

Broad HIV neutralization by a vaccine-induced cow antibody

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Potent broadly neutralizing antibodies to HIV have been very challenging to elicit by vaccination in wild-type animals. Using x-ray crystallography, cryo-electron microscopy and site-directed mutagenesis, we have analyzed the mode of binding of a potent bnAb (NC-Cow1) elicited in cows by immunization with the HIV gp140 Envelope trimer BG505 SOSIP.664. The exceptionally long (60 residues) third complementarity determining region of the NC-Cow1 heavy chain forms a knob-shaped mini-domain on an extended stalk that navigates through the dense glycan shield on the HIV envelope trimer to target a small footprint at the gp120 CD4 receptor binding site with no contact of the other CDRs to the rest of the Env trimer. These findings illustrate how an unusual vaccine-induced cow bnAb to HIV Env can neutralize with high potency and breadth.

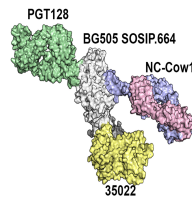


Figure 1