Submitter Name: Christiann Gaines
Submitter Email: hatalya@email.unc.edu
PI Name: Lisa Tarantino
PI Email: lisat@med.unc.edu

# Assessing the impact of compositionally distinct gut microbiotas on differences in initial cocaine sensitivity in closely related inbred mouse substrains

Christiann H. Gaines[1,2], Sarah H. Schoenrock[1], Ian M. Carroll[3], Fernando Pardo Manuel de Villena[1], Martin T. Ferris[1], Lisa M. Tarantino[1,4]

[1]Department of Genetics, [2]Neuroscience Curriculum, School of Medicine, [3]Department of Nutrition, Gillings School of Public Health and [4]Division of Pharmacotherapy and Experimental Therapeutics, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC

Substance use disorders are highly prevalent and impose a significant burden on society. Despite the prevalence of SUDs, there exist very few effective treatments. The lack of treatments is due, in part, to gaps in our understanding of the etiology of these devastating disorders. Risk for developing a SUD is influenced by genetics, the environment and gene by environment interactions. Identifying genetic mechanisms that increase SUD risk provides a potential avenue for novel treatments.

I performed genetic mapping in a reduced complexity cross (RCC) between two closely related inbred mouse substrains, C3H/HeJ (HeJ) and C3H/HeNTac (NTac), that differ in cocaine-induced locomotor activation. RCC mapping identified a suggestive locus on Chr 19 indicating that behavioral differences in C3H substrains may be influenced by non-genetic factors. I identified prominent differences in the composition of the gut microbiota in HeJ and NTac and hypothesized that the microbiota may play a role in substrain differences in locomotor sensitivity to cocaine. I cross fostered pups to dams of the alternate substrain to shift the composition of gut microbiota. 16S rRNA sequencing of fecal boli from foster dams and pups indicated that the microbiome of the foster pups matched that of the foster dams regardless of substrain. However, cross-fostered substrains maintained divergent locomotor response to cocaine. These data eliminated the gut microbiome as the cause of divergent cocaine-induced locomotor activation in these C3H substrains. We are currently testing candidate genes in the Chr 19 interval and investigating alternative hypotheses to explain the observed behavioral differences.