DNA methylation markers associated with injection drug use status and HIV infection among chronic injection drug users in the ALIVE study

Chang Shu[1], Kelly M. Bakulski[2], Kelly S. Benke[1], Andrew E. Jaffe[3], Shaocheng Wang[1], Sarven H. Sabunciyan[1], Shruti H. Mehta[1], Gregory D. Kirk[1], Brion S. Maher[1]

[1]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA, [2]University of Michigan, Ann Arbor, MI, USA [3]Lieber Institute for Brain Development, Baltimore, MD, USA

Background: Injection drug use (IDU) is associated with epigenetics marks such as DNA methylation. However, the biological mechanisms of how substance use affects epigenetic outcomes remain largely unknown.

Objective: To conduct the epigenome-wide association analyses(EWAS) among injection drug users to identify whether injection drug use and HIV status during the past six months is associated with genome-wide blood epigenetic changes.

Methods: In the AIDS Linked to the Intravenous Experience (ALIVE) study, blood was obtained from 288 current IDUs, resampled after cessation and then again after relapse (total samples = 774). Blood DNA methylation marks were measured using the Illumina Infinium MethylationEPIC BeadChip. Standard procedures in the minfi R package were used for preprocessing. Differences in DNA methylation at individual probes by current injection status, heroin, cocaine, speedball and HIV were tested separately using generalized estimating equations including age, gender, race, smoking status and cell heterogeneity as covariates. A joint analysis was also conducted. DNA methylation age was estimated for study subjects using the epigenetic clock method developed by Horvath et al. 2013. Gene ontology enrichment test was done by the missMethyl R package.

Results: DNA methylation at individual loci (cg03012169, $p=7.5\times10^{-8}$) is significantly associated with current injection drug use status after correction for multiple testing. HIV positive individual's average biological age is about 3 years older than their chronological age, but no differences were observed among HIV negative individuals, injection drug users and non-users.

Conclusion: In a preliminary study, we performed a genome-wide scan of methylation changes in a longitudinal study of injection drug use and identified genomic locations exhibiting significant changes in peripheral DNA methylation associated with injection drug use status. Individuals with HIV infection's biological age is older than their chronological age, which is consistent with the literature.