

## Abstract

Cervicovaginal HIV-1-neutralizing immunoglobulin A (IgA) was associated with reduced HIV-1 acquisition in a cohort of commercial sex workers. We aimed to define the prevalence and correlates of HIV-1-neutralizing IgA from HIV-1-exposed seronegative (HESN) women in HIV-1-serodiscordant relationships. **METHODS:** HIV-1-serodiscordant couples in Nairobi were enrolled and followed quarterly up to 2 years, and women in concordant HIV-1-negative relationships were enrolled as controls. Cervicovaginal, seminal, and blood samples were collected at enrollment and follow-up. Cervicovaginal IgA was assessed for HIV-1-neutralizing activity by a peripheral blood mononuclear cell-based assay using an HIV-1 clade A primary isolate. **RESULTS:** HESN women in discordant relationships had significantly more HIV-1-neutralizing IgA detected in genital secretions compared with control women [36 of 155 (23%) vs. four of 70 (6%), respectively; odds ratio (OR) 5.0; 95% confidence interval (CI) 1.70-14.64;  $P = 0.003$ ]. These responses persisted over time in all available follow-up cervicovaginal samples from women with detectable HIV-1-neutralizing IgA at baseline. Partner median HIV-1 plasma viral load was lower among women who had HIV-1-neutralizing IgA compared with women without detectable activity (4.3 vs. 4.8 log<sub>10</sub> copies/ml, respectively; OR 0.70; 95% CI 0.51-0.94;  $P = 0.02$ ). A similar trend was found with partner seminal viral load (OR 0.57; 95% CI 0.32-1.02;  $P = 0.06$ ). **CONCLUSION:** HESN women were five times more likely to have neutralizing IgA in cervicovaginal secretions than low-risk control women, and these responses were inversely associated with partner viral load. These observations support the existence of antiviral activity in the mucosal IgA fraction following sexual HIV-1 exposure.