

Submitter Name: Hongsheng Gui

Submitter Email: hgui1@hfhs.org

Integrative Omics for studying opioid use disorder and suicidality in African Americans

Hongsheng Gui^{1,2,3}, Brian K. Ahmedani^{1,2}, Hsueh-Han Yeh², Xiaoyu Liang⁴, Albert M. Levin⁵

¹Behavioral Health Services and Psychiatry Research, Henry Ford Health, Detroit, MI, USA;

²Center for Health Policy and Health Services Research, Henry Ford Health, Detroit, MI, USA;

³Department of Psychiatry, Michigan State University, East Lansing, MI, USA;

⁴Department of Biostatistics and Epidemiology, Michigan State University, East Lansing, MI, USA;

⁵Department of Public Health Sciences, Henry Ford Health, Detroit, MI, USA.

African Americans have been disproportionately affected by both opioid epidemic and suicide crisis in the last decade. While certain social determinants of health are known to increase the risk for both conditions, there remains a lack of genetics- or epigenetics-level mechanistic evidence for their higher co-occurrence. In addition, a better understanding of the development of OUD-suicidality needs to be achieved by integrating multiple types of biologic data together. Though collecting multi-Omics data on the same cohort is challenging, we propose integrative omics approaches that combine raw phenome-genome data with publicly available functional genomics data as a new solution. In this study, we have assembled multiple Omics data (genomics, transcriptomics, and epigenomics) with respect to African descent samples, accessed from All of Us (AoU) program, H3Africa Consortium, Joint Addiction, Aging, and Mental Health collection in dbGaP, and Gene Expression Omnibus (GEO) database. Epidemiology analysis in AoU revealed significant observational associations ($P < 0.001$), between OUD and suicide attempts, as well as between prescription opioid use and suicide ideation in African Americans. However, polygenic risk scoring (with training data from Million Veteran Program and target data from AoU) did not identify significant cross-phenotype genetic association (odds ratio=1.01, $P > 0.05$). Transcriptome- and epigenome-wide association tests were performed with PLACO, E-MAGMA and H-MAGMA tools; and they highlighted *DRD2* expression in brain and neurotransmitter catabolic process as potential contributor to shared biological pathway between OUD and suicidality. These combined analyses provide new insights into disease pathogenesis and will guide future suicide prevention among opioid users in African Americans.