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## Antigenic Comparison of HIV Envelope Complexes Containing Either sCD4, Human Anti-envelope Monoclonal Antibody A32, or CD4 Mimic Protein CD4M9

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There is growing interest in using antigens that replicate the envelope transition state structures that occur during HIV entry as vaccine immunogens. Three such immunogens have been developed – complexes between gp120 and sCD4 (CD4/gp120), gp120 and a human monoclonal antibody A32 (A32/gp120), and gp120 and a CD4 mimic molecule CD4M9, SCBaL/M9. Antigenic comparisons of these immunogens revealed key differences between these complexes. Coreceptor binding is 3-fold higher with the gp120/sCD4 over gp120/A32 and gp120/CD4M9 complexes. However, the CD4 induced epitopes (CD4i) recognized by 17b and FabX5 are expressed equally between all three complexes. 19e, which recognizes an epitope that is completely dependent upon CD4 binding (CD4d), binds to gp120/sCD4 but not to A32/gp120 or SCBaL/M9 complexes. Another CD4d epitope recognized by ED47 is similarly prominent in CD4/gp120 complexes but significant less so in A32/gp120 and SCBaL/M9. These data indicate that the antigenic features of the A32/gp120 and SCBaL/M9 are more consistent with a transition structure between unligated gp120 and the CD4/gp120. Chemical crosslinking can obscure these CD4i and CD4d epitopes. These antigenic differences may also explain the differences in the neutralizing antibody profiles generated by CD4/gp120 and A32/gp120 complexes in animal experiments.