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Intrasubtype C superinfected individuals mount delayed and low-titer autologous neutralizing antibody responses prior to superinfection

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Background

The potential role of neutralizing antibody in protecting against intra-subtype HIV-1 superinfection remains to be understood. We compared the early neutralizing antibody responses in three individuals, who were superinfected within one year of primary infection, to ten case-matched non-superinfected controls from a Zambian cohort of subtype C transmission cases. Sequence analysis of single genome amplified full-length env showed minimal diversification in the individuals who became superinfected with the same subtype of HIV-1 within year one post-seroconversion. We hypothesized that these superinfected individuals had a muted neutralizing antibody response that elicited little pressure on the founder virus to escape.

Methods

We molecularly cloned envs from virus at the time of seroconversion and from virus at the time point that superinfection was detected. Using a TZM-BL pseudovirus reporter assay, we tested plasma neutralization of these autologous variants over the first year of infection.

Results

Neutralization assays showed that autologous plasma NAb titers to founder virus were low to undetectable in all three superinfected individuals prior to superinfection. In contrast, neutralizing antibodies with a median IC50 of 1:1896 were detected as early as three months post-seroconversion in non-superinfected matched controls. There was no evidence, prior to superinfection, of cross-neutralization of superinfecting variants in any of the three cases, although cross-neutralization breadth and potency to the subtype C pseudovirus reference panel was also limited in the plasma from non-superinfected individuals. Although there was a trend towards superinfected individuals having reduced levels of gp120 binding antibodies prior to superinfection compared to non-superinfected controls, this difference was not statistically significant between the groups.

Conclusion

These data suggest that development of antibodies, as reflected in autologous neutralizing antibodies to the primary infection variants, may provide protection and decrease susceptibility to superinfection.

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