Shared Genetic Architecture between Substance-Use Disorders and Psychiatric Disorders

My research aims to identify biological principles underlying shared genetic architecture between psychiatric disorders and substance use disorders. I specifically looked into the comorbidities between three psychiatric disorders: Major Depressive Disorder (MDD), Schizophrenia (SCZ), and ADHD; and two substance use disorders (SUD): Alcohol Use Disorder (AUD) and Cigarettes per Day (CPD, a measure of nicotine addiction). My analysis began with summary statistics from Genome-Wide Association Studies (GWAS), which identify genetic variants that are associated with a particular trait, and corresponding association statistics. However, these variants are often located in the non-coding genome with unclear biological function. Therefore, we previously developed a computational tool, H-MAGMA, to aggregate variant-level statistics to their corresponding genes. H-MAGMA identifies gene-variant relationships in part based on data from the 3-D interaction of chromatin inside the nuclei. Because chromatin 3D interactions differ in different cell types, we generated different H-MAGMA frameworks using data from different cell types, namely cortical neurons and dopaminergic neurons. By identifying where these genes were most expressed using sc-RNA seq data, I was able to identify specific brain areas and cell-types that are likely affected in both disorders. Once common neurobiological mechanisms between psychiatric and substance use disorders are better understood, more targeted treatments and drugs can be developed to better help individuals impacted by both psychiatric and substance-use disorders.