Table 14: **Env**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp160( )		intranasal immunization with: HIV-gp160, peptide E7, LT(R192G) adjuvant	murine($H2^d$)	[Morris (2000)]
	• Mice were intranasally immunized with 20 ug of HIV-gp160 and 5 ug of peptide E7 (RIHIGPGRAFYAARK) with the adjuvant LT(R192G), a heat-labile enterotoxin produced by *E. coli* • Adjuvant LT(R192G) was required for stimulation of antigen-specific IgG1, IgG2 antibodies, and Th1 and Th2 cytokines responses to gp160, and peptide-specific CTL responses • Increased IFN-γ, IL-10 and IL-6 cytokine production specific to gp160 was measured with co-immunization of gp160 with LT(R192G)				
Env( )	gp160( )		DNA vaccine pCMV160IIIB and pCMVREV with Br-cAMP	murine($H2^d$)	[Arai (2000)]
	• The CMV promotor responds to the intracellular level of cAMP, and 8 Br-cAMP can increase transgene expression so it was co-administered with a CMV-based DNA vaccine both intranasally and intramuscularly • 8 Br-cAMP increased serum IgG responses, HIV-specific CTL, DTH and Th1 responses, and IgA in the intranasal vaccination • A CAT assay study showed adjuvant effect was due to CMV promotor activation				
Env( )	gp120( )		gp120 or gp160 DNA vaccine	murine( )	[Shiver (1997)]
	• DNA vaccinations of BALBc mice with a gp120 or gp160 DNA vaccine elicited a strong T-cell proliferative response with Th1-like secretion of γ interferon and IL-2, with little or no IL-4, as well as antigen specific gp120 Abs • An intramuscular route of inoculation gave a stronger proliferative response than intradermal • A proliferative response could be detected in all lymph tissues tested: spleen, PBMC, and mesenteric, iliac, and inguinal lymph nodes				
Env( )	gp120( )		DNA gag/pol, or env vaccine with a CD86 expression vector	murine( )	[Kim (1997b)]
	• A gp160 DNA vaccine, when delivered in conjunction with the plasmid encoding the co-stimulatory molecule CD86, gives an increase in the proliferative responses to gp120 in mice				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp120( )		DNA gag/pol, or env vaccine + IL-2, IL-4, IFN-γ, or IL-13 expression vectors	murine(H-2^d)	[Kim (2000)]
	• Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used to enhance the immune response – co-expression of Th1 cytokine IFN-γ drove Th1 immune responses and enhanced CTL responses				
Env( )	gp120( )			human( )	[De Berardinis (1997)]
	• Sequences flanking helper T-cell immunogenic domains can be important for immunogenicity				
Env( )	gp120( )	polyclonal	HIV-1 infection	human( )	[Rosenberg (1997)]
	• A strong proliferative response to p24 and gp160 was found in a healthy long term survivor				
Env( )	gp120( )	polyclonal	HIV-1 infection	*Macaca nemestrina*( )	[Kent (1997)]
	• *Macaca nemestrina* 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 proliferative response against gp160 with IL-4 production, indicating a Th2 response, was found with 4 weeks of infection • The gp160 proliferative response by 8 weeks produces both IL-4 and γ interferon, indicating both Th1 and Th2 responses				
Env( )	gp120( )	polyclonal	gp160 DNA vaccine, env protein boost	*Macaca mulatta*( )	[Letvin (1997)]
	• Vaccination of *Macaca mulatta* (rhesus monkeys) with a 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 • All three groups showed an increased proliferative response after vaccination				

HIV Helper-T Cell Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	Env( )		HIV-1 exposure	human( )	[Mazzoli (1997)]
	• Study of HIV-specific immunity in seronegative partners of HIV-positive individuals – Env peptides could stimulate IL-2 production in 9/16 HIV-exposed seronegative individuals, and only 1/50 low-risk controls • Exposed-uninfected produced more IL-2 and less IL-10 then HIV-infected individuals • 8/9 of those whose PBMC produce IL-2 in response to Env peptides had concomitantly detected urinary or vaginal tract anti-HIV IgA				
Env( )	Env( )		HIV-1 infection	human( )	[Plana (1998)]
	• Patients from later stages of infection given HAART do not show restoration of HIV-1 specific Th proliferative responses				
Env( )	Env( )		HIV-1 infection	human( )	[Kelleher (1998a)]
	• Env and gag Th epitopes were pooled and used to test Th proliferative responses after IL2 therapy – while IL2 therapy causes an increase in CD4+ lymphocyte count, it does not increase HIV-1 specific proliferative responses				
Env( )	gp160( )		HIV-1 infection + rgp160 vaccine	human( )	[Ratto-Kim (1999)]
	• Vaccinations with rgp160 did not enhance Th immunoproliferative responses in individuals who were immunized every 2 months for 5 years starting early in infection				
Env( )	gp160( )		HIV-1 infection + rgp160 vaccine	human( )	[Leandersson (2000)]
	• 27 HIV subtype B, 4 subtype C, 2 D and one of each subtype E, F, G were either given rgp160 B clade immunizations or placebo – all rgp160 immunized individuals showed increased proliferation responses to the B clade immunizing antigen rgp160 • gp120 was prepared from A, B, C, D, and E subtype virions and used as antigenic stimulus – 7 of 10 tested individuals responded to native gp120 from at least one additional subtype in addition to B subtype, while a placebo recipient did not respond to any gp120 • This study shows that cross-subtype HIV-specific T-cell proliferative responses can be stimulated in patients already infected with another HIV-1 subtype – all immunized subjects could respond to the subtype B immunogen, but many developed responses to at least one more subtype				
Env( )	gp160( )		rgp160 MN	human( )	[Gorse (1999)]
	• Helper T-cell memory responses were induced by MN rgp160 as measured by proliferation and Th1 and Th2 cytokine release – this response could be boosted by MN rgp120				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp120( )		SF2 envelope IS-COM or chimeric Fowlpox vaccine	*Macaca mulatta*( )	[Heeney (1998)]
	• Vaccinated monkeys with the highest level of Th1 and Th2 responses and the highest levels of NAbs were protected against a SHIV SF13 challenge – the ISCOM strategy gave more potent anti -gp120 responses than the Fowl pox strategy • When animals were challenged 4 months after boost, those that maintained high levels of HIV-1 specific IFN-γ responses, indicative of a Th 1 response, were still protected				
Env( )	( )		DNA env and rev vaccine	human( )	[Boyer (1999)]
	• A DNA vaccine containing env and rev was tested for safety and immune response in 15 HIV+ asymptomatic individuals • Enhanced proliferative activity and higher levels of MIP-1 alpha were detected in multiple study subjects				
Env( )	Env( )		vaccinia env vaccine	murine BALB/c( )	[Rodriguez (1999)]
	• A chimeric GM-CSF-env antigen expressed in a vaccinia vector elicits a higher HIV-specific env cellular immune response than when native env is used				
Env( )	Env( )		HIV-DNA prime - HIV vaccinia boost	*Macaca nemest-rina*( )	[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( )	gp120( )		10 different vaccines	*Macaca mulatta*( )	[Heeney (1999)]
	• Ten different vaccine strategies were evaluated for their ability to protect from infection in a rhesus macaque model using a non-pathogenic SHIV challenge. Protection correlated with the magnitude of NAb responses, beta-chemokines, and a balanced Th response. DNA, protein+adjuvant, VLP and ISCOM vaccines were tested. • HIV-1/ISCOMS gave the highest NAb titers, Th1 and Th2 responses, was the only vaccine formulation tested with a detectable CTL response, and gave enhanced beta-chemokine production.				
Env( )	gp160( )		rgp160 MN	human( )	[Kundu (1998)]
	• This study followed 10 HLA-A2 asymptomatic HIV+ individuals as they received MN gp160 vaccinations over a two year period. • There was an increased lymphoproliferative response but this did not impact viral load or CTL response.				

HIV Helper-T Cell Epitopes

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Env( )	gp120( )		rgp120, DNA env, gp120/ISCOM	*Macaca mulatta*( )	[Verschoor (1999)]
	• 16 rhesus Macaques were vaccinated with either an epidermal SF2 gp120 DNA vaccine, rgp120 with a MF59 adjuvant, or rgp120 incorporated into ISCOMs • DNA vaccination elicited a weak Th type 1 response and low antibody response, rgp120/MF59 triggered a strong antibody response, and rgp120/ISCOM induced both kinds of Th cells, and a strong humoral response. • Animals were challenged with SF13 SHIV. Early induction of Th type 1 and type 2 responses with the rgp120/ISCOM vaccine provided the most effective immunity, protecting from infection				
Env( )	Env( )		DNA vaccine + CD80 and CD86 expression vectors	murine( )	[Kim (1998)]
	• Co-stimulatory molecules co-expressed with an HIV-1 immunogen in a DNA vaccine used 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( )	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				