Table 18: **Env**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env(306–322)	gp160( )	SIRIQGPGRAFVTIGI	HIV-1 gp160/alum/CpG	murine(H-2D^d)	[Deml (1999)]
	• Addition of CpG oligodeoxynucleotide to a gp160/alum vaccine given to BALB/c mice shifted the response to Th0/Th1 from Th2, but no still CTL response to this immunodominant epitope was induced				
Env( )	gp160( )		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				
Env( )	gp160( )		HIV-1 infection	human( )	[Zheng (1999)]
	• Protein delivery (gp160 LAV, p66 LAV, and p24 NY5) to human dendritic cells (DC) with liposomes provides enhanced memory CTL response relative to delivery of protein alone				
	• Chloroquine administration enhanced epitope presentation, and brefeldin A and peptide aldehyde inhibitors inhibited antigen presentation, suggesting epitopes were processed by classical proteasome pathway				
Env( )	Env( )		HIV-1 infection	human( )	[Wasik (2000)]
	• HIV+ infants that progressed rapidly to AIDS had lower Th1 responses and decreased production of IL-2, as well as β-chemokines, 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				
Env( )	gp120( )		HIV infection	human( )	[Soudeyns (2000)]
	• Analysis of T cell receptor β chain variable region repertoire indicates that antiretroviral therapy (ART) and highly active antiretroviral therapy (HAART) decrease global CD8 T cell oligoclonality during primary HIV infection				
	• A sharp decline in HIV-1 gp120-specific CTL clones was observed in HAART-treated subjects				

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	Env( )		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				
Env( )	Env( )		HIV-1 infection	human( )	[Gamberg (1999)]
	• 13/13 subjects with advanced HIV infections showed CD8 T cell proliferation and differentiation of CTL *in vitro*, and six individuals showed HIV-specific responses to Gag, Pol, Env or Nef antigens • Data suggests that the functional and genetic integrity of the CD8 T cell repertoire (TCR βV gene intrafamily genetic diversity) remains intact through advanced HIV infection, although HIV-specific CTL activity decreases				
Env( )	Env( )		rec canarypox vaccine expressing HIV-1 Env, Gag, Pol, Nef and protease (vCP300) with or without administration of HIV-1 SF-2 rgp120	human( )	[Gorse (1999)]
	• *In vitro* inducible CTL activity against HIV-1 Env, Gag, Pol, and Nef antigens was observed in 79% (15 of 19) of vaccine recipients • The combination of vCP300 and vP1291 together resulted in an overall increase in CTL induction and detection sensitivity				
Env( )	Env( )		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				
Env( )	gp120( )		gp120 or gp160 DNA vaccine	Rhesus monkeys( )	[Shiver (1997)]
	• DNA vaccinations of Rhesus monkeys with a gp120 or gp160 DNA vaccine elicited a strong CD8 cytotoxic T cell response				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp160( )	Polyclonal	HIV-1 infection	*Macaca nemestrina*( )	[Kent (1997b)]
• Macaques can be infected with HIV, and clear the infection within 6 months, so it is of interest to examine their initial immune response • A strong CTL response against Env, Pol and Gag antigens can be detected • The CTL response peaked by 4 weeks and declined dramatically by 8 weeks • The response in the lymph nodes and peripheral blood was comparable					
Env( )	gp160( )		DNA Gag/Pol, Vif, and Env vaccine	murine( )	[Kim (1997b)]
• A Gag/Pol, Vif or Env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules B7 and IL-12, gave a dramatic increase in both the cytotoxic and proliferative responses in mice • When IL-12 was present, CTL response could be detected even without *in vitro* stimulation					
Env( )	gp160( )		DNA Gag/Pol, and Env vaccine	murine( )	[Kim (1997c)]
• A Gag/Pol or Env DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecules CD86, gave a dramatic increase in both the cytotoxic and proliferative responses in mice • When CD86 was present, CTL response could be detected even without *in vitro* stimulation					
Env( )	gp120( )	Polyclonal	gp160 DNA vaccine, Env protein boost	*Macaca mulatta*( )	[Letvin (1997)]
• Vaccination of Macaques mulatta (Rhesus monkeys) with an HXBc2 Env DNA prime and a protein boost elicited a T cell proliferative response, a CTL response, and type-specific neutralizing antibodies • Vaccinated animals challenged with SHIV-HXB2 were protected from infection					
Env( )	gp120( )	Polyclonal	Env + Rev MN DNA vaccine	human( )	[MacGregor (1998)]
• An HIV DNA Env and Rev vaccine given to 15 asymptomatic HIV+ individuals at three different dosages, 30,100 or 300 μg, was safe • The CTL response to gp120 was enhanced in 0/4 patients in the 30 μg group, 2/3 patients in the 100 μg group, and 0/3 in the 300 μg group – but the non-responding patients in the 300 μg group had a strong CTL response prior to vaccination, and the CTL results are inconclusive					
Env( )	gp120( )		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 Env was seen in one patient					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp120( )		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					
Env( )	gp120( )		HIV infection	human( )	[Corey (1998)]
• Vaccinia-naive subjects were vaccinated with vaccinia-gp160 LAI and boosted with gp120 SF2, LAI, MN, or 160 MN • 26/51 had an anti-Env CTL response, and those that were boosted with gp120 tended to produce Abs that neutralized autologous laboratory strains with some cross-reactivity					
Env( )	Env( )		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					
Env( )	Env( )		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					
Env( )	Env( )		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					
Env( )	Env( )		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					
Env( )	Env( )		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					

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	Env( )		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					
Env( )	Env( )		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					
Env( )	Env( )		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					
Env( )	Env( )		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					
Env( )	gp120( )		VLP SIVmac Pr56 – gp120	*Macaca mulatta*( )	[Notka (1999)]
• Immunization of SIV Pr56Gag-derived VLPs with HIV-1 gp120 anchored on their surface induced Abs, CTL and Th responses to HIV gp120; priming with the HIV antigens in Semliki-Forest Viruses enhanced the immunological outcome • Immunized monkeys challenged with SHIV showed a more rapid reduction of plasma viremia					
Env( )	Env( )		HIV-1 exposure	human( )	[Akridge (1999)]
• This study suggests that HIV-1-resistance in exposed and uninfected individuals is not only associated with the 32-bp deletion in the HIV-1 co-receptor CCR5, but can be related to HIV-1 specific CTL immunity					

HIV CTL Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp120( )		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				
Env( )	gp120( )		HIV-1 infection	human( )	[Aladdin (2000)]
	• The administration of IL-2 caused an initial enhancement of CD4 cell counts that was accompanied by a decrease in CTL activity – IL-2 therapy did not reduce initial HIV viral load and viral replication was ultimately enhanced				
Env( )	gp41(842–850 IIIB BH8)		HIV-1 infection	human(B7)	[Pantaleo (1997), Soudeyns & Pantaleo(1997)]
	• Clonotype-specific PCR and analysis of *in vivo* HIV-specific CTL showed that in early infection HIV-specific CTL clones preferentially accumulate in blood rather than lymph nodes and that they accumulate prior to down-regulation of virus				
Env( )	Env( )		DNA vaccine pCMV160/Rev	murine(H-2^d)	[Ishii (1997)]
	• pCMV160/Rev is a DNA vaccine candidate carrying gp160 and Rev linked to a cytomegalovirus (CMV promotor)				
Env( )	gp160( )		codon-optimized HIV-1 gp160 DNA vaccination	murine(H-2^d)	[Vinner (1999)]
	• Mammalian codon optimization renders gp160 expression Rev independent, increases gp160 expression levels, and DNA vaccination of BALB/c mice yields a higher antibody response with an earlier onset than wild type • Secreted gp120 gave higher antibody titers than membrane bound gp160 • In contrast to antibodies, synthetic codon-optimized DNA did not alter the CTL response, wild type genes generated equally strong CTL responses				
Env( )	( )		multicomponent peptide vaccine VC1 with cholera toxin adjuvant	murine(H-2^d)	[Kato (2000)]
	• Immunization of BALB/c mice with VC1 and CT induced a strong CTL response which was enhanced by IL-12 expressing plasmids • Immunization with VC1 and CT resulted in HIV-1 specific IgA antibody responses, which were increased by the combination of IL-4 or GM-CSF expressing plasmids				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp160( )		PLG-microparticle encapsulated DNA encoding gp160	murine(H-2^d)	[Kaneko (2000)]
	• Oral DNA vaccination of BALB/c mice induced mucosal and systemic gp160 glycoprotein-specific cellular and humoral immune responses, and mice vaccinated orally had higher resistance to HIV-Env expressing vaccinia intrarectal challenge than mice vaccinated i.m.				
Env( )	Env( )	SIV Nef and Env CTL epitopes	SIV-infection	Rhesus macaques(Mamu-A*11, -B*03, -B*04, and -B*17)	[Dzuris (2000)]
	• Cell binding assays for Mamu molecules were employed to describe the peptide binding motifs for Mamu-A*11, -B*03, -B*03, -B*04, and -B*17 CTL epitopes – a similarity for Mamu-A*11 and -B*03 and human HLA-B*44 and -B*27, respectively, was observed – all epitopes studied were SIV epitopes, so not specifically listed here				