

Genome wide association study of behavioral, physiological and gene expression traits in a multigenerational mouse intercross

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Genome wide association analyses (**GWAS**) in model organisms have numerous advantages compared to human GWAS, including the ability to use populations with well-defined genetic diversity, the ability to collect tissue for gene expression analysis and the ability to perform experimental manipulations. We examined behavioral, physiological, and gene expression traits in 1,063 male and female mice from a 50-generation intercross between two inbred strains. We used genotyping by sequencing (**GBS**) in conjunction with whole genome sequence data from the two founder strains to obtain genotypes at 4.3M SNPs. As expected, all alleles were common (mean MAF=0.35) and linkage disequilibrium degraded rapidly, providing excellent power and mapping precision. We identified 126 genome-wide significant loci for 50 traits, 7,081 *cis*-eQTLs and 1,476 *trans*-eQTLs from hippocampus, striatum and prefrontal cortex. We replicated several loci that were identified using an earlier generation of this intercross, including an association between locomotor activity and a locus containing a single gene, *Csmd1*. We also identified a *cis*-eQTL for *Csmd1* that mapped to this locus. Finally, we showed that *Csmd1* mutant mice recapitulated the phenotype associated with this locus. Our results demonstrate the utility of this population, identify numerous novel associations, and provide examples of replication in an independent cohort, which is customary in human genetics, and of replication by experimental manipulation, which is a unique advantage of model organisms.