Name: Eamonn Duffy
PI Name: Ryan Bachtell

Email: eamonn.duffy@colorado.edu
PI Email: ryan.bachtell@colorado.edu

Oxycodone Self-Administration Alters the Diversity and Composition of the Fecal and Cecal Microbiome in Two Genetically Divergent Rat Strains

Eamonn P. Duffy[1,2], John D. Sterrett[1], Luanne H. Hale[3], Jonathan O. Ward[3], Erika A. Mehrhoff[1,2], Daniel N. Frank[5], Laura M. Saba[2,4], Marissa A. Ehringer[1,2], Ryan K. Bachtell[2,3]

[1]Department of Integrative Physiology, University of Colorado Boulder;
[2]Institute for Behavioral Genetics, University of Colorado Boulder;
[3]Department of Psychology and Neuroscience, University of Colorado Boulder;
[4]Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus;
[5]Department of Medicine, Division of Infectious Diseases, University of Colorado Anschutz Medical Campus

Opioid use disorder (OUD) is an ongoing worldwide public health concern. The gut microbiome and genetic factors contribute to OUD-related phenotypes, including oxycodone-induced analgesia and reward. Here, we examine the effects of genetic background and oxycodone self-administration on the composition and structure of the fecal and cecal microbiome in two genetically divergent, inbred rat strains. Rats from the ACI/EurMcwi (n= 25F/20M) and M520/N (n = 17F/14M) strains self-administered intravenous oxycodone or saline. Both strains self-administered more oxycodone compared with saline with the M520/N strain consuming more oxycodone than the ACI/EurMcwi strain. Fecal and cecal samples were collected after the self-administration period and sequenced with 16S amplicon sequencing. Data were processed and analyzed using QIIME2 and R. Measures of alpha diversity (e.g., observed ASVs, Faith's PD) in the fecal microbiome was influenced by a strain-sex interaction, while diversity in the cecal microbiome had additive influences of strain and sex. Beta diversity analysis using unweighted and weighed UniFrac distances demonstrated that strain and oxycodone alter the community structure of the fecal and cecal microbiome. Several bacterial taxa were differentially abundant between strains and self-administration groups. These findings suggest that genetic background influences oxycodone self-administration, and both host genetics and oxycodone self-administration influence the diversity and composition of the gut microbiome.