

Submitter Name: Dong-Binh Tran
Submitter email: dong-binh.tran@jax.org
PI Name (if different): George Weinstock
PI email (if different): george.weinstock@jax.org

Associations between microbiota and novelty behavior in mice with reference to cocaine addiction

Thi Dong Binh Tran², Hoan Nguyen², Jason A. Bubier¹, Erica Sodergren², Yanjiao Zhou³, Elissa J. Chesler¹, George Weinstock²

¹ The Jackson Laboratory Mammalian Genetics, 600 Main St, Bar Harbor ME,

² The Jackson Laboratory Genomic Medicine, 10 Discovery Way, Farmington CT,

³ Uconn Health, 263 Farmington Avenue, Farmington CT.

The gut microbiome plays a critical role in the onset and development of depression and substance use disorder through effects on the vagus nerve. Very few studies have looked at both stool and cecum as gut microbiome to evaluate which part of the gut is implicated in microbiome communication with the brain. Using cecal content and fecal pellets, obtained from cohorts of Diversity Outbred mice also characterized in novelty behavior assays revealed that cecal samples had higher alpha diversity than fecal ones. Cecal and fecal bacterial structures were very different, and high community similarity was observed among cecal contents. The whole microbial composition was mostly shared between cecum and feces, suggesting stable presence of bacteria in the large intestine. To test the hypothesis that gut microbiome affects the brain and novelty response behavior, we performed an integrative analysis using multiple approaches (Spearman correlation, generalized linear model, and feature selection-LASSO). We have observed that cecum cohort generated larger number of associations between microbes and novelty behaviors with stronger magnitude than the feces cohort. Associations were also opposed between cohorts. Depending on the method used, each cohort showed a specific association with novelty behaviors. However, three common genera in both cohorts such as *Chlostridium_XIVa*, *Intestinimonas*, and *Syntrophococcus*, were found to be significantly correlated to at least one novelty behavior in three different methods. These findings suggest that a primary difference in the microbial composition might lead to different implications for behavior, and provide new insight into gut-brain axis involved in novelty-related behavior.