Transcriptional alterations in opioid use disorder reveal the interplay between neuroinflammation and synaptic remodeling across corticostrital circuits

Marianne L. Seney1, Sam Moon-Kim1,2,3, Jill R. Glausier1, Mariah A. Hildebrand1, Xiangning Xue4, Wei Zong4, Jiebiao Wang4, Micah A. Shelton1, BaDoi N. Phan5, Chaitanya Srinivasan5, Andreas R. Pfenning5,6, George C. Tseng4, David A. Lewis1, Zachary Freyberg1,7 and Ryan W. Logan2,3,8

1Department of Psychiatry, University of Pittsburgh School of Medicine; 2Center for Adolescent Reward, Rhythms, and Sleep, University of Pittsburgh; 3Center for Systems Neurogenetics of Addiction, The Jackson Laboratory; 4Department of Biostatistics, University of Pittsburgh; 5Department of Computational Biology, Carnegie Mellon University; 6Neuroscience Institute, Carnegie Mellon University; 7Department of Cell Biology, University of Pittsburgh; 8Department of Pharmacology and Experimental Therapeutics, Boston University School of Medicine

Prevalence rates of opioid use disorder (OUD) have increased dramatically, accompanied by a surge of overdose deaths. While opioid dependence has been extensively studied in preclinical models, we still have a very limited understanding of the biological changes that occur in the brains of people who chronically use opioids and who are diagnosed with OUD. To address this, we conducted the largest transcriptomics study to date using postmortem brains from subjects with OUD. We focused on the dorsolateral prefrontal cortex (DLPFC) and nucleus accumbens (NAc), two regions heavily implicated in OUD. We discovered a high degree of overlap in transcripts between DLPFC and NAc in OUD, primarily associated with neuroinflammation. Moreover, additional transcripts were enriched for factors that control pro-inflammatory cytokine-mediated signaling and remodeling of the extracellular matrix. Our results also implicate a role for microglia as a critical driver for opioid-induced neuroplasticity. Overall, our findings reveal new connections between the brain’s immune system and opioid dependence in the human brain.