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Session Day and Time: Monday, 10 am - 12 noon

Presentation Time: 10:00 am

Room: Room 408

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**Superinfection Susceptibility and Low Neutralizing Serum Responses in Treated Persons with Suppressed Plasma Viral RNA Levels**J McConnell<sup>1</sup>, T Wrin<sup>2</sup>, Y Liu<sup>2</sup>, C Kreis<sup>1</sup>, L Bragg<sup>1</sup>, F Hecht<sup>3</sup>, N Parkin<sup>2</sup>, Robert M Grant\*<sup>1,3</sup>, and Robert M Grant\*<sup>1,3</sup><sup>1</sup>Gladstone Inst of Virology and Immunology, Univ of California, San Francisco, US; <sup>2</sup>Monogram Biosci, South San Francisco, CA, US; and <sup>3</sup>Univ of California, San Francisco, US

**Background:** Sequential appearance of HIV-1 variants suggestive of HIV-1 superinfection is observed in 2 to 5% of persons in the first year after primary infection, and less frequently thereafter. Viral suppression during treatment could increase susceptibility to superinfection by allowing antiviral immune responses to wane while increasing the availability of target cells.

**Methods:** We evaluated viral populations and serum neutralization in chronically infected seroconcordant couples with no evidence of systemic superinfection despite high levels of exposure, recently infected individuals with apparent superinfections, and multiply infected persons with suppressed plasma RNA levels on therapy. A drug-resistant RT/PR was cloned into a genomic test vector derived from a highly exposed individual's isolate. Drug-resistant PR/RT is used in the test pseudotype viruses to evaluate antibody neutralization in the presence of PR/RT inhibitors in serum of treated individuals. HIV envelope sequences isolated from plasma samples of local controls and sexual partners are inserted into the vector to provide a panel of test vectors. Neutralizing antibody titers, reported as the inverse of the dilution giving 50% inhibition, were determined using a modification of the PhenoSense Entry assay (Monogram).

**Results:** Viral clonal analysis revealed multiple infections in blood cell DNA populations in 28% (7 of 25) of persons with suppressed plasma RNA levels. Serum neutralization titers were evaluated in these 7, and 18 highly exposed and viremic individuals. Neutralizing antibody titers against the test vectors were evident in 79.6% of serum/virus pairs among those with no evidence of superinfection, but only 22.9% of those with multiple infections. Responses to a laboratory strain in treated multiply infected individuals and 5 apparent superinfection cases among recently infected individuals were similar, and lower than observed in exposed persons without superinfection.

**Conclusions:** Multiple infections suggestive of superinfection were observed frequently in groups having negligible serum neutralizing levels, including those with suppressed viral load on therapy and those in the first 3 years of primary infection. Broad serum neutralization including partner-derived viruses may block superinfection or prevent systemic spread of additional infections.