

Submitter Name: Chang (April) Shu
Submitted email: c.shu@yale.edu
PI Name: Brion Maher
PI email: brion@jhu.edu

Epigenome-Wide Association Scan (EWAS) of opioid use among chronic injection drug users and in a post-mortem opioid overdose brain sample.

Chang Shu^{1,2}, Andrew E. Jaffe³, Amy Deep-Soboslay³, Sarven H. Sabunciyani², Jing Sun², Ross Felder², Thomas M. Hyde³, Daniel R. Weinberger³, Ran Tao³, Joel Kleinman³, Shruti H. Mehta², Gregory D. Kirk², Brion S. Maher²

¹Department of Psychiatry, Yale School of Medicine, ²Johns Hopkins Bloomberg School of Public Health, ³Lieber Institute for Brain Development

Background: Opioid use is associated with changes in DNA methylation. However, the precise biological pathways and the overlap between peripheral and brain changes in DNA methylation remain largely unknown.

Rationale/Significance/Hypotheses: To explore the peripheral and brain changes in methylation associated with opioid use, we conducted epigenome-wide association analyses (EWAS) among a cohort of persons who inject drugs during periods of frequent injection, cessation and relapse, and also in a post-mortem brain sample of individuals with opioid intoxication as a cause of death vs controls.

Methods: In the AIDS Linked to the Intravenous Experience (ALIVE) study, blood was obtained from 415 persons who inject drugs, resampled after cessation and then again after relapse (total samples = 1092). DLPFC samples from the Lieber Brain Repository were selected from 73 subjects with opioid intoxication as the cause of death versus 87 controls matched on age, sex, race and psychiatric disorders. Blood DNA methylation was measured using the Illumina Infinium MethylationEPIC BeadChip and tested for differences at individual probes by opioid status in both samples.

Results: In preliminary work, DNA methylation at an individual locus is significantly associated with current injection drug use status after correction for multiple testing. Additional analyses are ongoing.

Discussion: We performed a genome-wide scan of methylation changes in both a longitudinal study of injection drug use and in a post-mortem brain sample of subjects selected for opioid intoxication as a cause of death. Additional work is ongoing.