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Association between elevated markers of DNA damage and higher frequency of somatic mutations in neurons in opioid use disorder

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Opioid use disorder (OUD) has been an increasingly serious health and social issue. Many health comorbidities are associated with OUD, including sleep problems. We characterized the RNA and protein level changes in OUD brain, especially to investigate if OUD, at the molecular level, was associated with changes in pathways related to cancer and neurodegeneration such as neuroinflammation, DNA damage, and DNA methylation. As nucleus accumbens (NAc) is connected to prefrontal cortex, amygdala and hippocampus, it plays the role of neural integration between motivation and action, contributing to behaviors such as feeding, sexual, and drug self-administration. Dorsolateral prefrontal cortex (DLPFC) is mainly involved in cognitive deficits associated with drug addiction. We want to study on these 2 brain regions to understand the mechanism of development and cognitive effect of OUD.
We collected NAc and DLPFC tissues from postmortem human brain (12 OUD and 12 unaffected subjects), first round of analysis on single nuclei RNA-seq and proteomic data showed DNA damage-related genes were enriched in RNA and protein level changes associated with OUD. As a next step, we proposed to characterize the somatic mutation pattern in different cell types in the brains of subjects with OUD compared to unaffected subjects.
Using *SComatic* software, single nuclei RNA-seq data detected somatic mutations potentially associated with OUD. We believe this line of research could shed light on the neurobiology of opioid addiction with the goal of identifying new avenues for treating OUD and co-occurring psychiatric disorders.