

**Title:** Circulating DNA methylation markers associated with injection status and HIV infection among chronic injection drug users in the ALIVE study.

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Liability to drug addiction has a complex etiology with substantial contributions from both genetic and environmental factors. Epigenetic status represents an intersection of these factors that has not yet been explored in longitudinal drug addiction epidemiologic studies. The goals of this AIDS Linked to the Intravenous Experience (ALIVE) study are to identify in longitudinal methylation data whether chronic injection drug use, abstinence and relapse are associated with blood DNA methylation marks and to test whether these marks are associated with DNA methylation differences comparing subjects with HIV (HIV+) to those without (HIV-). Among an ALIVE study subsample, 792 samples were selected longitudinally during periods of daily drug injection, cessation and relapse. DNA was isolated from peripheral blood buffy coat at multiple time points. Samples were taken at baseline from individuals with at least 10 years of IDU+, and the second sample followed at least six months of IDU-. An additional subset of samples was selected for 2+ years of abstinence followed by relapse and Genome-wide DNA methylation was assessed using the Illumina Infinium MethylationEPIC array. We will compare methylation status at each site during chronic use versus after cessation, during cessation versus after relapse, and in HIV+ versus HIV- subjects.