# DNA methylation levels as a biomarker for severity of opioid use

Allison N. Tegge

Department of Statistics, Virginia Tech, Blacksburg, VA; Virginia Tech Carilion School of Medicine and Research Institute, Roanoke, VA

Opioids are the leading cause of drug related overdose deaths. Several genomic mutations have been associated with increased risk for opioid dependence and addiction. These indicators do not provide insights into molecular alterations as a function of opioid use. In contrast, gene-level DNA methylation status can change over time and may serve as a biomarker for opioid dependence. Previous studies have shown differences in the DNA methylation levels of genes between opioid-dependent and opioid-naïve individuals. This work hypothesizes that the level of DNA methylation for opioid related genes would change as a function of the length of time an individual has used opioids. Preliminary results indicate that in publically available brain tissue of heroin overdoses, 6851 CpG sites show a large effect size (Pearson correlation $|\rho| > 0.5$, uncorrected p-value $< 0.01$) between age and duration of heroin with 45% showing an increase in methylation as the years of use increase and 55% of the sites showing a decrease in methylation. These sites annotate to 4191 genes, including 271 transcription factors, 181 cellular receptor proteins, and 47 miRNAs. Of importance is the inclusion of the Opioid Receptor Mu 1 OPRM1, and the dopamine receptor D3 (DRD3), two pivotal proteins responsible for signaling and previously found to be methylated and associated with addiction. Functional enrichment analysis using pathways from the KEGG database found eight significant pathways including Morphine Addiction, GABAergic Synapse, and TGF-beta Signaling (adj. p-value $< 0.05$). Quantifying a patient's DNA methylation may provide a useful biomarker for understanding the severity of their dependence and determining a personalized treatment protocol.