Part II-A: Table of CTL Epitopes

All CTL epitopes arranged by protein position

Table 1: **p17**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(11–19)	Gag(11–19 HXB2)	GELDRWEKI	HIV-1 infection	human(B*4002)	[Mulligan (2001)]
• Epitope G2 from Patient 12129 with HLA genotypes A*0207, A*0217, B*0801, B*4002, Cw*0303, Cw*07(01, 06)					
p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK		human(A*0301)	[Brander & Goulder(2001)]
• C. Brander notes that this is an A*0301 epitope					
p17(18–26)	p17(18–26 SF2)	KIRLRPGGK	HIV-1 infection	human(A*0301)	[Altfeld (2001a)]
• 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 seven proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study					
• The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK					
p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human(A3)	[Wilson (1996)]
• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study					
• KIRLRPGGR and RIRLRPGGR, naturally occurring variants, were found in the mother, and are escape mutants					
p17(18–26)	p17(18–26)	KIRLRPGGK	*in vitro* stimulation	human(A3)	[Zarling (1999)]
• 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					
p17(18–26)	Gag(18–26)	KIRLRPGGK	HIV-1 infection	human(A3)	[Brodie (1999)]
• CTL effector cells were studied by expanding autologous HIV-1 Gag-specific CTL *in vitro*, and adoptive transfer					
• 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					
p17(18–26)	(18–26)	KIRLRPGGK	HIV-1 infection	human(A3)	[Brodie (2000)]
• Study tracks and quantifies *in vivo* 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 *in vivo*

p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK	HIV-1 infection	SJL/J HLA transgenic mice(A3)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- KIRLRPGGR and RIRLRPGGR were escape mutants
- This epitope was recognized and many escape mutants were detected in an HLA A3 transmitting mother, and was recognized but invariant in an HLA A3 non-transmitting mother

p17(18–26)	p17(18–26 IIIB)	KIRLRPGGK	HIV-1 infection	human(A3)	[Goulder (1997e), Goulder (1997a)]

- Identical twin hemophiliac brothers were both infected with the same batch of factor VIII. One had a response to this epitope, the other did not. [Goulder (1997e)] is a review of immune escape that summarizes this study.

p17(18–26)	p17( )	KIRLRPGGK	HIV-1 exposed seronegative	human(A3)	[Kaul (2000)]

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses
- Low risk individuals did not have such CD8+ cells
- CD8+ 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

p17(18–26)	p17( )	KIRLRPGGK	HIV-1 infection	human(A3)	[Goulder (2000a)]

- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK (this tally comes from the tables, not the text of the paper)
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(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

p17(18–26)	p17( )	KIRLRPGGK	HIV-1 infection	human(A3)	[Seth (2001)]

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized

p17(18–26)	p17(18–26 SF2)	KIRLRPGGK	HIV-1 infection	human(A3)	[Altfeld (2001c)]

- 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 were 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-A3+ individuals that had a CTL response to this epitope broken down by group: 3/7 group 1, 0/4 group 2, and 2/2 group 3

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p17(18–26)	p17(18–26)	KIRLRPGGK	HIV-1 exposed seronegative, HIV-1 infection	human(A3)	[Kaul (2001a)]

- KIRLRPGGK is cross-reactive for A, B, and D 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

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p17(18–26)	p17( )	KIRLRPGGK	HIV-1 infection	human(A3)	[Severino (2000)]

- Primary HLA-A3+ CD4+ and HLA-mismatched lymphocytes from uninfected donors were infected with JRCSF after isolation then cocultured with the A3-restricted CTL clone 11504/A7 specific for KIRLRPGGK, and viral inhibition was MHC-restricted
- Primary monocytes and monocyte-derived DC were generated from the same donors, replication of HIV-1 in these cell types was less efficient than in lymphocytes and could also be inhibited by MHC-restricted CTL
- DC-lymphocyte cluster cultures allowed vigorous viral replication and MHC-restricted CTL viral inhibition was blunted or lost depending on the ratio of DC to CD4+ lymphocyte in the culture

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p17(18–26)	p17(18–26)	KIRLRPGGK	HIV-1 infection	human(A3)	[Day (2001)]

- 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
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant

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p17(18–26)	p17(18–26)	KIRLRPGGK	HIV-1 infection	human(A3)	[Ostrowski (2000)]

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T-cell help in 9/10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T-cell help to a variable degree in most of patients
- Those CTL that didn't respond to CD40LT could expand with IL-2 present, and IL-15 produced by dendritic cells also contributes
- The T-helper epitope used for CD4+ T-cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

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p17(18–26)	p17(18–26)	KIRLRPGGK	HIV-1 infection	human(A3, A3.1, B27)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

p17(18–26)	( )	KIRLRPGGK	HIV-1 infection	human(B*0301)	[Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

p17(18–27)	p17(18–27 LAI)	KIRLRPGGKK		human(B27)	[Brander & Walker(1996)]

- D. Lewinsohn, pers. comm.

p17(18–27)	p17(18–27)	KIRLRPGGKK	HIV-1 infection	human(B27)	[Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

p17(18–31)	p17(18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human(A3)	[Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

p17(18–31)	p17(18–31)	KIRLRPGGKKKYKL	HIV-1 infection	human(B62)	[Lubaki (1997)]

- Eighty-two HIV-1-specific CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of CTL 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 HLA-B62+ had CTL that recognized this peptide, and p24 LGLNKIVRMYS, and one additional unknown epitope

p17(18–42)	p17(18–42 IIIB)	KIRLRPGGKKKYKLK-HIVWASRELE	HIV-1 infection	human(A3)	[Jassoy (1992)]

- Epitope recognized by CTL clone derived from CSF

p17(18–42)	p17(18–42 PV22)	KIRLRPGGKKKYKLK-HIVWASRELE	HIV-1 infection	human(A3)	[Jassoy (1993)]
	• HIV-1 specific CTLs release γ-IFN, and α- and β-TNF				
p17(18–42)	p17(18–42 BH10)	KIRLRPGGKKKYKLK-HIVWASRELE	HIV-1 infection	human(Bw62)	[Johnson (1991)]
	• Gag CTL response was studied in three individuals				
p17(19–27)	p17(19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse(B*2705)	[Brander & Goulder(2001)]
	• Noted by Brander to be B*2705 (Pers. Comm. D. Lewinsohn)				
p17(19–27)	p17(19–27 LAI)	IRLRPGGKK		human(B27)	[Brander & Walker(1996)]
p17(19–27)	p17(19–27 JRCSF)	IRLRPGGKK	HIV-1 infection	scid-hu mouse(B27)	[McKinney (1999)]
	• Epitope-specific CTL were infused in infected human PBL-SCID mice, and transient decreases in viral load were observed, however virus was not eradicated and the HIV-specific CTL rapidly disappeared • No escape mutants were observed • Control CTL were long lived in both infected and uninfected mice, showing the rapid loss of CTL was due to target interaction				
p17(19–27)	p17( )	IRLRPGGKK	HIV-1 infection	human(B27)	[Goulder (2000a)]
	• WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 2/3 individuals that were B27+ had a dominant response to this epitope • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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				
p17(19–27)	p17(19–27)	IRLRPGGKK	HIV-1 infection	human(B27)	[Day (2001)]
p17(19–27)	p17(19–27)	IRLRPGGKK	HIV-1 infection	human(B27)	[Goulder (2001c)]
	• Epitope name: IK9. This B27 epitope is generally recognized only if there is escape in the B27 dominant epitope, p24 KRWIILGLNK				
p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human( )	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes • Three of the four individuals that responded to SLYNTVATL recognized HIV epitopes, and one individual who was A*0201, A31 and B51 and B58w4 recognized this epitope (previously described as HLA A3.1), as well as one other				

p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A*03)	[Goulder (1997e), Goulder (1997a)]

- Identical twin hemophiliac brothers were both infected with the same batch of factor VIII
- One had a response to gag A3 epitope RLRPGGKKK, the other non-responder carried the sequence RLRPGGKKC
- [Goulder (1997a)] is a review of immune escape that summarizes this study

p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]

- C. Brander notes that this is an A*0301

p17(20–28)	p17( )	RLRPGGKKK	HIV-1 infection	human(A*0301)	[Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
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- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

p17(20–28)	p17(20–28 SF2)	RLRPGGKKK	HIV-1 infection	human(A*0301)	[Altfeld (2001a)]

- 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 seven proteins, suggesting that the breadth of CTL responses are underestimated if accessory proteins are not included in the study
- The reactive peptide p17 gag WEKIRLRPGGKKKYK contained two A*0301-restricted epitopes, KIRLRPGGK and RLRPGGKKK A*0301

p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (2000c)]

- Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten
- A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC

p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (1997f)]

- A control CTL line that reacts with this peptide was included in the study

p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Cao (1997)]

- The consensus peptide of A, B, and D clade viruses is RLRPGGKKK
- The consensus peptide of C clade viruses is RLRPGGKKH and is equally reactive

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p17(20–28)	p17( )	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (2000a)]

- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – 7/10 that had a dominant response to this epitope were A3, and 5/7 targeted RLRPGGKKK while 2/7 targeted KIRLRPGGK (this tally comes from the tables, not the text of the paper which stated 6/7 RLRPGGKKK)
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPGGKKKYKLK(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

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p17(20–28)	p17(20–28 SF2)	RLRPGGKKK	HIV-1 infection	human(A3)	[Altfeld (2001c)]

- 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 were 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-A3+ individuals that had a CTL response to this epitope broken down by group: 5/7 group 1, 2/4 group 2, and 2/2 group 3

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p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Day (2001)]

- 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
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant

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p17(20–28)	p17(20–28)	RLRPGGKKK	HIV-1 infection	human(A3)	[Goulder (2001c)]

- Epitope name: RK9. 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 A3-positive with a higher frequency than those who were A3-negative (P = 0.0002)
- These mutations are being sexually transmitted in adult infections

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p17(20–29)	p17(20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(A3)	[Goulder (2000c)]
	• Two clonal CTL responses were generated in donor 021-BMC (HLA A3/3001, B42/-, Cw17/-) against different optimal versions of this epitope, one nine amino acids long, one ten • A previously described optimal A3 epitope overlapping this region, KIRLRPGGK, was not recognized by CTL from 021-BMC				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(A3.1)	[Brander & Walker(1995)]
	• Unpublished, C. Jassoy and Beatrice Culman, pers. comm.				
p17(20–29)	p17(20–29 LAI)	RLRPGGKKKY	HIV-1 infection	human(A3.1)	[Wilkens & Ruhl(1999)]
	• Pers. comm., B. Wilkens and D. Ruhl				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(A30, A3.1)	[Betts (2000)]
	• 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 A30, and one was A3, and both responded to RLRPGGKKKY • The A2+ A3 individual also reacted with two other A3.1 epitopes				
p17(20–29)	p17(20–29 IIIB)	RLRPGGKKKY	HIV-1 infection	human(B42)	[Wilson (1996)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study • RLRPGGKKRY, a naturally occurring variant, was found in non-transmitting mother and is recognized • Binds HLA-A3 and Bw62 as well				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(B42, Bw62)	[Ferrari (2000)]
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17(20–29)	p17(20–29)	RLRPGGKKKY	HIV-1 infection	human(B62)	[Brodie (2000)]
	• Study tracks and quantifies *in vivo* 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 *in vivo*				
p17(20–29)	p17(20–29 LAI)	RLRPGGKKKY		human(Bw62)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • Also P. Johnson, pers. comm.				

p17(20–30)	p17( )	RLRPGGKKKYK	HIV-1 infection	human( )	[Goulder (2000a)]

- WEKIRLRPGGKKKYKLK was the target of the dominant response in Caucasoids (38%) more frequently than non-Caucasoids (12%) – the dominant response in a Haitian immigrant living in Boston who was HLA A24/29 B7/B44 Cw6/7 was to this epitope, although the restricting element was not determined
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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
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p17(20–35)	p17(90–105 SF2)	CLRPGGKKKYKLKHIV	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 A-2, A-24, B-13, B-35

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p17(21–35)	Gag( )	LRPGGKKKYKLKHIV	HIV-1 infection	human( )	[Weekes (1999a)]

- Peptide 703.3: Memory CTL specific for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations

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p17(21–35)	p17(91–105 SF2)	LRPGGKKKYKLKHIV	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-A1, A2, B50, B57

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p17(21–35)	Gag( )	LRPGGKKKYKLKHIV	HIV-1 infection	human(A3)	[Weekes (1999b)]

- Peptide 703.3: 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 in the CD28 depleted cell population
- HIV CTL responses to 3 Env and 2 Gag peptides were studied
- The clonal composition of TCR Vβ responses was 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 Vβ13.1 and Vβ5.2

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p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV		human(B8)	[Nixon & McMichael(1991)]

- Two CTL epitopes defined (see also p24(191-205))

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p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV	HIV-1 infection	human(not B8)	[van Baalen (1996)]

- Unknown HLA specificity, but not B8

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p17(21–40)	p17(21–40 clade A)	LRPGGKKKYRLKHLV-WASRE	HIV-1 infection	human(Cw4)	[Dorrell (1999)]

- 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 was defined in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTL from this patient were not A-B cross-reactive

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p17(22–31)	Gag(22–31)	RPGGKKRYKL	HIV-1 infection	human(B7)	[Jin (2000b)]

- This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor
- A dominant B7 epitope was defined using conventional methods, and three additional sub-dominant HLA B7 epitopes were defined by first using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing

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p17(24–31)	p17(24–31)	GGKKKYKL		human(B8)	[Goulder (1997g)]

- The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation
- The predictions were experimentally confirmed
- The anchors for HLA-B8 epitopes, as defined by peptide elution data, are P3 (K), P5 (K/R), and P8 (L)
- Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe
- Small hydrophobic residues at P2 may be favorable for binding
- A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor

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p17(24–31)	p17(24–31 SF2)	GGKKKYKL	HIV-1 infection	human(B8)	[McAdam (1998)]

- CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope

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p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Reid (1996)]

- The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied
- Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined
- 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement
- 7Q and 7R alter the TCR exposed surface, and retain some recognition
- Reactivity of 5R depends on the T-cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound
- Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues

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p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Price (1997)]

- A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual
- Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present

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p17(24–31)	p17(24–31 SF2)	GGKKKYKL	HIV-1 infection	human(B8)	[Altfeld (2001c)]

- 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: 0/3 group 1, 1/3 group 2, and 2/2 group 3				
p17(24–31)	p17(24–31)	GGKKKYRL	HIV-1 exposed seronegative, HIV-1 infection	human(B8)	[Kaul (2001a)]
	• 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				
p17(24–31)	p17(24–31)	GGKKKYKL	HIV-1 infection	human(B8)	[Day (2001)]
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes epitope to be presented by B*0801				
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Sutton (1993)]
	• Exploration of HLA-B8 binding motif through peptide elution				
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Rowland-Jones (1993)]
	• Study of an individual with partially defective antigen processing				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1994)]
	• Naturally-occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1995)]
	• Naturally-occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Nowak (1995)]
	• Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Dyer (1999)]
	• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
p17(24–32)	p17( )	GGKKKYKLK		human(B8)	[Rowland-Jones (1999)]
	• 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: GGKKKYKMK – no cross-reactivity [Phillips (1991)]

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p17(24–33) p17(24–32) GGKKKKYKLK HIV-1 infection human(B8) [Oxenius (2000)]

- Epitope name: GGK. 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 by 1/7 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 FLKEKGGL throughout and minor responses to GEIYKRWII, DCKTILKAL, GGKKKYKLK – GEIYKRWII and GGKKKYKLK responses were stimulated by a brief period off therapy

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p17(24–33) p17( ) GGKKKKYKKL HIV-1 infection human(B8) [Seth (2001)]

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized

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p17(24–35) p17(25–35 SF2) GGKKKYKLKHIV HIV-1 infection human(B8) [Goulder (1997a), Phillips (1991)]

- 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

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p17(24–35) p17(25–35) GGKKKYKLKHIV HIV-1 infection human(B8) [Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

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p17(28–36) ( ) KYRLKHLVW HIV-1 infection human( ) [Kaul (2001b)]

- 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 (ML1573)

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p17(28–36) p17(28–36 LAI) KYKLKHIVW human(A*2402) [Brander & Goulder(2001)]

- Ikeda-Moore(1998) and D. Lewinsohn, pers. comm.
- C. Brander notes that this is an A*2402 epitope

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p17(28–36)	p17(28–36 SF2)	KYKLKHIVW	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1998)]

- Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+
- HLA A24 is very common in Japanese (70% carry it) and is common globally
- This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.

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p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A23)	[Goulder & Walker(1999)]

- P. Goulder, pers. comm.

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p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A24)	[Brander & Walker(1996)]

- D. Lewinsohn, pers. comm.

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p17(28–36)	p17(28–36 SF2)	KYKLKHIVW	HIV-1 infection	human(A24)	[Altfeld (2001c)]

- 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-A24+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 2/3 group 2, and 0/0 group 3

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p17(28–36)	p17(28–36 93TH253 CRF01)	KYKLKHIVW	HIV-1 infection	human(A24)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- The only HLA-A24 FSWs tested did not recognized the E clade version of this epitope KYKMKHLVW, which differs from the previously defined B clade version by two amino acids, KYKLKHIVW
- This epitope was only conserved in CRF01 (subtype E), and identities were rare

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p17(28–36)	p17(728–736 subtype A)	KYRLKHLVW	HIV-1 exposed seronegative, HIV-1 infection	human(Cw4)	[Kaul (2001a)]

- 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-Cw4 women, 2/2 HEPS and 7/11 HIV-1-infected women recognized this epitope
- The dominant response to this HLA allele was to this epitope in both of the 2/2 HEPS cases and in 3 of the 7/11 HIV-1-infected women

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p17(28–36) p17(28–36) KYRLKHLVW HIV-1 infection human(Cw4) [Appay (2000)]

- This epitope is newly-defined in this study
- 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

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p17(36–44) p17( ) WASRELERF HIV-1 infection human( ) [Goulder (2000a)]

- The dominant response in an African American who was HLA A3/33 B35/B53 Cw4/7 was to this epitope, although the restricting element was not determined – this epitope fell outside the most recognized peptides in the study
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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

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p17(36–44) p17(35–43 LAI) WASRELERF HIV-1 infection human(B*3501) [Goulder (1997d)]

- Optimal epitope defined from within p17(30-44), LKHIVWASRELERFA
- Dominant CTL response in an HIV+ asymptomatic donor was to this epitope
- The Phe in the C-term anchor is distinct from the previously-defined Tyr for B*3501 C-term anchors

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p17(36–44) p17(36–44 LAI) WASRELERF human(B*3501) [Brander & Goulder(2001), Goulder (1997b)]

- C. Brander notes this is a B*3501 epitope

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p17(36–44) p17(36–44) WASRELERF HIV-1 infection human(B35) [Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

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p17(36–44) p17(36–44) WASRELERF HIV-1 infection human(B35) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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p17(36–44)	p17(36–44 SF2)	WASRELERF	HIV-1 infection	human(B35)	[Altfeld (2001c)]

- 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

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p17(69–93)	p17(69–93 BH10)	QTGSEELRSLYNTVAT-LYCVHQRIE	HIV-1 infection	human(A2)	[Johnson (1991)]

- Gag CTL response studied in three individuals

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p17(71–79)	p17(71–79 LAI)	GSEELRSLY		human(A1)	[Brander & Walker(1996)]

- P. Goulder, pers. comm.

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p17(71–79)	p17(71–79)	GSEELRSLY	HIV-1 infection	human(A1)	[Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

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p17(71–79)	p17(71–79 HXB2)	GSEELRSLY	HIV-1 infection	human(A1)	[Oxenius (2000)]

- Epitope name: GSE. 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 not recognized by the 6/8 study subjects that were HLA-A1

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p17(71–79)	p17(71–79)	GSEELRSLY	HIV-1 exposed seronegative, HIV-1 infection	human(A1)	[Kaul (2001a)]

- 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-A1 women, 1/1 HEPS and 3/3 HIV-1-infected women recognized this epitope, and the response was the dominant HLA-A1 response in all cases

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p17(71–85)	p17(71–85 SF2)	GSEELRSLYNTVATL	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-A1, A11, B8, B27				
p17(74–82)	p17( )	ELRSLYNTV		human(B*0801)	[Brander & Goulder(2001)]
	• Noted by Brander to be a B*0801 epitope				
p17(74–82)	p17( )	ELRSLYNTV		human(B8)	[Goulder (1997g)]
	• Defined in a study of the B8 binding motif				
p17(74–82)	p17(74–82)	ELRSLYNTV	HIV-1 infection	human(B8)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(74–82)	p17(74–82)	ELRSLYNTV	HIV-1 infection	human(B8)	[Ferrari (2000)]
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17(74–82)	p17(74–82)	ELRSLYNTV	HIV-1 infection	human(B8)	[Day (2001)]
	• B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual				
p17(76–86)	p17(74–86 LAI)	RSLYNTVATLY		human(A*3002)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*3002 epitope				
p17(76–86)	p17( )	RSLYNTVATLY	HIV-1 infection	human(A*3002)	[Goulder (2000a)]
	• The CTL-dominant response was focused on this epitope in a single HIV+ individual from Boston – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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				
p17(76–86)	Gag(76–86 HXB2)	RSLTNTVATLY	HIV-1 infection	human(A*3002)	[Mulligan (2001)]
	• Epitope G8 from Patient 07107 with HLA genotypes A*3002, A*3201, B*4501, B*5301, Cw*0401, Cw*1202				

p17(76–86)	Gag( )	RLSYNTVATLY		human(A*3002)	[Novitsky (2001)]

- This study provides a survey of CTL responses and full length HIV-1 genome sequences from a C subtype infected Botswanan cohort
- Only 3/13 (23.1%) A*3002-positive subjects demonstrated moderate CTL responses to the peptide GTEELRSLYNTVATLYCVHE (residues 71 to 90), which contains the previously described A*3002 epitope RLSYNTVATLY

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p17(76–86)	p17(76–86)	RSLYNTVATLY	HIV-1 infection	human(A*3002)	[Goulder (2001a)]

- Epitope name: RY11 (p17). HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)
- HLA-A*3001-positive targets do not present RSLYNTVATLY

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p17(76–86)	p17(74–86 SF2)	RSLYNTVATLY	HIV-1 infection	human(A30)	[Altfeld (2001c)]

- 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-A30+ individuals that had a CTL response to this epitope broken down by group: 0/1 group 1, 0/0 group 2, and 1/1 group 3

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p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human( )	[Sewell (2000)]

- Review of the impact of CTL on viral immunity and escape that notes that SLYNTVATL-tetramer binding cells in individuals that react to this epitope inversely correlate with plasma viral load

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*02)	[Huang (2000)]

- 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 IFN producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT
- 4/8 A*02 subjects had a positive response to this epitope indicating that it is a major epitope for CD8+ γ IFN production
- 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 a B27 epitope, p24(263-272), not the A2 SLYNTVATL epitope

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*02)	[Rinaldo (2000)]

- Epitope name: SL9. 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

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A*02) [Scott-Algara (2001)]

- Epitope name: SL9. This study examined with CTL response in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV
- 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV)
- There were no differences observed in children that had therapy versus those that did not
- Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells

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p17(77–85) p17(77–85 HXB2) SLYNTVATL HIV-1 infection human(A*0201) [Brander (1999)]

- 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 substitution Y79F was an escape mutation in that it interfered with CTL recognition by one CTL clone from an A*0201 infected individual, clone 13010.B17, but it was still recognized by another CTL clone, 115.D4

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p17(77–85) Gag( ) SLYNTVATL HIV-1 infection human(A*0201) [Tan (1999)]

- Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninty five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- Individuals that did not respond to SLYNTVATL recognized other HIV epitopes, and 2/4 SLYNTVATL responders had stronger responses to epitopes restricted by other class I alleles
- SLYNTVATL was the only response detected in a one individual that was HLA A*0201, B44, B70

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Ogg (1999)]

- Epitope name: SL9. CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SLYNTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient
- Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy
- After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Altman (1996)]

- Epitope name: SL9. This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs – HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and can quantitate HIV-specific CD8+ cell lines in freshly isolated PBMCs

		• Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%)			
p17(77–85)	Gag( )	SLYNTVATL	HIV-1 infection	human(A*0201)	[Gray (1999)]
	• Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL				
p17(77–85)	p17(77–85 SF2)	SLYNTVATL	HIV-1 infection	human(A*0201)	[McAdam (1998)]
	• Epitope name: SL9. CTL from a patient infected with clade B virus did not recognize the clade A analog of this epitope				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Wilson (1998a)]
	• Epitope name: SL9. 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 *in vivo* • 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 • An A2-Gag specific line from one patient was found to be BV8, and at its highest level represented 17.5% of the patient's CD8+ T-cells				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Ogg (1998b)]
	• Epitope name: SL9. HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load • Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity • No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells				
p17(77–85)	p17(77–85)	SLYNTVATL	*in vitro* stimulation	human(A*0201)	[Walter (1997)]
	• Epitope name: SL9. HLA-A2 heavy chain and β2-microglobulin expressed in *E. coli* were refolded in the presence of this peptide • The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2 • Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens				
p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Lalvani (1997)]
	• Epitope name: SL9. 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 test peptides for optimizing the protocol				
p17(77–85)	p17(76–84)	SLYNTVATL	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]
	• Epitope name: SL9. Slow dissociation rate is associated with immunogenicity • CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual				

p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Goulder (1997e), Goulder (1997a)]

- Epitope name: SL9. Identical twin hemophiliac brothers were both infected with the same batch of factor VIII
- One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV
- Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL
- 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL
- Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL
- An additional subject went from SLYNTVATL responder to non-responder coincident with a switch to the variant SLFNTVATL
- [Goulder (1997a)] is a review of immune escape that summarizes this study

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p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Gray (1999)]

- Epitope name: SL9. Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T-cells
- 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL
- After HAART, the majority of the epitope-specific CTL were apparently memory cells

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p17(77–85)	p17(77–85 clade A)	SLFNTVATL	HIV-1 infection	human(A*0201)	[Dorrell (1999)]

- Epitope name: SL9. 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
- This epitope is most commonly SLYNTVATL in B subtype, and CTL from the C subtype infection did not recognize B clade gag or the 3Y form of the epitope, but do recognize the predominant A and C clade form, SLFNTVATL

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Brander (1998)]

- Epitope name: SL9. Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope
- Only one subject had CTL against all three epitopes
- There was significant heterogeneity in the CTL response to this immunodominant epitope
- The overall variation in this epitope among the 17 who had a CTL response and 11 non-HLA A*0201 HIV-1+ individuals was similar, suggesting a lack of immune pressure
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area

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p17(77–85) p17(77–85 HXB2) SLYNTVATL HIV-1 infection human(A*0201) [Hay (1999)]

- Epitope name: SL9. CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201
- The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted
- Despite the initial narrow response to two epitopes, no other CTL responses developed
- No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak
- A variant of this epitope was observed *in vivo* (`--F----V-`), but this mutation is recognized by SLYNTVATL-specific CTL, and in this case the patient's cells could present the peptide to SLYNTVATL-specific CTL

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Kalams (1999b)]

- Two patients were followed before and after HAART – reduced plasma HIV-1 RNA levels resulted in a decline in HIV-specific *in vivo*-activated CTL such that by day 260 CTL activities were undetectable
- ERYLKDQQL was the dominant response in one of the individuals, SLYNTVATL subdominant
- Sporadic breakthrough in viremia resulted in transient increases in CTLp
- Memory CTL frequency directed against Vac-Gag, Vac-RT, Vac-Env, and Vac-Nef initially increased with HAART and then decreased with the decline of the viral load

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p17(77–85) Gag(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Spiegel (2000)]

- High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T-cell mediated effector activity was not seen
- Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy

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p17(77–85) Gag(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Larsson (1999)]

- ELISPOT was used to assay the CD8 T-cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia vectors in 19 HIV+ people
- The highest CTL frequency was directed at Pol epitopes
- In A*0201 individuals, higher numbers of spot-forming T-cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A*0201) [Goulder (2000a)]

- The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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

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p17(77–85) p17(77–85 LAI) SLYNTVATL human(A*0201) [Brander & Goulder(2001)]

- C. Brander notes this is an A*0201 epitope

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p17(77–85) p17(77–85 SF2) SLYNTVATL HIV-1 infection human(A*0201) [Goulder (2001b)]

- Epitope name: SL9. This epitope is targeted by 75% of HLA-A*0201, HIV+ adults, and the magnitude of the response is inversely correlated with viral load
- CTL responses to SL9 and autologous SL9 variants were not detected in 11 HLA-A*0201 positive subjects during acute infection
- Longitudinal studies of two individuals (AC13 and PI004) showed that the initial control of viremia was independent of the SL9 CTL response
- Low Gag expression levels did not correlate with the delayed CTL response to this epitope
- Autologous SL9 variants SLYNTIAVL, SLYNTVAVL, SLFNTVATL, SLFNTVATL, and SLFNTVATL are each capable of inducing a range of CTL responses, sometimes strong, sometimes diminished, and sometimes complete escape relative to the wild type variant SLYNTVATL in patients with chronic HIV-1 infection – the ability to cross-react with a particular variant was patient dependent

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A*0201) [Altfeld (2001d)]

- Epitope name: p17 SL9. HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested
- Three additional previously described HLA-A2 epitopes were added to the set of 20, including p17 SL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acutely infected individuals recognized at least 1 (median of 1 and maximum of 2)
- p17 SL9 was recognized in 12/22 patients with chronic HIV-1 infection
- Only 1/13 patients with acute HIV-1 infection recognized p17 SL9

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p17(77–85) Gag( ) SLYNTVATL HIV-1 infection human(A*0201) [Goepfert (2000)]

- Epitope name: (SL9). This paper describes a comparison of results of different CTL assays, an SL9 tetramer assay and IFN-γ ELISPOT, using 7 HIV-positive patients
- The IFN-γ ELISPOT assay was compared using the single SL9, a pool of overlapping 20 mers, and recombinant vaccinia encoding Gag as antigen – pooled peptides gave the highest number of spot forming cells, vaccinia gave high background
- A correlation with results of the tetramer assay was found only for ELISPOT using the Gag epitope as antigen, but the tetramer assay detected a 10-fold higher number of cells than could produce IFN-γ in the ELISPOT assay – the authors suggest not all tetramer-positive cells may produce IFN-γ, some may be undergoing apoptosis, some may be producing other cytokines
- The tetramer assay could detect a reaction to SLYNTVATL in most of the HLA-A*0201 chronically HIV-1 infected study subjects

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p17(77–85)	Gag( )	SLYNTVATL	*in vitro* stimulation	human(A*0201)	[Engelmayer (2001)]

- Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors
- Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses

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p17(77–85)	p17(77–85 LAI)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Mollet (2000)]

- 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 tetramer staining or 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

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p17(77–85)	Gag( )	SLYNTVATL	HIV-1 infection	human(A*0201)	[Gea-Banacloche (2000)]

- In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found
- High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products
- 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patient 3 and 19) tested positive to this epitope

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p17(77–85)	p17(77–85 SF2)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Propato (2001)]

- 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
- Tetramer staining with A2, β2-microglobulin, and either SLYNTVATL, KLVGKLNWA, or LTFGWCFKL revealed that tetramers detected more HIV-specific cells in LTNP than in progressors, activated effector cells were the minority population, and ELISPOT correlated better with the effector cell subpopulation than the total tetramer stained population

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p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Jin (2000a)]

- The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay
- LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A*0201)	[Appay (2000)]

- 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

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A*0201) [Goulder (2000b)]

- 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

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A*0201) [Ostrowski (2000)]

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T-cell help in 9/10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T-cell help to a variable degree in most of patients
- Those CTL that didn't respond to CD40LT could expand with IL-2 present, and IL-15 produced by dendritic cells also contributes
- The T-helper epitope used for CD4+ T-cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

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p17(77–85) p17(77–85) SLYNTVATL human(A*0202) [Brander & Goulder(2001)]

- C. Brander notes that this epitope can be presented by A*0201 and A*0202

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A*0202) [Goulder (2000a)]

- The CTL-dominant response was focused on this epitope in 11/25 HLA A2 (A*0201 or A*0202) HIV+ individuals from Boston and in 1/8 HLA A2 HIV+ individuals from Durban
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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

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p17(77–85) p17(77–85 LAI) SLYNTVATL human(A*0205) [Brander & Goulder(2001)]

- C. Brander notes that this epitope can be presented by A*0201 and A*0202

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p17(77–85) p17( ) SLYNTVATL HIV-1 exposed seronegative human(A*0214, A*0201) [Kaul (2000)]

- 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-specific CD8 γ-IFN responses in the cervix – systemic CD8+ T-cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T-cell responses
- Low risk individuals did not have such CD8+ cells
- CD8+ 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
- The epitope variants SLYNTVATL and SLFNTVATL were both recognized

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p17(77–85) Gag(77–85) SLYNTVATL Vaccine human(A2) [Woodberry (1999)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested
- SLYNTVATL was recognized by 5/16 HLA-A2 patients

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p17(77–85) p17(77–85) SLYNTVATL Vaccine human(A2) [Carruth (1999)]

Vaccine: *Vector/type:* canarypox *Strain:* MN, LAI *HIV component:* gp120, gp41, Gag, Protease

- The vaccine used was a live recombinant canarypox (CP) virus vaccine containing multiple HIV-1 genes (HIV-1 MN gp120, HIV-1 LAI gp41, HIV-1 LAI Gag, HIV-1 LAI protease)
- CD4+ and CD8+ Gag and Env specific CTL responses were detected in only 1/5 vaccinated volunteers, and were not detectable 1 year after vaccination
- CTL responses to epitopes SLYNTVATL and TVYYGVPVWK from HIV+ control patients were used as positive controls
- The study explored why vaccinees were non-responsive – non-response was not due to inherent defects or differences in the ability of these individuals to process and present antigen
- Lack of response to SLYNTVATL led the authors to speculate that the immunodominance of this epitope in natural infections may not be recapitulated by vaccine antigen

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A2) [Birk (1998)]

- Epitope name: SL9. A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A2) [Callan (1998)]

- Epitope name: SL9. Included as a negative control in a tetramer study of A2-EBV CTL response

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A2) [Wagner (1998a)]

- Epitope name: SL9. CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules

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p17(77–85)	p17(77–85 HXB2)	SLYNTVATL	HIV-1 infection	human(A2)	[Collins (1998)]

- Epitope name: SL9. Two CTL clones recognize this epitope, but not the NL4-3 form of the epitope SLYNTIAVL
- Nef down-regulates MHC class I molecules, which inhibits CTL killing, and this down-regulation can be partially compensated for by adding excess soluble peptide

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Durali (1998)]

- Epitope name: SL9. Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia
- Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested
- Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag
- Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef
- Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env
- Patient B18 had the greatest breadth and diversity of response, and recognized Gag SLYNTVATL and Nef PLTFGWCFKL

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Kundu (1998b)]

- Epitope name: SL9. Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated
- SLYNTVATL is a conserved HLA-A2 epitope included in this study – 3/6 patients had this sequence as their HIV direct sequence, one had the form SLYNTVAVL and all four of these had a detectable CTL response – the other two had either the sequence SLFSAVAVL or SLFSAVAAL and no detectable CTL response

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p17(77–85)	p17(77–85 IIIB)	SLYNTVATL	HIV-1 infection	human(A2)	[Sipsas (1997)]

- Epitope name: SL9. HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB
- SLYNTVAVL, a variant found in HIV-1 MANC, was also recognized
- SLFNTVAVL, a variant found in HIV-1 NY5CG, was also recognized

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p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A2)	[Rowland-Jones (1998a)]

- Epitope name: SL9. 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 SLfNtvatL
- The D subtype consensus is SLyNTvATL

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p17(77–85)	p17( )	SLYNTVATL	HIV-1 infection	human(A2)	[Sewell (1997)]

- Epitope name: SL9. Naturally-occurring variants of this epitope escaped killing and acted as antagonists

- The following variants were found in HIV-1 infected patients who mounted a strong response against this epitope: `--F------`, `--F----V-`, `--S------`, `-SF------`, `--L------`, `-----I---`, `-----I-V-`, `--F--I---`, `--F--I-V-`, `--F-A----`
- All variants bound to A2 with at least half the affinity of SLYNTVATL except the triple mutant: `--F--I-V-`
- Antagonism could be observed at low concentrations, abrogating lysis at an antagonist:agonist ratio of 1:10 – the antagonism was observed in one SLYNTVATL-specific CTL line but not another

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p17(77–85)	p17(77–85 HXB2)	SLYNTVATL	HIV-1 infection	human(A2)	[Yang (1997b)]

- Epitope name: SL9. 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 transduced into CD8+ cells
- The response using universal-receptor-bearing CD8+ cells to lyse infected cells *in vitro* 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

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p17(77–85)	p17(77–85)	SLYNTVATL	*in vitro* stimulation	human(A2)	[Stuhler & Schlossman(1997)]

- Epitope name: SL9. Keyhole limpit hemocyanin or tetanus toxoid Th epitope co-expression with peptide CTL epitopes on the same APC was required for induction of peptide-specific CTL

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Yang (1996)]

- Epitope name: SL9. 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

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Yang (1997a)]

- Epitope name: SL9. CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation
- CTL suppress HIV replication more efficiently in HLA-matched cells

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p17(77–85)	p17(77–85 LAI)	SLYNTVATL	HIV-1 infection	human(A2)	[Parker (1992), Parker (1994)]

- Epitope name: SL9. Examined in the context of motifs important for HLA-A2 binding

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p17(77–85)	p17(77–85 LAI)	SLYNTVATL	HIV-1 infection	human(A2)	[McMichael & Walker(1994)]

- Epitope name: SL9. Review of HIV CTL epitopes

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Tsomides (1994)]

- Epitope name: SL9. CTL clones recognize naturally processed peptide

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p17(77–85)	p17(77–85)	SLYNTVATL	*in vitro* stimulation	human(A2)	[Stuhler & Schlossman(1997)]

- Epitope name: SL9. A three cell-type cluster consisting of APCs, Th, and CTLs is the minimal regulatory unit required for Th cell-dependent induction of CTLs

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Cao (1997)]

- Epitope name: SL9. The consensus peptides of B and D clade viruses and some Cs have the sequence SLYNTVATL
- The consensus peptide of A, and some C strains have SLFNTVATL, a form that is cross-reactive

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p17(77–85)	Gag(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Dyer (1999)]

- Epitope name: SL9. CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Harrer (1998)]

- Epitope name: SL9. Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL)
- Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape

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p17(77–85)	p17(77–85 SF2)	SLYNTVATL	HIV-1 infection	human(A2)	[Altfeld (2001a)]

- The relative contribution of CTL responses against HIV-1 Vpr, Vpu, and Vif were analyzed in multiple HIV-1-infected individuals
- Individuals with long-term nonprogressive and treated chronic HIV-1 infection targeted Vpr more frequently than individuals with treated acute infection
- Vpr is a frequent target of HIV-1 specific CD8+ T-cells – a response was detected in 45% of individuals tested and Vpr and p17 were the most preferentially targeted proteins per unit length by CD8+ T-cells
- The A2 epitopes Vpr AIIRLLQQL and p17 SLYNTVATL do not account for the dominance of Vpr and p17, the result holds even when HLA-A2+ individuals are excluded

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p17(77–85)	p17( )	SLYNTVATL	*in vitro* stimulation	human(A2)	[Buseyne (2001)]

- Epitope name: SL9. 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 SLYNTVATL specific CTL line EM71-1 without protein synthesis, while macrophages demonstrated a decreased presentation efficiency
- Exogenous Gag epitope presentation was Env-dependent and required receptor-dependent fusion

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p17(77–85)	p17( )	SLYNVATL	HIV-1 infection	human(A2)	[Kostense (2001)]

- 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
- In one patient with a SLYNVATL response, no SLYNVATL mutations were found among 21 clones despite high viral load (260,000 RNA copies/ml serum), suggesting low *in vivo* efficacy of the SLYNVATL response

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

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p17(77–85)	p17( )	SLYNVATL	HIV-1 infection	human(A2)	[Seth (2001)]

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized
- 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these declined upon successful therapy
- 4/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope
- Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV

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p17(77–85)	p17(77–85)	SLYNTVATL	HIV-1 infection	human(A2)	[Islam (2001)]

- Epitope name: SL9. Transcript frequencies were followed for four CTL clones from patient 115, with a chronic and stable HIV-1 infection, were tracked in a longitudinal study of samples collected 6-11 years post infection: clone M21 and E15 recognize ERYLKDQQL,and clone D87 recognizes variant ERYLQDQQL, and clone p175b recognizes the A2 epitope SLYNTVATL
- This epitope sequence from clone p175b uses the Vβ5, CDR3 (FDS), Jβ2.7 TCR β gene
- Responses were stable even through HAART with undetectable viral loads, but frequencies varied over time by 100-fold, ranging from 0.012% of the total population for SLYNTVATL at its lowest point to 3.78% for M21, with the relative frequencies of clones shifting over time

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p17(77–85)	p17(77–85 SF2)	SLYNTVATL	HIV-1 infection	human(A2)	[Altfeld (2001c)]

- 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-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 2/6 group 2, and 2/4 group 3

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p17(77–85)	p17(77–85)	SLFNTVATL	HIV-1 exposed seronegative, HIV-1 infection	human(A2)	[Kaul (2001a)]

- Variants SL(F/Y)NTVATL 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
- 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-A2 women, 1/10 HEPS and 22/26 HIV-1-infected women recognized this epitope, likelihood ratio 18.3, p value < 0.003, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women
- The dominant response to this HLA allele was to this epitope in the 1/10 HEPS cases and in 18 of the 22/26 HIV-1-infected women that responded
- 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 1250 had an A2 response to ILKD/EPVHGV prior to seroconversion, which switched to SLF/YNTVATL post-seroconversion
- Subjects ML 1575 and ML 1592 had no response to SLF/YNTVATL prior to seroconversion, but made responses post-seroconversion
- Subject ML 1760 had an A2 response to ILKD/EPVHGV prior to seroconversion, and gained responses to epitopes A2 SLF/YNTVATL and B27 KRWIIL/MGLNK post-seroconversion

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p17(77–85) p17(77–85 93TH253 CRF01) SLYNTIATL HIV-1 infection human(A2) [Sriwanthana (2001)]

- Epitope name: G77-85. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was reactive in HIV+ control study subjects 125 and 144 who carried HLA-A2

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p17(77–85) p17(77–85 93TH253 CRF01) SLYNTIATL HIV-1 infection human(A2) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- 2/4 tested FSWs recognized the E clade version of this epitope, SLYNTIATL, the B clade version is SLYNTVATL
- This epitope was only conserved in CRF01 and subtypes B and D, and exact matches were uncommon

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A2) [Day (2001)]

- 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
- SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes
- Three subjects only had an A2 response to SLYNTVATL
- The two subjects with acute infection did not respond to SLYNTVATL

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(A2) [Goulder (2001d)]

- Epitope name: SL9. Immune escape variants in this epitope where transmitted both horizontally and vertically in two families
- Eight transmitting mothers and 14 non-transmitters mothers were studied and variation within the SL9 epitope was associated carrying HLA-A2 (P=0.04), but no link between variation from the SL9 consensus and vertical transmission was established

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(A2) [Altfeld (2000)]

- 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

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p17(77–85) p17( ) SLYNTVATL HIV-1 exposed seronegative human(A2, A*0202) [Rowland-Jones (1998b)]

- Epitope name: SL9. 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, SLFNTVATL, was preferentially recognized by CTL
- This epitope was recognized by two different exposed seronegative prostitutes

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p17(77–85) p17( ) SLYNTVATL HIV-1 infection human(B*0201) [Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and 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 KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705

- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

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p17(77–85) p17(77–85) SLYNTVATL HIV-1 infection human(B62) [Goulder (1997a)]

- Epitope name: SL9. 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
- 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

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p17(82–91) p17(82–91 93TH253 CRF01) IATLWCVHQR HIV-1 exposed seronegative, HIV-1 infection human(A11) [Sriwanthana (2001)]

- Epitope name: G82-91. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11
- This epitope was strongly reactive in HIV+ study subject 053 who carried HLA-A11

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p17(82–91) p17(82–91 93TH253 CRF01) IATLWCVHQR HIV-1 infection human(A11) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined
- 3/8 tested FSWs recognized this epitope
- This epitope was not conserved in other subtypes, and exact matches were uncommon

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p17(84–91) p17(83–91) TLYCVHQR HIV-1 infection human(A11) [Harrer (1998)]

- Two overlapping epitopes were recognized in a long-term survivor, restricted by two different HLA molecules, HLA-A11(TLYCVHQR) and -A2 (SLYNTVATL)
- Viral sequence substitutions were present in this individual which did not affect viral replication and did not alter CTL-recognition of the A2 epitope, but reduced recognition of the A11 epitope, indicative of immune escape
- A Q90E substitution resulted in a loss of the ability of the peptide to induce lysis, R91K substitution was still reactive, and R91Q substitution showed a reduced ability to stimulate lysis

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p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes that this is an A*1101 epitope				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A11)	[Brander & Walker(1995)]
	• Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A11)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 infection	human(A11)	[Ferrari (2000)]
	• One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles				
p17(84–92)	p17(84–92 SF2)	TLYCVHQRI	HIV-1 infection	human(A11)	[Altfeld (2001c)]
	• 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 1/2 group 3				
p17(84–92)	p17(84–92)	TLYCVHQRI	HIV-1 exposed seronegative, HIV-1 infection	human(A11)	[Kaul (2001a)]
	• 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				
p17(86–101)	p17( )	YCVHQRIEIKDTKEAL	HIV-1 infection	human( )	[Altfeld (2000)]
	• 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				
p17(86–101)	p17( )	YCVHQRIEIKDTKEAL	HIV-1 infection	human( )	[Altfeld (2000)]
	• 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				
p17(87–105)	p17(91–105 SF2)	CRIDVKDTKEALEKIE	HIV-1 infection	human( )	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				

p17(88–115)	p17(88–115 ARV)	VHQRIEIKDTKEALDK-IEEEQNKSKKKA	HIV-1 infection	human(A2)	[Achour (1990)]

- B cell epitope HGP-30 also serves as a CTL epitope

p17(88–115)	p17(88–115 ARV)	VHQRIEIKDTKEALDK-IEEEQNKSKKKA	Vaccine	murine BALB/c(H-2^d)	[Hamajima (1997)]

Vaccine: *Vector/type:* peptide *HIV component:* V3, HPG30, CD4BS *Stimulatory Agents:* IL-12

- B cell epitope HGP-30 also serves as a CTL epitope
- Vaccine combined HGP-30, V3 loop peptide variants, and CD4 binding site peptide
- IL-12 expression plasmid included with the vaccination enhanced the CTL response

p17(90–101)	p17( )	RIDVKDTKEAL	HIV-1 infection	human( )	[Goulder (2000a)]

- The CTL-dominant response was focused on this epitope in an HIV+ Haitian living in Boston, who was A23/68 B45/72 Cw2/16 – this epitope fell outside the most recognized peptides in the study
- Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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

p17(91–105)	p17(91–105 SF2)	RIDVKDTKEALEKIE	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-A3, A24, B8, B55

p17(92–101)	p17(92–101)	IEIKDTKEAL	HIV-1 infection	human(B*4001)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*4001 epitope

p17(92–101)	p17( )	IEIKDTKEAL	HIV-1 infection	human(B60)	[Wagner (1998a)]

- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules

p17(92–101)	p17(92–101 SF2)	IEIKDTKEAL	HIV-1 infection	human(B60)	[Altfeld (2001c)]

- 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-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3				
p17(92–101)	p17( )	IEIKDTKEAL	HIV-1 infection	human(B60(B*4001)	[Altfeld (2000)]
	• 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				
p17(92–101)	p17(92–101)	IEIKDTKEAL	HIV-1 infection	human(B60/B61)	[Day (2001)]
	• No immunodominant responses were detected to five B61-restricted epitopes tested • All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response				
p17(93–101)	p17( )	DVKDTKEAL	HIV-1 infection	human( )	[Goulder (2000a)]
	• The CTL-dominant response was focused on this epitope in an HIV+ Caucasian from Boston, who was A1/*0201 B8/63 Cw7/- – this epitope fell outside the most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (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), 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				
p17(93–101)	p17(93–101)	EIKDTKEAL	Peptide-HLA interaction	human(B8)	[DiBrino (1994b)]
	• Examined in the context of motifs important for HLA-B8 binding, predicted epitope based on Achour *et al*.				
p17(93–101)	p17(93–101)	EIKDTKEAL	HIV-1 infection	human(B8)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs				
p17(93–101)	p17(93–101 LAI)	EIKDTKEAL		human(B8,B60)	[Brander & Walker(1997)]
	• Pers. Comm. from A. Trocha and S. Kalams to C. Brander and B. Walker				
p17(121–132)	p17(121–132 HXB2R)	DTGHSNQVSQNY	HIV-1 infection	human(A33)	[Buseyne (1993b)]
	• Clustering of Gag p24 CTL epitopes recognized in 29 HIV-infected people				

p17(121–132)	Gag(121–132 LAI)	DTGHSNQVSQNY	HIV-1 infection	human(A33)	[Buseyne (1993a)]

- Vertical transmission of HIV ranges from 13% to 39%
- Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children
- Epitopes recognized in five children were mapped using synthetic peptides and secondary cultures
- Patient EM17 (CDC P2A+C+D2) had a CTL response to two epitopes in Gag

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p17(124–132)	p17(124–132 SF2)	NSSKVSQNY	HIV-1 infection	human(B35)	[Altfeld (2001c)]

- 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

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p17(124–132)	p17(124–132 LAI)	NSSKVSQNY	HIV-1 or HIV-2 infection	human(B*3501)	[Brander & Goulder(2001)]

- Noted by Brander to be B*3501 epitope

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p17(124–132)	p17( )	NSSQVSQNY	HIV-1 infection	human(B*3501)	[Dorrell (2001)]

- The crystal structure of this epitope bound to HLA-B*3501 shows that a serine can fit into the B pocket, which is shared between B35 and B53, with the hydroxyl group of the P2 serine occupying a position almost identical to the P2 proline that was previously considered the anchor motif
- Novel B53 epitopes (DTINEEAAEW and QATQEVKNM) were defined in this study that showed that A and T can also serve as P2 anchor residues for the B pocket of HLA-B35 and B53 – while S, T, and P could all fit into the 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

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p17(124–132)	p17( )	NSSKVSQNY	HIV-1 infection	human(B35)	[Seth (2001)]

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized

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p17(124–132)	p17(124–132 LAI)	NSSKVSQNY	HIV-1 infection	human(B35)	[McMichael & Walker(1994)]

- Review of HIV CTL epitopes

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p17(124–132)	( )	NSSKVSQNY	HIV-1 infection	human(B35)	[Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and 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 KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

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p17(124–132) p17(124–132) NSSKVSQNY HIV-1 infection human(B35) [Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is influenced by immune pressure from CTLs

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p17(124–132) p17(124–132 LAI) NSSKVSQNY HIV-1 or HIV-2 infection human(B35) [Rowland-Jones (1995)]

- Established by titration

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p17(124–132) p17(124–132 LAI) NSSKVSQNY *in vitro* stimulation human(B35) [Lalvani (1997)]

- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers
- This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors

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p17(124–132) p17( ) NSSKVSQNY human(B35) [Rowland-Jones (1999)]

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no 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
- HIV-2 version of this epitope is not conserved: PPSGKGGNY, but the CTLs are cross-reactive – this is one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]
