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# Natural and engineered antibodies against HIV

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The humoral arm of the immune system exerts continual selective pressure on HIV replication in the infected person. We have described a conserved epitope within the gp120 V3 loop that is masked in the native Env trimer on CCR5-restricted (R5) HIV-1 virions, but fully exposed on CXCR4-using (X4, R5X4) virions. The ability of a monoclonal antibody against this epitope to selectively neutralize CXCR4-using but not CCR5-restricted primary isolates raises the question of whether in vivo neutralizing antibody selection pressure in the acutely infected person plays a major role in the selective transmission of R5 viruses.

We are exploiting antibodies to engineer novel bifunctional proteins against HIV infection. One agent, designated sCD4-17b, is based on the sequential receptor binding mechanism of gp120: first to CD4, then to coreceptor. The sCD4 moiety of the chimeric protein binds and induces the conformational change required to expose/create the highly conserved "bridging sheet" involved in coreceptor binding and containing the 17b epitope. The potent neutralizing activity of sCD4-17b against diverse HIV-1 primary isolates suggests its potential utility as a topical microbicide to protect against HIV-1 sexual transmission. [1,2].

## References

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