Name: Lisa Tarantino   Email: lisat@med.unc.edu

Genetic mapping of initial locomotor sensitivity to cocaine in two divergent Collaborative Cross inbred mouse strains

Sarah A. Schoenrock[1,3], Christiann H. Gaines[1,3], Padam Kumar[1], Saad Khan[1], Center for Systems Neurogenetics of Addiction[3] and Lisa M. Tarantino[1,2,3]

[1]Department of Genetics, School of Medicine, [2]Division of Pharmacotherapy and Experimental Therapeutics, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC USA and [3]Center for Systems Neurogenetics of Addiction (CSNA), The Jackson Laboratory, Bar Harbor, ME USA

The Collaborative Cross (CC) is a heterogeneous mouse population derived from 8 inbred mouse strains and designed for systems genetics analyses. The genetic heterogeneity present in the CC yields phenotypic diversity far exceeding that found in commonly used inbred mouse strains. Phenotypic screens yield identification of CC mouse strains suitable for studying biological and pharmacological mechanisms underlying disease. The CC also provides a platform for mapping and identification of genes that contribute to complex traits. The Center for Systems Neurogenetics of Addiction (CSNA) is using the CC and the Diversity Outbred (DO) population derived from the same 8 inbred strains, to identify biological relationships between stages of cocaine addiction and behaviors that predict drug abuse. We identified two CC strains, CC004/TauUncJ and CC041/TauUncJ, that differ for initial locomotor sensitivity to cocaine, acquisition of intravenous cocaine self-administration, and other addiction-relevant behaviors. In order to identify genomic regions association with initial sensitivity to cocaine, we crossed males and females from each CC strain with C57BL/6NJ mice to produce two F2 intercross populations for genetic mapping. Combined cross mapping identified genome-wide significant QTL on Chrs 7 and 11. CSNA mapping and gene expression data from the CC and DO were used along with bioinformatics strategies to identify high-priority candidate genes in those regions.