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Session Day and Time: Tuesday, 10 am - 12:30 pm

Presentation Time: 10:15 am

Room: Ballroom 5-6

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Broad Neutralization of HIV-1 Variants in Couples without Evidence of Systemic Superinfection Despite ExposureJ McConnell¹, Y Liu², C Kreis¹, J Marcus¹, L Bragg¹, C Chappey², E Stawiski², T Wrin², F Hecht³, and Robert Grant*¹¹Gladstone Inst, San Francisco, CA, US; ²Monogram Biosci, South San Francisco, CA, US; and ³Univ of California, San Francisco, US

Background: Apparent cases of systemic superinfection have predominantly occurred in persons who have recently acquired HIV-1 infection, which is consistent with non-human primate research that indicates a short period of susceptibility to superinfection. Superinfection occurs rarely, if at all, in cohorts of viremic individuals with longer-term infections.

Methods: Persons with acute or recent infection were identified in the San Francisco Options Project and followed over at least 6 months for evidence of systemic superinfection, defined as overgrowth of a resident HIV-1 population by a highly divergent variant. Chronically infected persons were enrolled in the San Francisco Positive Partners study as couples, if they had genetically distinguishable viruses at baseline, and were followed for approximately 12 months. Neutralizing antibody titers, reported as the inverse of the dilution giving 50% inhibition, were determined using a modification of the PhenoSense Entry assay.

Results: Among 104 persons with acute or recent infection, we identified 4 cases in whom a highly divergent virus appeared 1 to 3 years after seroconversion. Heteroduplex assays and clonal analysis indicated no evidence of the subsequent virus in baseline specimens, consistent with sequential acquisition of the second variant. In contrast, there was no evidence of systemic superinfection among 35 chronically infected couples despite frequent unprotected intercourse. In the 4 recently infected persons with apparent superinfection, there was weak or no neutralization of autologous virus from 18 concomitant timepoints (median <20, range <20 to 149). In contrast, serum from 6 couples involving 12 individuals without evidence of superinfection had detectable neutralization of autologous concomitant viruses (median 135, range 39 to 253), sexual partners' viruses (median 173, range 49 to 978), and the viruses of 10 epidemiologically unrelated individuals (median 173, range 56 to 457). Neutralization was stronger to the partner's virus than to the autologous virus in 8 of 12 individuals having no evidence of superinfection.

Conclusions: We observed development of broad neutralization activity during the first 2 years of infection, including activity against viruses in sexual partners. Broad serum neutralizing responses may be a mechanism that blocks superinfection in chronically infected couples and other highly exposed individuals.