Table 6: **Gag**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Gag(223–231)	( )	GPGHKARVL		(B7)	[Brander & Goulder(2001), Goulder(1999)]
Gag( )	Gag( )		HIV-1 p55 Gag VLPs	Rhesus macaques( )	[Paliard (2000)]
	• CTLs primed by HIV-1 p55 Gag virus-like particle (VLP) vaccination recognized epitopes in four different 20 amino acid peptides p17/4, p17/8, p24/13 and p14/9 • Cytotoxic T cell response lasted greater than 8.5 months				
Gag( )	Gag( )		HIV-1 infection	human( )	[Wasik (2000)]
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of β-chemokines and IL-2 relative to other HIV+ infants • No HIV+ infants had no demonstrable CTL at birth, but Th1 responses accompanied by CTL responses developed in children with slowly progressive disease, and not in rapid progressors • CTLp frequencies were determined by limiting dilution using autologous B cells infected with vaccina/HIV constructs				
Gag( )	Gag( )		rec canarypox vector with HIV-1 gp120 MN, tm/Gag/protease LAI (vCP205), alone or with p24E-V3 MN synthetic peptide (CLTB-36)	human( )	[Salmon-Ceron (1999)]
	• Twenty HIV negative subjects were vaccinated in phase I trial with combinations of vCP205 and CLTB-36 • Immunization with vCP205 induced HIV-1-specific ABs to gp120, V3, and p24 antigens, and CTL immune responses against vCP205 were detected after the fourth immunization in 33% of the subjects against Env, Gag and Pol, but the CLTB-36 peptide did not produce AB or CTL immune responses against p24 or gp160				
Gag( )	p24( )		p24-VLP virus-like particle	human( )	[Klein (1997)]
	• Immunization of HIV+ people with an HIV-1 p17/p24 Ty virus-like particle (p24-VLP) resulted in a marginal, short-lived increased proliferative response to p24 and p17 and a transient elevation in viral load • Two of four subjects that received 500 or 1000 μg of p24-VLP had an increase in Gag-specific CTL				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Gag( )	p24( )		PLG microparticles containing rec gp120 and p24 in emulsion adjuvant MF59	murine and baboon( )	[O'Hagan (2000)]
	• PLG (Polylactide co-glycolide Polymer) microparticles administered in MF59 emulsion induced gp120 Ab responses and CTL immune responses against p24 Gag				
Gag( )	Gag( )		HIV-infection	human( )	[Lubaki (1999)]
	• Three strategies were used to analyze CTL activity: area under the net HIV-specific lysis curve (ACU), linear regression (LR) of net specific lysis, and the standard method, lytic units (LU20) • A correlation between low HIV plasma viral load and increased levels of HIV-specific Gag and Nef CTL activity was observed using ACU and LR, but not LU20				
Gag( )	Gag( )		HIV-1 infection	human( )	[Kalams (1999a)]
	• The presence of HIV-1 p24-specific proliferative responses was positively correlated with Gag-specific memory CTL and negatively correlated with viral load in untreated subjects • Gag proliferative responses were the most readily detected – Gag CTL responses were the only responses with a significant correlation with Gag stimulated help, although there was a positive trend with Nef, Env and RT				
Gag( )	p55( )		HIV-1 infection	human( )	[Greenough (1999)]
	• 7/128 HIV-1 infected hemophiliacs were identified as long-term non-progressors (LTNPs) and were monitored for viral and host immune parameters over 15 years – LTNPs maintained a low viral load, high frequencies of CTL precursors directed against Gag antigen and low levels of HIV-specific effector CTL activity – effector cell activity suggests low level ongoing viral replication				
Gag( )	Gag( )		HIV infection	human( )	[Trickett (1998)]
	• Twelve HIV-1 infected patients were re-infused with their own lymphocytes, cryopreserved from an earlier time point in the infection • Improvement in CD4+ and CD8+ T cells was seen in 7/12, and an increase in the CTL response to Gag was seen in one patient				
Gag( )	Gag( )		HIV-1 infection	human( )	[Betts (1999)]
	• This study demonstrated an inverse correlation between HIV Type I plasma viral load and CTL activity directed against HIV-1 Pol, and stronger combined effects of Pol- and Env-specific CTL, in long-term survivors (LTS) of HIV-1 infection				
Gag( )	Gag( )		HIV infection	human( )	[Legrand (1997)]
	• Seventeen recently infected patients were tested for CTL response to HIV proteins Env, Gag, Pol, Rev, Nef, Vif and Tat • An early response (within a month following PI) was noted in 87% of the subjects to Gag, 75% to Env, and 50% to Nef • Early responses to Pol, Rev, Vif and Tat were rare				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Gag( )	Gag( )		HIV-1 infection	human( )	[Betts (1997)]
	• 6/8 individuals from Zambia infected with C clade virus had CTL that were able to make response to B clade HIV-1 IIIB vaccinia-expressed Gag, Pol and Env proteins • A vigorous cross-clade response was not limited to a particular protein, and the level of recognition of different proteins varied among the six patients				
Gag( )	Gag( )		HIV-1 infection	human( )	[De Maria (1997)]
	• CD3+ cells that also carry a natural killer cell receptor (NKR+) can exhibit down regulation of T cell function • Anti-NKR IgM MAb masked this inhibitory function and increased HIV-1 specific CTL activity in phytohemagglutinin-activated PBMC cultured in the presence of IL-2 from 3/5 patients, and in one other case anti-NKR MAb brought HIV-1 specific CTL activity to detectable levels				
Gag( )	Gag( )		HIV-1 canarypox vaccine	human( )	[Belshe (1998)]
	• The live canarypox vaccine ALVAC-HIV(vCP205) carrying MN gp120, LAI gp41, Gag and Protease, and boosted with SF-2 rpg120, was given to HIV-1 seronegative volunteers – HIV-specific Env or Gag CD8+ CTL were detected in 64% of the volunteers				
Gag( )	Gag( )		HIV-1 infection	human( )	[Buseyne (1998a)]
	• This study showed a correlation between strong CTL memory and breadth of response in 7–12 month old infants, and remaining AIDS-free for the first year of life, higher absolute CD4 and CD8 cells, and lower viral load				
Gag( )	Gag( )		HIV-1 infection	human( )	[Buseyne (1998b)]
	• In infants with positive CTL responses, most responses showed cross-clade reactivity with somewhat diminished recognition of epitopes from different subtypes				
Gag( )	Gag( )		HIV-1 exposure	human( )	[Goh (1999)]
	• 13/37 exposed uninfected individuals with repeated high-risk sexual exposure had HIV-1 specific CTL against Env, Gag, Pol, or a combination of proteins – CTL activity was correlated with a CCR5 wildtype genotype • In this group, the highest CTLp frequencies were directed at Gag, but the most common response was to Env and four individuals had responses to multiple HIV-1 proteins				
Gag( )	Gag( )		canarypox HIV vaccine	human( )	[Evans (1999)]
	• A canarypox vaccine expressing gp120, gp41, Gag, Protease, Nef and Pol CTL epitopes gave rise to CTL that could be detected in 61% of the volunteers – responses to Gag, Env, Nef and Pol were detected 3–6 months after the last vaccination				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Gag( )	p17( )		HIV-1 infection	human( )	[Kuiken (1999)]
• A correlation between conserved regions of p17 or Nef and CTL epitope density was noted – the authors suggest that this may be due to a biological reason such as epitope processing, or may possibly be an artifact of experimental strategy for epitope definition such that conserved epitopes would tend to be identified because they would be more likely to be cross-reactive with the test reagents • In contrast to p17 and Nef, p24 is a more conserved protein and known epitopes are evenly distributed across p24					
Gag( )	Gag( )		HIV-DNA prime - HIV vaccinia boost	Macaca nemestrina( )	[Kent (1998)]
• Priming with an HIV-DNA vaccine and boosting with a vaccinia construct induced greater levels of HIV T cell immunity than either vaccine alone • The proliferative response to Env and Gag after the DNA vaccination had a mean SI of 1.5–4, but after boosting with rHIV-fowlpox virus, there was a 6–17 fold increase in the mean SI for HIV Gag and Env. The T help response happened despite a fall in antibody titers, suggesting that the Th response was primarily Th1, not Th2. The CTL response was also enhanced					
Gag( )	Gag/Pol( )		ALVAC HIV vaccine	human( )	[Salmon-Ceron (1999)]
• A live attenuated canarypox vector expressing MN gp120 and LAI gp41/Gag/protease could induce CTL and a lymphoproliferative response in healthy, uninfected volunteers					
Gag( )	Gag/Pol( )		DNA vaccine + CD80 and CD86 expression cassettes	chimpanzee( )	[Kim (1998)]
• The study explores the use of co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine to enhance the immune response – co-expression of CD86, but not CD80, dramatically increased both HIV Env and Gag/Pol specific CTL and Th proliferative responses					
Gag( )	Gag( )		HIV-1 infection	human( )	[Aladdin (1999)]
• *In vitro* measurements of CTL-activity by Cr release assay in bulk culture showed no correlation between CTL-activity (gp120, Gag, Pol and Nef) and disease progression as measured by viral load, CD4 and time to death					
Gag( )	Gag( )		HIV-1 infection	human(A*0201 and Cw*08)	[Shacklett (2000)]
• HIV-1 specific, MHC class I-restricted CTL killing was detected in duodenal and rectal gut associated lymphoid tissue (GALT) sites from three infected individuals – the distribution of class I restricted CTL was different in the peripheral blood samples and GALT samples					

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Gag( )	p24( )		HIV-1 Gag DNA vaccine with secreted Gag protein	murine(H-2^d)	[Qiu and B Liu (2000)]
	• Mice were injected with plasmid DNA at 0, 2 and 4 weeks and lymphocyte proliferation was measured after 6 weeks with recombinant p24 protein • Secreted HIV-1 Gag expression vectors generated a stronger response than standard Gag or cytoplasmic Gag expression vectors • IFN-gamma levels were increased compared to an undetectable IL-4 response • CTL levels were also increased in secreted Gag expression vaccination studies				
Gag( )	Gag( )		rec vaccinia with codon-optimized Gag or Gag-Protease	murine and Rhesus monkeys (*Macaca mulatta*)(H-2^d)	[zur Megede (2000)]
	• Sequence-modified Rev-independent Gag and Gag-protease gene constructs lead to increased expression levels and elevated CTL and antibody immunogenicity in BALB/c and CB6F1 mice • A CTL response in mice could be detected after a single immunization with codon-optimized Gag, using 2 ng of plasmid; wild type Gag required 200 ng to detect a response • Recognition of 3 different Gag peptide pools was observed, indicating a Polyclonal CTL response • Significant Gag-specific CTL responses were detected in 4/4 rhesus monkeys, in contrast to 1/4 using wildtype Gag				