Submitter Name: Thao Vu
Submitted Email: thao.3.vu@cuanschutz.edu
PI Names: Katerina Kechris
PI Emails: katerina.kechris@cuanschutz.edu
Laura M. Saba
laura.saba@cuanschutz.edu

Identification of blood metabolite biomarkers for oxycodone exposure in rats through metabolomics

Thao Vu[1], Suneeta Godbole[1], Lisa Maturin[2], Olivier George[2], Laura M. Saba[3], Katerina Kechris[1]

[1]Department of Biostatistics & Informatics, Colorado School of Public Health, University of Colorado Anschutz Medical Campus;
[2]Department of Psychiatry, School of Medicine, University of California San Diego;
[3]Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus

Metabolomics studies of prescription opioid medications including oxycodone provide insights into biochemical mechanisms of the addiction cycle and prognosis prediction. Although oxycodone has an elevated abuse liability profile compared to other opioids, many human and rodent metabolomics studies have not been specifically focused on oxycodone. In this study, we investigated metabolomics changes associated with oxycodone exposure using plasma samples from 16 rats at pre-exposure and intoxication time points. The samples were profiled on the Metabolon platform to characterize a total of 941 metabolites. We employed k-Nearest Neighbor and binarization to impute metabolites with low and moderate levels of missingness, respectively. Of the 136 binarized metabolites, 6 showed differentially expression, including 5 present at pre-exposure but absent at intoxication (e.g., *adenine*), while *linoleamide* exhibited the opposite behavior. Among the 798 low-missing metabolites, 364 showed significant changes between pre-exposure and intoxication including *succinate*, *oleamide*, and *sarcosine*. We identified four pathways including *tryptophan metabolism* that were nominally enriched among the metabolites that change with oxycodone exposure. Furthermore, we identified several metabolites that showed nominal correlations with the Addiction Index (composite of oxycodone behaviors), 17 at pre-exposure and 9 at intoxication. In addition, there were 9 metabolites with their oxy-induced changes nominally correlated with the Addiction Index, including *sphingomyelins*, *methylhistidines*, and *glycerols*. In summary, not only were we able to capture oxy-induced changes in metabolic pathways using easily accessible blood samples, but we also demonstrated the potential of blood metabolomics to better understand addiction liability. This work is partially supported by NIDA (DA044451).