

VRC01

VRC01 is the founding member of the "VRC01 class" of CD4-binding site (CD4bs) broadly neutralizing antibodies, isolated from donor 45, a person living with HIV-1 clade B ([Wu et al., 2010, *Science*](#)). It neutralizes approximately 91% of diverse HIV-1 isolates by mimicking the host CD4 receptor, engaging the CD4-binding site primarily through its CDRH2 ([Zhou et al., 2010, *Science*](#)). VRC01-class antibodies are defined by their use of the VH1-2*02 heavy chain gene and a rare 5-amino-acid CDRL3, and have been independently isolated from at least ten different donors — a remarkable example of convergent evolution in the immune system ([Zhou et al., 2015, *Cell*](#)). Despite being up to 50% divergent in amino acid sequence, these independently arising antibodies adopt nearly identical binding orientations, suggesting the evolutionary landscape strongly constrains the structural solutions for effective CD4bs recognition. VRC01 was the first CD4bs bnAb tested in large-scale human efficacy trials (the AMP trials), which showed it could protect against sensitive viral strains but not resistant ones — highlighting the importance of understanding which mutations confer resistance and at what fitness cost ([Corey et al., 2021, *N. Engl. J. Med.*](#)).