Submitter Name: Sierra Simpson
Submitted email: sisimpson@health.ucsd.edu
PI Name (if different): Olivier George
PI email (if different): Olgeorge@health.ucsd.edu

Drugs, Bugs, and SUDs: Leveraging the Microbiome and Metabolome to Predict Addiction Liability.

Sierra Simpson[1], Allegra Aaron[2], Molly Brennan[1], Brent Boomhower[1], Fred Matalon[1], Lani Tieu[1], McKenzie Palvich[1], Lisa Maturin[1], Leah-Solberg-Woods[3], Giordano de Guglielmo[1], Pieter Dorrestein[2], and Olivier George[1]

[1] Department of Psychiatry, University of California San Diego, La Jolla, CA 92093, USA
[2] UCSD School of Medicine, University of California San Diego, La Jolla, CA 92093, USA
[3] Wake Forest University Health Sciences, Winston-Salem, NC 27157, USA

Mounting evidence calls for a precision approach for the treatment and diagnosis of substance use disorders. There is a significant unmet medical need to expand the identification of biomarkers to determine the risk of addiction liability and develop novel therapeutics. Shifts in microbial communities impact the functionalization of bile acids and the release of metabolites such as short chain fatty acids, as well as intestinal permeability and the immune system. Recent evidence indicates that alterations of the gut microbiome modulates the neuronal ensembles active during intoxication and withdrawal states, making the gut-brain axis an appealing new target for translational investigation.

We leveraged a large dataset containing behavioral, microbiome, and metabolomic measures, from Heterogenous Strain (HS) rats obtained through the Cocaine and Oxycodone biobanks, to explore the microbiome and metabolome's potential to predict addiction risk. We hypothesized that novel biomarkers could be identified from the microbiome and metabolome using unbiased machine learning and artificial intelligence approaches.

Indeed, biomarkers from both microbiome and metabolome emerged in populations with both high and low addiction liability. The potential mechanism and durations of change have yet to be determined, however this work provides a foundation to use an unbiased multi-omic approach to evaluate potential targets that impact drug intake.