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Poster Hall

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**Highly Divergent Viral Lineages in Blood DNA Appear Frequently during Suppressive Therapy in Persons Exposed to Superinfection**J Marcus<sup>1</sup>, J McConnell<sup>1</sup>, T Liegler<sup>2</sup>, L Chow<sup>2</sup>, J Javier<sup>2</sup>, C Kreis<sup>1</sup>, L Bragg<sup>1</sup>, J Krek<sup>1</sup>, and Robert Grant\*<sup>1</sup><sup>1</sup>*Gladstone Inst, San Francisco, CA, US and* <sup>2</sup>*Univ of California, San Francisco, US*

**Background:** Systemic superinfection involving overgrowth of plasma viral RNA populations with newly acquired variants is rare in persons with well-established infection, including couples extensively exposed to genetically distinguishable viral variants. In contrast, persons with suppressed plasma viral RNA on therapy may have higher risk of acquiring new variants of HIV due to diminished viral interference or waning immune responses.

**Methods:** Couples were enrolled in the San Francisco Positive Partners study if they had genetically distinguishable viruses at baseline, and were followed for 12 months. Persons with suppressed plasma RNA (<100 copies/mL) were selected for *pol* sequencing of PBMC DNA using a modified genotyping assay (TRUGENE).

**Results:** Viral DNA *pol* sequences were available from 19 individuals on suppressive therapy. When enrolled, 2 had been recently infected, and the other 17 reported a longer time since their first positive HIV antibody tests (median 10 years, range 2.3 to 19.3 years). Highly divergent variants of HIV-1 appeared in the PBMC DNA of both recently infected persons (2 of 2), and in 3 of 17 (18%) of those infected for longer than 2 years. In all of these cases, the new viral variant did not cluster with the baseline variant in phylogenetic analysis involving epidemiologically unrelated local controls. In 1 case, the genetically divergent virus that appeared was similar to the virus circulating in the individual's sexual partner, but epidemiological history could not rule out the possibility that one initially infected the other. In another case, the acquired virus did not match the partner's virus. Drug-resistant mutants were acquired in 3 of 5 cases, although none had a rebound of plasma viral RNA on therapy.

**Conclusions:** The viral variants that appeared in PBMC DNA of these persons on suppressive therapy are much more divergent (and polyphyletic) than expected from endogenous evolution and archiving of previously circulating variants. Among chronically infected individuals, the finding of frequent limited superinfection in DNA populations during suppressive therapy contrasts markedly with the rarity of systemic superinfection during which plasma RNA populations are overgrown by new variants of HIV-1. The mechanisms that make systemic superinfection rare (as expressed in plasma RNA populations) in chronic infection may not prevent limited superinfection of DNA populations.