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Characterization of Single cell multiomic changes during chronic HIV infection and cocaine self-administration in mice

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Previous studies have illustrated the reciprocal exacerbation of symptoms between substance use disorder (SUD) and HIV, indicating the development of these conditions within shared neurobiological systems. However, the molecular pathways and circuits underlying the interactions between SUD and HIV are poorly understood. As a part of Single Cell Opioid Responses in the Context of HIV (SCORCH) consortium, we used cutting-edge single-nuclei multiomic profiling and spatially resolved transcriptomics technologies to characterize transcriptional and epigenetic changes in addiction-relevant brain regions (10 ROIs) of EcoHIV-infected mice which compulsively self-administer cocaine (extended cocaine access) in a molecular cell type-specific and spatially resolved manner. Briefly, we have collected 185 10x Multiome libraries, and >1.2 million QC-passed cells (783,359 neurons and 480,165 non-neuronal) which are mapped onto our latest whole-mouse brain cell type atlas to obtain their cell type identity. To identify multiomic responses to EcoHIV infection and cocaine addiction, we calculated numbers of differentially expressed genes (DEGs) and differentially accessible ATAC peaks (DAPs) between different experimental groups. Our preliminary analysis identified some region- and cell-type-specific DEG/DAP induction patterns. For example, only “HIV + Extended Cocaine” condition induced many DEGs/DAPs in D1/D2 medium spiny neurons in the ventral striatum, whereas “PBS + Extended Cocaine” induced high level of DAPs in the astrocytes of the dorsal striatum and layer 4/5 intratelencephalic (IT) neurons in the prefrontal cortex (PL-ILA-ORB-TT-DP) with different transcription factor binding motif enrichment patterns. Together, these results will lead to new insights into pathophysiological interactions between HIV and SUD in our brain.