

Name: Jessica Zhou
PI Name: Francesca Telese
Presentation preference: Oral

Email: jlz014@eng.ucsd.edu
PI email: ftelese@health.ucsd.edu

Computational analysis of snATAC-seq from amygdalae reveals cell type-specific chromatin regions associated with cocaine addiction

Jessica Zhou^{1,2}, Hairi Li³, Olivier George⁴, Abraham Palmer⁴, Graham McVicker², and Telese Francesca³

¹Bioinformatics and Systems Biology Graduate Program, University of California San Diego; ²Integrative Biology Laboratory, Salk Institute for Biological Studies, University; ³Department of Medicine, University of California San Diego; ⁴Department of Psychiatry, University of California San Diego

Cocaine dependence is a devastating illness that is difficult to treat. Developing a better understanding of how chronic cocaine use drives long-term addictive behavior will lead to more effective therapies for cocaine use disorders. We performed extensive bioinformatics analyses of single-nucleus ATAC-sequencing (snATAC-seq) data from the amygdalae of outbred rats subjected to a validated model of extended access to cocaine intravenous self-administration (IVSA) to study the regulatory mechanisms associated with addictive behavior at cell type-specific resolution. Rats from the study were displayed either a high or low addiction index (based on several behavioral metrics), enabling us to perform cell type-specific differential chromatin accessibility analyses to identify genomic regions that drive the neuroadaptations underlying cocaine addiction-like behaviors. We identified differentially accessible chromatin regions in both neuronal and glial cell types, including both specific and shared regions. Motif enrichment analyses of these cell type-specific differentially accessible regions revealed transcription factors (TF) likely to be involved in driving addiction-related changes in the brain. We integrated single-nucleus RNA-sequencing (snRNA-seq) data from the amygdalae of rats subjected to the same IVSA model and identified putative target genes regulated by the TFs previously identified from the differentially accessible regions. Finally, we leveraged data from genome wide association studies of various addiction related traits to perform a linkage disequilibrium score regression. This revealed significant enrichment of addiction risk in cell type-specific chromatin regions associated with cocaine addiction-like behavior. Our findings illuminate the pathways involved in cocaine dependence and yield promising targets for future therapeutic approaches.