A046 · Integrative transcriptomic analysis identifies long noncoding RNA dysregulation and circadian disruption in reward and executive circuits of opioid use disorder

Presenter: Lina Yan — UMass Chan Medical School

Authors: Chen Fu, Zixiu Li, Lina Yan, Peng Zhou, Ryan W. Logan, Chan Zhou

Session: Day 1 · Thu Oct 1, 2026 · 2:15–4:15 PM

Opioid use disorder (OUD) is characterized by compulsive drug seeking and impaired executive control resulting from maladaptive plasticity within corticostriatal circuits. Although transcriptomic studies have identified dysregulated protein-coding genes in the nucleus accumbens (NAc) and dorsolateral prefrontal cortex (DLPFC), the contribution of long noncoding RNAs (lncRNAs) remains largely unexplored. Here, we performed integrative transcriptomic analysis of postmortem human NAc and DLPFC to systematically identify and characterize long noncoding RNAs (lncRNAs) in OUD. We identified 36,225 expressed lncRNA loci expressed across reward and executive regions, approximately half of which were previously unannotated. OUD was associated with dysregulation of 375 lncRNAs in the NAc and 102 in the DLPFC. Co-expression analysis linked these lncRNAs to addiction-related genes and pathways involved in membrane excitability, synaptic transmission, neuronal development, and neurotrophic and MAPK signaling. Differential rhythmicity analysis further identified 105 lncRNAs in the NAc and 148 in the DLPFC with altered circadian rhythmicity. These rhythmic changes represent largely region-specific gains or losses of rhythmic expression that were mostly distinct from differential expression. Integration with single-nucleus transcriptomic data revealed pronounced neuronal and glial cell-type specificity among OUD-associated lncRNAs. Together, these findings define a broad landscape of OUD-associated lncRNAs in human brain reward and executive-control circuits. Spatial, temporal, and cell-type-specific remodeling of the noncoding transcriptome may represent an important regulatory layer contributing to brain circuit dysfunction in OUD.