Name: Benjamin Hunter Grissom
Email: BGrissom@som.umaryland.edu
PI Name: Seth A. Ament
PI email: SAment@som.umaryland.edu

# Heroin-induced genomic regulation of ventral pallidum and nucleus accumbens neuron subtypes

Benjamin Grissom[1], Rianne Campbell[1], Marcia Cortes-Gutierrez[1], Swarup Mitra[2], Seth A. Ament[1]*, David M. Dietz[2]*, and Mary Kay Lobo[1]*

[1]University of Maryland Baltimore, School of Medicine; [2]University at Buffalo, Jacobs School of Medicine and Biomedical Sciences; *Co-Principle Investigator

Opioid dependence is associated with long-lasting changes in the mesolimbic dopamine system, but the cell type-specific gene regulatory networks mediating these effects are poorly understood. To address this, we sequenced the nuclear transcriptomes (snRMA-seq) and chromatin accessibility states (snATAC-seq) of 279,219 single cells in the nucleus accumbens (NAc) and ventral pallidum (VP) from rats in the context of heroin self-administration. We produced detailed atlases for the cell type diversity in each brain region, characterizing ten transcriptionally distinct subtypes of spiny projection neurons in the NAc and >20 transcriptionally distinct neuronal subtypes in VP, representing the first detailed single-cell genomic atlas for this brain region. We characterized cell type-specific changes in gene expression and chromatin accessibility in rats that self-administered heroin vs. controls at 1 or 14 days of abstinence, to gain insight into both acute and persistent effects on gene regulation. We integrated these data to model the gene regulatory networks mediating the effects of heroin. Our results provide insight into the gene regulatory mechanisms mediating the persistent effects of opioids in the brain.