Functional Genomics Studies of Human Brain Diseases

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Brain disorders are complex, heterogeneous, and polygenic syndrome affecting millions of people worldwide without an effective cure. Given the high heritability, researchers were trying to identify disease loci by comparing the allele frequencies between patients and controls. We collected a large independent homogenous Han Chinese cohort (976 schizophrenia patients and 1043 controls) to achieve this goal. And we found CREB1 is involved in the pathogenesis of schizophrenia.

As genome-wide association studies identified more and more disease loci, an opening challenge is which genes and mutations are disease causal. We recently applied new approaches to identifying alternative transcripts and functional genetic variants by integrating multi-omics data. We discovered a specific cluster of SNX19 gene transcripts associated with schizophrenia using RNA-seq data and DNA methylation data combined with the genotype data generated from 495 postmortem brains. Then, we extended the investigation of functional genomic regions of schizophrenia from one gene to the whole-genome to analyze RNA-seq data from 1,479 human postmortem brains combined with their whole-genome sequencing data. While confirming SNX19 in schizophrenia risk, we also identified CYP2D6 is predisposed to schizophrenia.

Besides multi-omics data analysis, we are trying to determine our identified genes' molecular and cellular phenotypes such as SNX19 by CRISPR gene editing, followed by differentiating the bio-engineered human iPSCs to neurons and 3D brain organoids. These studies enable us to gain deeper mechanistic insights into the molecular mechanisms of brain diseases and help to identify novel therapeutic targets.

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Zoom Link for Remote Access:
https://bioinformatics.utep.edu/colloquium/zoom