24(298–306)	DRFYKTLRA	HIV-1 infection	human(B14)	[Yang (1996)]
	<ul style="list-style-type: none"> • CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL • Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones • The distinction was thought to be due to lower expression of RT relative to Env and Gag • CTL can lyse infected cells early after infection, possibly prior to viral production 				
p24(166–174)	p24(298–306)	DRFYKTLRA	HIV-1 infection	human(B14)	[Yang (1997a)]
	<ul style="list-style-type: none"> • CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found <i>in vivo</i> 				

HIV CTL Epitopes

- CTL produced HIV-1-suppressive soluble factors – MIP-1 α , MIP-1 β , RANTES, after antigen-specific activation
- CTL suppress HIV replication more efficiently in HLA-matched cells

p24(166–174)	p24(298–306)	DRFYKTLRA	<i>in vitro</i> stimulation	human(B14)	[Zarling (1999)]
					<ul style="list-style-type: none"> • This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL
p24(166–174)	p24()	DRFYKLTRA		human(B14)	[Rowland-Jones (1999)]
					<ul style="list-style-type: none"> • CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 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, and the B35 allele seems to be protective • HIV-2 sequence: DRFYKSLRA is cross-reactive, [Harrer1993]
p24(166–174)	p24(298–306 IIIB)	DRFYKTLRA	HIV-1 infection	human(B14)	[Wilson (1999a)]
					<ul style="list-style-type: none"> • 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 • DRFYKILRA and DQFYKTLRA were escape mutants
p24(166–174)	p24()	DRFYKTLRA	HIV-1 infection	human(B14)	[Goulder (2000a)]
					<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in 2/5 HIV+ individuals who were HLA B14 living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa
p24(166–174)	p24()	DRFYKTLRA	HIV-1 infection	human(B14)	[Goulder (2001b)]
					<ul style="list-style-type: none"> • Epitope name: DA9. Data from patient AC13 suggest a role for this epitope in initial control of viremia in acute infection, as it is one of several subdominant CTL epitopes recognized during the initial decline in viremia • A CTL response to SL9, SLYNTVATL, was not evident until 18 months post-presentation

p24(166–174)	p24(166–174)	DRFYKTLRA	HIV-1 infection	human(B14)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(166–174)	p24(298–306 SF2)	DRFYKTLRA	HIV-1 infection	human(B14)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B14+ individuals that had a CTL response to this epitope broken down by group: 3/3 group 1, 1/2 group 2, and 0/0 group 3 				
p24(166–174)	p24(298–306)	DRFFKTLRA	HIV-1 exposed seronegative, HIV-1 infection	human(B14)	[Kaul (2001a)]
	<ul style="list-style-type: none"> • Variants DRF(F/W)KTLRA are specific for clades A/B • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B14 women, 0/4 HEPS and 6/7 HIV-1-infected women recognized this epitope, likelihood ratio 14.4, p value 0.004 and HEPS women tended to respond to DLNMMLNIV/DLNTMLNVV, while infected women tended to respond to DRF(F/W)KTLRA • The dominant response to this HLA allele was to this epitope for all of the 6/7 HIV-1-infected women • Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort 				
p24(166–174)	p24()	DRFYKTLRA	HIV-1 infection	human(B14)	[Altfeld (2000)]
	<ul style="list-style-type: none"> • This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual 				
p24(166–174)	p24()	DRFYKTLRA	HIV-1 exposed seronegative	human(B14, B*1402)	[Rowland-Jones (1998b)]
	<ul style="list-style-type: none"> • 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 				

HIV CTL Epitopes

- The clade A version of the epitope, DRFFKLTRA, was preferentially recognized by CTL
- This epitope was recognized by two different exposed and uninfected prostitutes

p24(166–175)	p24(298–306 HX10)	DRFYKTLRAE	HIV-1 infection	human(B14)	[Wagner (1999)]
					<ul style="list-style-type: none"> • The immunodominant CTL response in a long-term survivor was to this highly conserved and functionally relevant epitope • By testing mutations in an HXB2 background, it was found that all mutations within the epitope that abrogated CTL recognition also abolished viral infectivity • The epitope in this study overlaps the major homology region for which highly conserved residues exist in all known lenti- and onco-viruses and yeast transposons • Patient was part of the study in [Harrer (1996a)]
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 infection	human(Cw8)	[Lubaki (1997)]
					<ul style="list-style-type: none"> • 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 • Despite this being a well defined conserved epitope, and thought to be presented by B14, none of the 11 gag-specific clones from a B-14 positive subject could recognize either it or p24 PQDLNTMLN • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)
p24(173–181)	()	RAEQASQEV	HIV-1 infection	human()	[Kaul (2001b)]
					<ul style="list-style-type: none"> • This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative • The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire • This epitope was 1/22 HEPS sex worker controls ML1792
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 exposed seronegative, HIV-1 infection	human(B14)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 infection	human(B14?)	[Price (1995)]
					<ul style="list-style-type: none"> • Study of cytokines released by HIV-1 specific activated CTL • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)
p24(173–181)	p24(305–313)	RAEQASQEV	HIV-1 infection	human(Cw8)	[Johnson (1991)]
					<ul style="list-style-type: none"> • Originally reported as HLA-B14 restricted, but subsequently found not to be presented by cells transfected with B14

- Thought to be HLA-Cw8 restricted (C. Brander and B. Walker)

p24(173–181)	p24()	RAEQASQEV	HIV-1 exposed seronegative	human(Cw8)	[Rowland-Jones (1998a)]
					<ul style="list-style-type: none"> • 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 RAeQAtQEY • The D subtype consensus is RAEQsQdV • Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)
p24(174–184)	p24(306–316 LAI)	AEQASQDVKNW	HIV-1 infection	human(B44)	[Mollet (2000)]
					<ul style="list-style-type: none"> • Epitope name: G3. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change
p24(174–184)	p24(306–316 LAI)	AEQASQDVKNW		human(B*4402)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*4402 epitope
p24(174–184)	p24(306–316 LAI)	AEQASQDVKNW		human(B*4402,B44)	[Brander & Walker(1997)]
					<ul style="list-style-type: none"> • Pers. Comm. from D. Lewinsohn to C. Brander and B. Walker, C Brander <i>et al.</i>, this database, 1999
p24(174–184)	Gag(306–316)	AEQASQEVKNW	HIV-1 infection	human(B44)	[Brodie (1999)]
					<ul style="list-style-type: none"> • The ability of CTL effector cells was studied by expanding autologous HIV-1 Gag-specific CTL <i>in vitro</i>, and adoptively transferring them • The transferred CTLs migrated to the lymph nodes and transiently reduced circulating productively infected CD4+ T-cells, showing that CTL move to appropriate target sites and mediate anti-viral effects
p24(174–184)	p24(306–316)	AEQASQEVKNW	HIV-1 infection	human(B44)	[Brodie (2000)]
					<ul style="list-style-type: none"> • Study tracks and quantifies <i>in vivo</i> migration of neo-marked CD8+ HIV-specific CTL • Adoptively transferred gene-marked HIV-specific CTL homed to specific lymph node sites, co-localizing within the parafollicular regions of the lymph node adjacent to cells expressing HIV tat-fusion transcripts, indicative of viral replication • The CTL clones expressed CCR5 and localized among HIV-1 infected cells expressing MIP-1α and MIP-1β, CC-chemokines produced at sites of viral replication, suggesting a possible homing mechanism • This study provides a methodology for tracking and studying antigen specific CTL <i>in vivo</i>
p24(174–184)	p24(174–184)	AEQASQDVKNW	HIV-1 infection	human(B44)	[Day (2001)]
					<ul style="list-style-type: none"> • B44-restricted CTL response was strongest to this epitope in one individual

HIV CTL Epitopes

p24(175–186)	p24(307–318)	EQASQEVKNWMT	HIV-1 infection	human(B44)	[Quayle (1998)]
					<ul style="list-style-type: none"> • HIV is found in semen both as cell-associated and cell-free forms, and HIV-specific CTL could be found in the semen of 5/5 men with CD4 greater than 500 – 3 of the men were analyzed in detail and had broad CTL to Gag, Env, and Pol • Two CTL lines from one donor recognized this epitope • Isolation of CTLs specific to HIV in both male and female urinal tracts provide evidence that virus-specific lymphocytes come from the urogenital mucosa, and the authors speculate that CTL in mucosal tissues may be correlated with lower viral load in semen and reduced transmission
p24(176–184)	p24(308–316 LAI)	QASQEVKNW	HIV-1 infection	human(B*5301)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5301 epitope
p24(176–184)	Gag(308–316 HXB2)	QASQEVKNW	HIV-1 infection	human(B*5301)	[Mulligan (2001)]
					<ul style="list-style-type: none"> • Epitope G31 from Patient 07118 with HLA genotypes A*0209, A*3201, B*4002, B*5301, Cw*0202, Cw*0401 • Epitope G31 Patient 07118 has 4 more optimal peptides P55, PIQKETWETW with HLA A*3201; N10, KEKGGLEGL with HLA B*4002; G21 and G22, AEWDRVHPV with HLA B*4002;G43, TERQANFL with HLA B*4002
p24(176–184)	p24(309–317 LAI)	QASQEVKNW	HIV-1 infection	human(B*5701)	[Goulder (1996b)]
					<ul style="list-style-type: none"> • Recognition of this peptide by two long-term non-progressors • Peptide defined on the basis of B*5801 binding motif, yet not cross-restricted except at high concentrations • Described as B*5701 in C. Brander <i>et al.</i>, this database, 1999
p24(176–184)	p24(311–319 LAI)	QASQEVKNW	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*5701 epitope
p24(176–184)	p24(308–316 LAI)	QASQEVKNW	HIV-1 infection	human(B53)	[Buseyne (1997)]
					<ul style="list-style-type: none"> • Minimal sequence determined through epitope mapping • This is a relatively conserved epitope • HLA-Cw*0401 was defined as the restricting element, but cells that carry Cw*0401 varied in their ability to present this epitope – this could be the result of diminished cell-surface expression of Cw*0401 in some cells • The HLA presenting molecule for this epitope was originally described as Cw*0401, but subsequent experiments with an HLA B53+ C4- cell line and with C1R cells transfected with HLA-B53 have shown that the HLA restricting element is HLA-B53 (Pers. Comm., Dr. Florence Buseyne, 2000)
p24(176–184)	()	QASQEVKNW		(B53)	[Brander & Goulder(2001), Buseyne (1996), Buseyne (1997), Buseyne(1999)]
p24(176–184)	p24()	QASQEVKNW	<i>in vitro</i> stimulation	human(B53)	[Buseyne (2001)]
					<ul style="list-style-type: none"> • Epitope name: QW9. Exogenous presentation or cross-presentation of epitopes by antigen presenting cells (APC) without protein synthesis is an alternative pathway for CTL epitope processing that may be important in the initial generation of viral specific CTL

- Dendritic cells treated with AZT to inhibit protein synthesis were able to elicit a strong specific CTL response in QASQEVKNW specific CTL clone 141 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency
- Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion

p24(176–184)	p24(308–316)	QATQEVKNW	HIV-1 exposed seronegative, HIV-1 infection	human(B53)	[Kaul (2001a)]
			<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B53 women, 1/2 HEPS and 7/9 HIV-1-infected women recognized this epitope 		
p24(176–184)	p24(308–316 subtype A consensus)	QATQEVKNM	HIV-1 infection	human(B53)	[Dorrell (2001)]
			<ul style="list-style-type: none"> • In clade A infected Gambians, three HLA-B53 epitopes were defined in Gag p24 using ELISPOT, tetramer, and cytotoxicity assays • Two of the new epitopes lacked the predicted P2 anchors, DTINEEAIEW and QATQEVKNM, and bound to B53 with high affinity, thus extending the anchor residue motif for B53 and the related B35 • While S, T, and P could all fit into the HLA-B35 or HLA-B53 B pocket and form a hydrogen bond, A would not form a bond, so the authors propose compensatory interactions account for the high affinity of QATQEVKNM for B53 • QATQEVKNM was recognized in 6/7 HLA-B53 subjects • Cross-recognition of QATQEVKNM was not studied here, but it was noted that both the A, QATQEVKNM, and B, QASQDVKNW, subtype version of this epitope, are also presented by HLA-B57 and B58, common HLA alleles in Africans 		
p24(176–184)	Gag()	QASQEVKNW	HIV-1 infection	human(B57)	[Goulder (2001b)]
			<ul style="list-style-type: none"> • Epitope name: QW9. This peptide elicited a weak CTL response during acute infection of patient PI004 • Three CTL responses, to epitopes TSTLQEQIGW, ISPRTLNAW, and KAFSPEVIPMF, were evident early after infection; CTL responses to SLYNTVATL, QASQEVKNW, EIYKRWII, and FLKEKGGL were detectable at 5 months post-infection and beyond 		
p24(176–184)	()	QASQEVKNW		(Cw4)	[Brander & Goulder(2001), Buseyne (1997), Buseyne(1999)]

CTL

HIV CTL Epitopes

p24(176–184)	p24(176–184)	QASGEVKNW	HIV-1 exposed seronegative, HIV-1 infection	human(Cw4)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
p24(176–185)	p24(311–319 SF2)	QASKEVKNWV	HIV-1 infection	human(B57)	[Altfeld (2001c)]
					<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3
p24(177–185)	p24(177–185)	ATQEVKNWM	HIV-1 exposed seronegative, HIV-1 infection	human(B53)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • Variants A(T/S)QEVKNWM are specific for the A/B clades • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers • Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women • 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure • Among HLA-B53 women, 1/2 HEPS and 5/9 HIV-1-infected women recognized this epitope • The dominant response to this HLA allele was to this epitope in the 1/2 HEPS cases and in only one of the 5/9 HIV-1-infected women
p24(180–189)	p24(313–322)	EVKNWMTETL	HIV-1 exposed seronegative, HIV-1 infection	human(B53)	[Kaul (2001a)]
					<ul style="list-style-type: none"> • ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
p24(181–190)	p24(313–322 LAI)	VKNWMTETLL		human(B8)	[Brander & Walker(1996)]
					<ul style="list-style-type: none"> • P. Johnson, pers. comm.

p24(191–205)	p24(191–205)	VQNANPDCKTILKAL	HIV-1 infection	human(B51)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(191–205)	p24(323–337)	VQNANPDCKTILKAL	HIV-1 infection	human(B8)	[Nixon & McMichael(1991)]
	<ul style="list-style-type: none"> • Two CTL epitopes defined (see also p17(21-35)) 				
p24(191–205)	p24(325–339 SF2)	VQNANPDCKTILKAL	HIV-1 infection	human(B8)	[Goulder (1997a), Phillips (1991)]
	<ul style="list-style-type: none"> • Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to the B8 epitopes, which varied over time • [Goulder (1997a)] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients 				
p24(191–210)	p24(323–342 SF2)	VQNANPDCKTILKAL- GPAAT	HIV-1 infection	human()	[Lieberman (1997a)]
	<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • Three of these 12 had CTL response to this peptide • The responding subjects were HLA-A3, A24, B8, B55; HLA-A1, A11, B8, B27 				
p24(191–210)	p24(323–342 SF2)	VQNANPDCKTILKAL- GPAAT	HIV-1 infection	human()	[Lieberman (1997b)]
	<ul style="list-style-type: none"> • CTL expanded <i>ex vivo</i> were later infused into HIV-1 infected patients 				
p24(193–201)	Gag(327–335 SF2)	NANPDCKTI	HIV-1 infection	human(B*5101)	[Tomiyama (1999)]
	<ul style="list-style-type: none"> • HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995) • 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3% • Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed • Four of the six epitopes were highly conserved among B subtype sequences, NANPDCKTI is conserved 				
p24(193–201)	p24(325–333)	NANPDCKTI?	HIV-1 infection	human(B51)	[Betts (2000)]
	<ul style="list-style-type: none"> • Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes • 3/11 of the HLA A2+ individuals were HLA B51 and two of these responded to this epitope as well as to other epitopes 				
p24(193–201)	p24(324–335 IIIB)	NANPDCKTI	HIV-1 infection	human(B51)	[Wilson (1999a)]
	<ul style="list-style-type: none"> • This study describes maternal CTL responses in the context of mother-to-infant transmission 				

HIV CTL Epitopes

- 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
- No variants of this epitope were found in a non-transmitting mother that had a CTL response to this epitope

p24(193–201)	p24(323–333)	NANPDCKTI	HIV-1 infection	human(B51)	[Oxenius (2000)]
					<ul style="list-style-type: none"> • Epitope name: NAN. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • None of the 8 study subjects recognized this epitope but none were HLA B51+
p24(193–201)	p24(191–205)	NANPDCKTI	HIV-1 infection	human(B8)	[Ferrari (2000)]
					<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles
p24(195–202)	p24(323–342)	NPDKTIL	HIV-1 infection	human(B35)	[Bernard (1998)]
					<ul style="list-style-type: none"> • This study focuses on six rare HIV-infected long-term survivors who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population • No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs • Epitope sequences were deduced from larger reactive peptides based on HLA binding motifs – XPXXXXXL is a B35 binding motif
p24(197–205)	p24(329–337 LAI)	DCKTILKAL		human(B*0801)	[Brander & Goulder(2001)]
					<ul style="list-style-type: none"> • C. Brander notes this is a B*0801 epitope
p24(197–205)	p24(329–337 LAI)	DCKTILKAL		human(B8)	[Sutton (1993)]
					<ul style="list-style-type: none"> • Predicted epitope based on B8-binding motifs, from larger peptide VQNANPDCKTILKAL
p24(197–205)	p24(329–337)	DCKTILKAL	HIV-1 infection	human(B8)	[Nowak (1995)]
					<ul style="list-style-type: none"> • In a longitudinal study of CTL response and immune escape – the variant DCRTILKAL was also found, binds to B8, but is not recognized
p24(197–205)	p24(329–337)	DCKTILKAL		human(B8)	[McAdam (1995)]
					<ul style="list-style-type: none"> • Defined as minimal epitope by titration and binding studies
p24(197–205)	p24(197–205)	DCKTILKAL		human(B8)	[Goulder (1997g)]
					<ul style="list-style-type: none"> • Included in a study of the B8 binding motif
p24(197–205)	p24(329–337)	DCKTILKAL	HIV-1 infection	human(B8)	[Oxenius (2000)]

- Epitope name: DCK. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable
- This epitope was recognized at a low level by only 1 of the 7/8 study subjects that were HLA B8
- Patient SC12(HLA A1, B8/39, Cw0701/0702, DR2/3, DR51/52, DQ2/6) had sustained therapy started during acute infection and maintained an immunodominant response to FLKEKGGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy

p24(197–205)	p24(197–205)	DCKTILKAL	HIV-1 infection	human(B8)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(197–205)	p24(197–205)	DCKTILKAL	HIV-1 infection	human(B8)	[Day (2001)]
	<ul style="list-style-type: none"> • B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual 				
p24(211–230)	p24(345–364 SF2)	LEEMMTACQGVGGPG-HKARV	HIV-1 infection	human()	[van Baalen (1993)]
	<ul style="list-style-type: none"> • Gag CTL epitope precursor frequencies estimated, peptide mapping 				
p24(211–230)	p24(343–362 SF2)	LEEMMTACQGVGGPG-HKARV	HIV-1 infection	human(B7)	[McAdam (1998)]
p24(211–231)	p24(343–362 SF2)	LEEMMTACQGVGGPG-HKARVL	HIV-1 infection	human()	[Lieberman (1997a)]
	<ul style="list-style-type: none"> • Of 25 patients, most had CTL specific for more than one HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A2, B50, B57 				
p24(217–227)	p24(349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	<ul style="list-style-type: none"> • C. Brander notes this is an A*1101 epitope 				
p24(217–227)	p24(349–359 IIIB)	ACQGVGGPGHK	HIV-1 infection	human(A11)	[Sipsas (1997)]
	<ul style="list-style-type: none"> • HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB • ACQGVGGPSHK, a variant found in HIV RF, was also recognized 				
p24(217–227)	p24()	ACQGVGGPGHK	HIV-1 infection	human(A11)	[Goulder (2000a)]
	<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study 				

HIV CTL Epitopes

- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses
- Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa

p24(217–227)	p24(349–359)	ACQGVGGPGHK	HIV-1 infection	human(A11)	[Oxenius (2000)]
	<ul style="list-style-type: none"> • Epitope name: ACQ. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Both of the 2/8 HLA-A11 study subjects recognized this CTL epitope • Patient SC19(HLA A11/12, B8/44, Cw06/0701, DR3/7, DR52/53, DQ 2/8) had a CTL response to epitopes FLKEKGGL, GEIYKR-WII, ACQGVGGPGHK, AVDLSHFLK, and FNCGGEFFY that declined during therapy initiated at day 197 • Patient SC18(HLA A2/11, B8/44, Cw06/0701, DR3/7, DR52/53, DQ2) recognizes the epitopes ACQGVGGPGHK, QVPLRPMTYK, AVDLSHFLK, and one called QIY but not fully described – he had brief therapy upon seroconversion and has had low viral load during 600 days of follow up 				
p24(217–227)	p24(216–226)	ACQGVGGPGHK	HIV-1 infection	human(A11)	[Ferrari (2000)]
	<ul style="list-style-type: none"> • One of the 51 HIV-1 epitopes selected by Ferrari <i>et al.</i> as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles 				
p24(217–227)	p24(349–359 SF2)	ACQGVGGPGHK	HIV-1 infection	human(A11)	[Altfeld (2001c)]
	<ul style="list-style-type: none"> • Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 2/2 group 3 				
p24(221–231)	p24(353–363 LAI)	VGGPGHKARVL	HIV-1 infection	human(B7)	[Mollet (2000)]
	<ul style="list-style-type: none"> • Epitope name: G1. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses • In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished • Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change 				

p24(223–231)	p24(223–231 SF2)	GPGHKARVL	HIV-1 infection	human(B*0702)	[Altfeld (2001a)]
	<ul style="list-style-type: none"> • Epitope name: GL9. HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses is underestimated if accessory proteins are not included in the study • The response to GPGHKARVL was dominant 				
p24(223–231)	p24(355–363 LAI)	GPGHKARVL	HIV-1 infection	human(B7)	[Goulder (1997e), Goulder (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 a weak response • [Goulder (1997a)] is a review of immune escape that summarizes this study 				
p24(223–231)	p24()	GPSHKARVL	HIV-1 infection	human(B7)	[Goulder (2000a)]
	<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ Caucasian living in Boston – this epitope did not fall within the three most recognized peptides in the study • Three peptides GSEELRSYNTVATL (p17 residues 71-85), SALSEGATPQDLNMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLLK(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 				
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HIV CTL Epitopes

- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 1/4 group 1, 2/3 group 2, and 0/1 group 3

p24(223–231)	p24(223–231)	GPGHKARVL	HIV-1 infection	human(B7)	[Day (2001)]
	<ul style="list-style-type: none"> • The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person • Subjects with chronic HIV-1 infection recognized between 2-8 out of 11 B7-restricted epitopes • An acute seroconverter homozygous for the B7 allele recognized five B7-restricted epitopes • The other acute seroconverter failed to recognize any of the 11 B7-restricted epitopes tested • The B7-restricted CTL response was highly variable and there was no clearly dominant epitope 				
p24(223–232)	Gag()	GPGHKARVLA		human(B7)	[De Groot (2001)]
	<ul style="list-style-type: none"> • The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay • GPGHKARVLA was confirmed as an HLA-B7 epitope in this study, and had been previously published 				
p24()	p24()		HIV-1 infection	human()	[Goulder (2000a)]
	<ul style="list-style-type: none"> • The CTL-dominant response was focused on this epitope in an HIV+ South African – this epitope did not fall within the five most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLG(p17 16-30) contained the dominant Gag-specific epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-specific epitopes in 32 out of 37 C-clade infected subjects from South Africa 				