# HIV-1 Superinfection Can Strengthen the Corresponding Antibody Response

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HIV-specific neutralizing antibodies (NAbs) that have been found in infected individuals have been shown to protect against infection in non-human primate models. Recently, several NAbs have been described from HIV-1 infected individuals that possess 'elite' neutralizing activity, which are classified this way based on their ability to neutralize multiple virus subtypes with high potency. However, it is unclear how such NAbs are elicited, and thus how to develop vaccination strategies that will induce similar antibodies.

In the study described here, Human Biology graduate student Valerie Cortez, postdoctoral fellow Dr. Katherine Odem-Davis, principal investigator Dr. Julie Overbaugh and collaborators in the Seattle/Kenya project tested the hypothesis that superinfected individuals develop broader and more potent NAb responses compared to non-superinfected individuals due to increased antigenic stimulation from multiple viruses.

The group studied 12 superinfected individuals from a cohort of high-risk women in Mombasa, Kenya. The women acquired a second infection two months to five years post-initial infection, with a median occurrence of 1.72 years post-infection. Three non-superinfected, singly infected individuals were matched to each superinfected case based on the initial infecting virus, time post-initial infection, and sample availability. NAb potency and breadth were analyzed both pre- and post-superinfection (SI), with the single post-SI time point taken when all 12 cases had been superinfected for at least one year, which occurred an average of five years post-initial infection for all individuals. Superinfected women had significantly lower mean viral loads than singly infected women pre-SI ($Log_{10}$VL: 4.24 vs. 4.79, p=0.034), but were comparable post-SI. Both groups also had similar mean CD4 T-cell counts post-SI, and none of the individuals were on antiretroviral therapy at any time point.

Pre- and post-SI serum samples were measured for NAb breadth and potency in a neutralization assay against eight viruses from four genetically diverse HIV subtypes. On average, superinfected women had 1.68 (CI: 1.23-2.30, p=0.001) times greater NAb breadth than non-superinfected women. Superinfected women also had 1.46 (CI: 1.03-2.06, p=0.033) times greater NAb potency

than the non-superinfected group. By longitudinally analyzing serum samples from two SI women with the broadest NAb responses post-SI, the authors found that NAb breadth developed early after SI in these women. This study revealed a previously unexplored source of naturally-occurring broadly NAbs, and suggests that a vaccination strategy that mimics SI may elicit development of a broad NAb response in vaccinees.

Cortez V, Odem-Davis K, McClelland RS, Jaoko W, Overbaugh J. 2012. HIV-1 superinfection in women broadens and strengthens the neutralizing antibody response. *PLoS Pathogens* 8:e1002611.

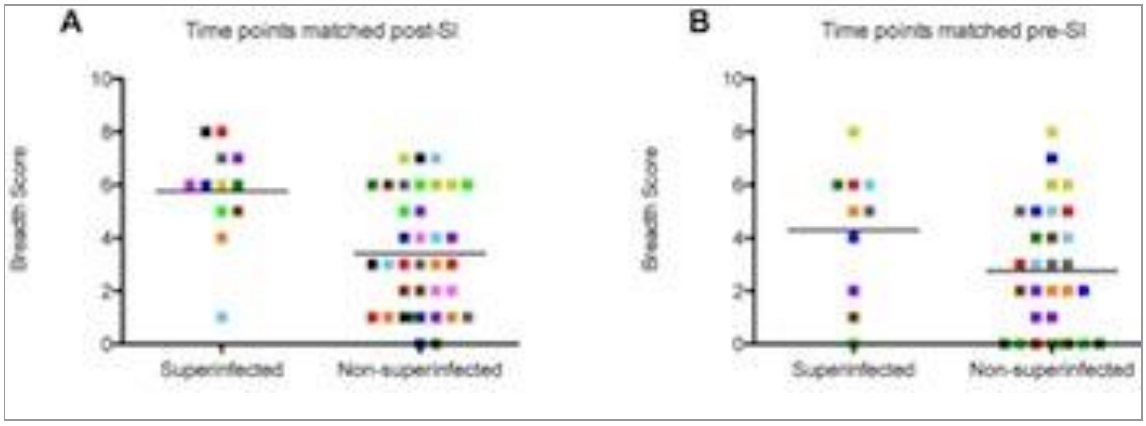


*Image courtesy of the Overbaugh Lab*

Summary of differences in HIV-1 neutralizing antibody (NAb) breadth scores between superinfected and non-superinfected women. Each case and the three matched controls are denoted by a single color. Mean scores shown with horizontal bar. Breadth comparisons post-SI and pre-SI are shown in panels A and B, respectively. The overall breadth is a composite score for each individual against all eight viruses in the panel, with a maximum score of 8 and a minimum score of 0.