Multi-omics approach identifies large list of candidate genes associated with alcohol use disorder
20 August 2021

Manav Kapoor, Ph.D., an Assistant Professor of Neuroscience and Genetics and Genomics at Mount Sinai at the time of the study.

To identify genes relevant to AUD and drinks per week (DPW), a measure used to evaluate alcohol consumption, the research team integrated multi-omics data, using Mendelian Randomization-based methods on the largest available transcriptomic and epigenomic data from brain tissues and myeloid cells. Using data derived from these tissues, the team fine mapped complex loci and identified likely variants and candidate genes, including SPI1 and MAPT genes, associated with alcoholism. SPI1 and MAPT have also been found to be associated with susceptibility for other psychiatric and neurodegenerative disorders including depression and Alzheimer's disease.

SPI1 (Spi-1 Proto-Oncogene) encodes an ETS-domain transcription factor (PU.1) that regulates gene expression during myeloid and B-lymphoid cell development and homeostasis. Given SPI1's control over expression of several downstream genes, this gene may be a major reason for enrichment of immune pathways in drinking behaviors, as observed in past transcriptomic analysis of human and animal brains.

The MAPT gene analyzed in the study encodes the tau protein, which is known for its role in central nervous system disorders such as Alzheimer's disease, frontotemporal dementia, Parkinson's disease, and other neurodegenerative disorders known as tauopathies.

"This work could lead to novel therapeutics for the treatment for alcohol use disorders," said senior author, Alison Goate, D.Phil., Professor of Genetics and Genomic Sciences and Neuroscience at Mount Sinai. "A number of anti-tau therapeutics are being..."
developed for treatment of tauopathies including Alzheimer's disease, these should also be tested in AUD models." Dr. Goate's lab also has funding to develop inhibitors of SPI1 for Alzheimer's Disease. The current study suggests these inhibitors may also be useful for treating alcoholism.


Provided by The Mount Sinai Hospital

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