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Epigenome Profiling in Prefrontal Cortex Neurons Exposed to Opiates

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Opioid addiction (OA) has emerged as one of the most pressing public health crises in recent US history. Genetics is a major contributor to OA with an estimated 60% heritability: only somewhat less than schizophrenia (80%) which has recently seen substantial gains in identified underlying genetics and in rapidly increasing knowledge on the neurogenomic alterations, including the transcriptome, that affect cerebral cortex and other regions of the brain from diseased subjects. The long-term goal of our multidisciplinary, NIDA-funded project is to take a novel, integrated 'omics' based strategy to investigate the molecular basis of OA and uncover both genetic and epigenetic factors.

Here, we present an update and initial results from the first phase of our project, which aims to fine-map, at base pair resolution on a genome-wide scale, the distribution of the transcriptional histone mark, H3-acetyl-lysine 27 (H3K27ac) in prefrontal cortex neurons of 100 subjects who overdosed on opioids, along with matched control brains. We expect our resource to provide the field with critically needed cell type-specific insights into cis-regulatory sequences associated with epigenomic alterations after opiate exposure. In conjunction with additional datasets, including transcriptome RNA-seq profiling, we expect to gain deeper understanding into genome organization and function in the context of opiate exposure, including potential implications for the underlying genetic risk architecture(s) of OA.

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