Submitter Name: Rebecca Veenhuis Submitted Email: rterill1@jh.edu

Past cocaine exposure durably alters CD4$^+$ T-cell reservoir seeding and reactivation SIV-infected ART-suppressed macaques

Mary Elizabeth Zipparo[1], Edna Ferreira[1], Celina Abreu[1], Lily Pohlenz[1], Jordin Dixson[1], Erin Shirk[1], Suzanne Queen[1], Janice Clements[1,2,3], and Rebecca T. Veenhuis[1,2]

Departments of [1]Molecular and Comparative Pathobiology,
[2]Neurology, and
[3]Pathology, Johns Hopkins School of Medicine, Baltimore MD, USA

Cocaine is one of the most commonly abused substances, with an estimated worldwide prevalence of 5-15% of people living with HIV (PLWH) having a history of cocaine use disorder (CUD). PLWH with CUD have weaker viral suppression, poorer ART adherence, lower CD4$^+$ T-cell counts, and increased viral load over time irrespective of ART. However, despite the prevalence of CUD, the long-term effect of cocaine exposure on the establishment and maintenance of the CD4$^+$ T-cell reservoir has yet to be determined. Therefore, we used the simian immunodeficiency virus (SIV)mac251 macaque model of HIV to determine the effect of cocaine exposure during acute infection and early suppression, on the establishment and maintenance of the CD4$^+$ T-cell reservoir. Twelve animals were infected with SIVmac251 and began ART at 42 days post inoculation (DPI). Prior to infection, 6 of the 12 animals were treated with cocaine and maintained on cocaine until fully suppressed (126 DPI). These animals were then weaned from cocaine and continued ART until their terminal timepoint (300 DPI). Cocaine had no effect on plasma viremia, time to suppression and terminal tissue SIV RNA levels. Cocaine treatment resulted CD4$^+$ T-cell reservoirs in blood, spleen, and lymph node that were easier to reactivate despite having lower levels of intact SIV genomes. These data suggest that while cocaine exposure during acute infection and early suppression may reduce reservoir seeding in CD4$^+$ T-cells, it likely results in a long-term effect on the quiescent state of CD4$^+$ T-cells, preventing the virus from becoming truly latent.