Effect of microRNA expression on alcoholism: A study in a panel of recombinant inbred mouse strains

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MicroRNAs (miRNAs) are small non-coding RNAs that bind messenger RNAs and potentially affect their functionality. We conducted a high-throughput investigation designed to discover differences in miRNA expression levels in alcohol naïve animals that influence predisposition to alcohol-related phenotypes in a panel of mouse strains. We examined expression quantitative trait loci (eQTL) affecting the miRNA expressions and compared them with known alcohol related QTL found by prior studies using Bayesian QTL mapping methods. We also found and studied eQTL hotspots and investigated their role in controlling the alcohol-related phenotypes.

The LXS RI panel is derived from two inbred progenitor strains (Inbred Long Sleep and Inbred Short Sleep), which were selectively bred for differences in sensitivity to the hypnotic effects of an acute dose of alcohol. Using existing genotype data on the panel and newly generated miRNA sequencing data, we explored the genetics of miRNA expression. Most of the usual statistical tools are inappropriate for this purpose due to the discrete nature of the sequencing. We used novel statistical model for the hypothesis testing and subsequently controlling the false discovery rate. A number of miRNA eQTL were identified and several of these miRNA eQTL are from to the same region of the genome that regulates the alcohol phenotypes of interest. In particular, several eQTL identified by this study were close to the QTL related to the 'Sleep time' and the 'Drinking in the dark' phenotypes. An enrichment method was used to detect eQTL hotspots. An alternative kernel-based method was also applied to find regions in the genome significantly associated with the miRNAs.

The miRNAs significantly related to such SNPs regulating the alcohol phenotypes can be important in the research of addiction and further studies can reveal their functional mechanism in controlling the alcohol phenotypes.

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