Name: Jennifer Kelschenbach
Email: jennifer.kelschenbach@mssm.edu
PI Name: David Volsky
PI email: david.volsky@mssm.edu

Morphine dependence accelerates HIV-associated neurocognitive impairment in EcoHIV infected mice

Jennifer Kelschenbach[1], Lauren Wills[2], Xiaokun Liu[1], Alejandra Borjabad[1], Richard O'Connor[2], Eran Hadas[1], Boe-hyun Kim[1], Wei Chao[1], Paul J. Kenny[2], David J. Volsky[1]

[1]Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine;
[2]Nash Family Department of Neuroscience, Icahn School of Medicine

Antiretroviral therapy (ART) has shifted HIV to a survivable infection, however, patients on ART experience chronic HIV-related diseases, including neurocognitive impairment (HIV-NCI). HIV-NCI can range in severity affecting quality of life and opioid use disorder (OUD) may facilitate HIV-NCI pathogenesis. We tested this hypothesis using EcoHIV, a chimeric mouse-tropic HIV that can chronically infect mice causing HIV-NCI like disease. Morphine (25 milligram) or placebo pellets were implanted subcutaneously once a week to induce dependence in male C57BL/6J mice. Three days after implantation, mice were inoculated intraperitoneally with EcoHIV or PBS, 10 days later animals were assessed for HIV-NCI using the radial arm water maze (RAWM), then euthanized. Spleens, peritoneal macrophages, and brain were collected for virological analysis while prefrontal cortex (PFC) was collected for snRNAseq analysis. EcoHIV infected, morphine dependent, but not infected placebo implanted mice, developed learning/memory deficits in 10 days after infection that correlated with elevated HIV burdens in the spleen, peritoneal macrophages, and a trend towards increased burdens in the brain accompanied by gene dysregulation in the PFC. A total of 2,489 differentially expressed genes (DEGs) were observed across 10 cell clusters, with over 700 DEGs identified in oligodendrocyte and pericyte clusters in EcoHIV infected, morphine dependent mice compared to EcoHIV infected, placebo mice. Morphine dependence accelerates disease in EcoHIV infected mice, potentially modeling acceleration of NCI in HIV patients with OUD. We attribute this acceleration to increased HIV replication in the presence of morphine and a potential convergence of neuropathogenic effects of HIV and morphine in the brain.