Name: Kuranosuke Yamada Email: kyamad23@colby.edu
PI Name: Elissa Chesler PhD. PI email: elissa.chesler@jax.org

Mapping and Analyses of Differential Co-expression Networks of Striatum Tissue in Cocaine-treated, high-diversity mouse populations

Kuranosuke Yamada[1,2], Vivek M. Philip[2], Robyn L. Ball[2], Michael C. Saul [2], Center for Systems Neurogenetics of Addiction[2], and Elissa J. Chesler[2]
[1]Computational Biology, Colby College; [2]The Jackson Laboratory

The study of individual variation in addiction-related behavior in mice can uncover genetic mechanisms related to addiction vulnerability or resistance. Exposure to cocaine and other addictive substances has been shown to alter the coupled activity of brain molecular networks. We performed differential co-expression analysis on a high-diversity, reproducible mouse population, the Collaborative-Cross (CC), to evaluate changes in striatum gene co-expression networks following exposure to cocaine. This will enable the identification of hub genes and co-expression modules that are differentially co-activated following cocaine exposure, and to interpret these findings by identifying the corresponding cell pathways that become involved before and after cocaine exposure. RNA-sequencing was performed on the Striatum of high-diversity cocaine-treated (six injections of 10 mg/kg i.p cocaine HCl during a 19-day sensitization protocol) and saline treated controls from the CC mouse population (134 samples over 34 strains) to quantify average gene expression across different treatments and strains. Using the R-package, Weighted Correlation Network Analysis (WGCNA), we identified several modules in the co-expression networks of CC mice that become coupled after exposure to cocaine. These modules show a lower mean preservation of adjacency between eigengenes of the cocaine derived co-expression modules. Several well-known genetic regulators of cocaine related behavior in mice are represented in these coupled modules, including *Cyfip2* and others. By understanding the nature of molecular network dysregulation following drug exposure, we may identify early processes in the neurobiological response to drug that differ among different strains and individuals, thereby elucidating the biological mechanisms of addiction vulnerability.

This work was funded by NIH P50 DA039841 and R01 DA037927 to EJC.