Name: Yasmine Sami
Email: yns@wi.mit.edu
PI Name: Olivia Corradin
PI email: corradin@wi.mit.edu

Differentially expressed genes in Opioid Use Disorder are enriched amongst genes with brain region specific regulatory activity

Yasmine Sami[1,2], Kate Hazel[1], Hannah Ramcharan[1,2], Olivia Corradin[1,2]

[1]Whitehead Institute for Biomedical Research, Cambridge, MA
[2]Massachusetts Institute of Technology, Cambridge, MA

Opioid use disorder (OUD) is a chronic, relapsing condition characterized by repeated cycling of three stages: opioid intoxication, withdrawal, and preoccupation. Specific brain regions are thought to engender each of these stages disparately. We aimed to investigate the contribution of different brain regions to OUD by identifying differences in gene regulation that occur across neurons from different brain regions. To do so, we generated H3K27ac ChIP-seq data from post-mortem human control neurons (NeuN+) from seven brain regions that have been associated with OUD: Nucleus Accumbens (NAc), Hypothalamus (HT), Hippocampus (HC), Dorsolateral Prefrontal Cortex (dlPFC), Orbitofrontal Cortex (OFC), Anterior Cingulate Gyrus (ACG), and Amygdala. Rather than evaluate each regulatory element separately, we devised an approach to identify genes with the most brain region specific regulatory activity by summating all regulatory elements associated with the same gene. Using neuronal Hi-C datasets, we identified regulatory elements linked to the same gene and summated ChIP peak scores. While the majority of genes have similar regulatory activity patterns across brain regions, approximately 10% of genes exhibited NAc specific activity. We next compared genes with region specific activity with previously published differentially expressed genes (DEGs) identified in OUD NAc tissue samples. Genes with high brain region specificity to the NAc were found to be significantly enriched for OUD DEGs. Notably, we identified 140 OUD DEGs with specific regulatory activity in the NAc. This included the genes USE1, CELF5, and ACHE which have been previously shown to have NAc specific function in rodent studies of OUD.