

**TOPIC 04: B CELL IMMUNOLOGY AND NEUTRALIZING ANTIBODIES****P04.18****Cross-neutralizing antibodies in HIV-1 infected individuals recognize novel epitopes on monomeric gp120**

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**Background:** Defining the epitopes recognized by broadly cross-neutralizing (BCN) antibodies will assist in identifying targets for an HIV-1 vaccine. Previously, we found BCN activity in 7 of 35 individuals from the CAPRISA 002 cohort infected with HIV-1 subtype C for at least 3 years. Here we describe the study of BCN antibodies directed against monomeric gp120.

**Methods:** Recombinant gp120s coupled to magnetic beads were used to adsorb antibodies from sera of the 7 individuals with BCN activity. Adsorbed plasmas were tested for neutralization against selected subtype A, B and C viruses. Envelope amplicons were generated at multiple time-points by single genome amplification and some were cloned to generate pseudoviruses for neutralization assays.

**Results:** In 2 of the 7 individuals tested, the bulk of the neutralizing activity observed at 3 years post-infection was adsorbed using gp120-coated beads. Gp120s with mutations in the CD4 (D368R) or the coreceptor (I420R) binding sites adsorbed the BCN activity equivalently to wildtype gp120 suggesting these sites are not involved. Heterologous neutralization developed gradually over time from the second year of infection with no subtype-specificity. Adsorptions of longitudinally collected plasmas suggested that the epitope(s) in gp120 was the target of the BCN activity from the initial development of breadth. However, the contemporaneous autologous neutralization was not adsorbed by gp120.

**Conclusion:** Our results indicate that a novel cross-clade neutralizing epitope in gp120 is recognized by the antibodies in two individuals with BCN activity. The failure to adsorb the autologous neutralizing activity suggests that these BCN antibodies constitute a minor proportion of the autologous neutralization.