

POSTER 49**GENETIC DIVERSITY IN HIV-1 *pro-pol* PERSISTS IN PATIENTS ON SUPPRESSIVE ANTIRETROVIRAL THERAPY**

S. Yu¹, M. Kearney¹, S. Palmer¹, Kristen Danley¹, J. Mican², R. Stephens³, D. Rock⁴, W. Shao¹, J. Mellors⁵, J. Coffin¹, F. Maldarelli¹

¹HIV Drug Resistance Program, NCI, NIH, Frederick MD; ²Laboratory of Immunoregulation, NIAID, NIH, Bethesda, MD; ³SAIC, Frederick, MD; ⁴NIAID/CCMD Clinic, NIH, Bethesda, MD; ⁵Division of Infectious Diseases, University of Pittsburgh, Pittsburgh, PA

HIV-1 drug-resistant variants emerge from diverse virus populations, but the effect of antiretroviral therapy on diversity remains poorly understood. Specifically, it is not known whether HIV-1 populations remain diverse or become more homogeneous with suppressive therapy. To address this question, we analyzed HIV-1 *pro-pol* sequences in patients initiating suppressive antiretroviral therapy. Antiretroviral naïve HIV-1 infected patients (N=10) were sampled within one month of initiating therapy. Individual HIV-1 *pro-pol* sequences were obtained using single-genome sequencing. 9-20 sequences per sample were obtained before therapy and during viral decline. HIV-1 diversity was measured in aligned sequences by average pairwise difference (APD). Genetic relatedness of sequences was determined by phylogenetic analysis. Before therapy HIV-1 sequences were highly diverse (APD=0.005-0.02 per site). After therapy, plasma HIV-1 RNA levels declined with first phase half-lives of c. 1-1.5 d. Up to three samples were analyzed for each patient on therapy when HIV-1 RNA had declined to less than 500 copies/ml (range <50-238 c/ml). Viral diversity on therapy was not different from that measured before therapy (APD 0.005-0.02 per site). Phylogenetic analyses revealed similar genetic relatedness among sequences before and after therapy. In patients who were treated with a non-nucleoside reverse transcriptase inhibitor based regimen, comparison of *pro* and *pol* sequences revealed similar viral population structure before and after therapy, indicating *pro* did not vary independently from *pol* in the absence of protease inhibition. In summary, HIV-1 *pro-pol* genetic diversity is not different before and after initial antiretroviral therapy, suggesting that suppression occurs without significant genetic bottlenecks. This result implies similar HIV-1 diversity in infected cell populations with long or short half-lives.