Submitter Name: Heidi S. Fisher
Submitted Email: heidi.fisher@jax.org
PI Name: Elissa J. Chesler
PI Email: elissa.chesler@jax.org

Identification of strain differences in transcriptional responses to cocaine across stages of drug self-administration in mice with high and low rates of acquisition and extinction

Heidi S. Fisher[1], Troy Wilcox[1], Leona Gagnon[1], Hao He[1], Vivek M. Philip[1], Robyn L. Ball,
[1] Erik B. Bloss[1], Elissa J. Chesler [1]

[1]The Jackson Laboratory, Bar Harbor, ME

Mounting evidence provides increased support for the association between genetic variation and susceptibility to substance use disorder in humans and related behaviors in model organisms. However, understanding how changes in neural gene expression differ across the behavioral phases of drug self-administration in genetically distinct populations remains unclear. Here we compared transcriptional profiles of three mouse stains with differing genetic backgrounds and disparate behavioral patterns of cocaine intravenous self-administration. Using a multifaceted design, we find that all strains share some transcriptional response patterns during acquisition and extinction of drug seeking behavior, as compared to mice with no cocaine exposure and those that were exposed but failed to acquire drug seeking behavior, while other changes in gene regulation are strain specific. In addition, we contrast these transcriptional changes with preliminary data on dendritic morphology and density suggesting that changes in cocaine self-administration may be associated with neuroplasticity. Together, these findings suggest that both previously discovered and unknown transcriptional correlates of drug self-administration differ among strains with different vulnerability to acquisition and maintenance of drug seeking behavior. Identifying these genes, their regulatory mechanisms, and the role they play in neurobiological mechanisms of addiction is critical to unraveling and addressing their effects on substance use disorder in people. Funded by The Jackson Laboratory, R01 DA37937, and P50 DA039841.