Submitter Name: Hongyu Gao
Submitter email: hongao@iu.edu
PI Name: Yunlong Liu; Howard Edenberg
PI email: yunliu@iu.edu; edenberg@iu.edu

# Single cell analyses of putamen region from subjects with alcohol use disorders

Hongyu Gao[1,2], Xiaona Chu[1], Patrick McGuire[2], Xiaoling Xuei[1,2], Yue Wang[1], Howard Edenberg[2,3], and Yunlong Liu[1,2]

[1]Department of Medical and Molecular Genetics, [2]Center for Medical Genomics, [3]Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, Indiana, United States of America

Single-nucleus RNA-seq (snRNA-seq) enables the investigation of cellular composition and states in complex tissues; although becoming affordable, it is still costly for large-scale studies. To reduce cost and minimize batch effects, samples can be multiplexed through DNA-tagged antibodies (cell hashing) or chemical labeling, or can be pooled and demultiplexed using natural genetic variations. Here we present our study utilizing snRNA-seq and snATAC-seq (single-nucleus ATAC-seq) to compare the transcriptome and chromatin accessibility of individuals with alcohol use disorders with those of controls. Frozen human putamen tissues from 40 donors were studied in pools of 10 samples (5 each cases and controls). Nuclei were extracted from the pools; half was used for snRNA-seq and half for snATAC-seq using the 10X Genomics Chromium single cell system. An average of 50,000-80,000 reads and 80,000 reads per sample were generated for the snRNA-seq and snATAC-seq, respectively. The nuclei detected from each pool were demultiplexed into individual donors using known genotype information. Doublets were identified and discarded in the downstream analysis. Singlets assigned to each donor from all pools were integrated. A total of about 110,000 nuclei from snRNA-seq and 60,000 nuclei for snATAC-seq were analyzed, demonstrating that the pools could be disambiguated. Analyses detected oligodendrocytes, oligodendrocyte progenitor cells, astrocytes, microglia, inhibitory and excitatory neurons. Analysis of cases vs controls is in progress.