Differential fear learning and anxiety-like behavior mediated by quantitative trait loci (QTL) on chromosome 10

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C57BL/6J (B6) and A/J (AJ) inbred mice differ in freezing to context with AJ mice displaying a greater degree of freezing to context compared to B6 mice. Previously, we used a standard fear conditioning paradigm (FC) in a panel of chromosome substitution strains (CSS) where each strain is created by introgressing a single chromosome from the AJ strain on an otherwise uniform B6 genetic background. In that study, C57BL/6J-Chr10^{A}/NaJ mice (CSS-10) showed higher freezing to context and to tone compared to B6 mice suggesting that pleiotropic alleles influencing both innate and learned fear may be present on chromosome 10. To determine the chromosomal region corresponding to these differences, a F_2 cross was produced between B6 and CSS-10 mice. We identified a region on the distal portion of chromosome 10 that corresponded to both freezing to context and to tone with a Bayesian 95% confidence interval spanning approximately 17.43 Mb (110.23-127.66 Mb). To distinguish between learning and innate fear, we have bred and phenotyped two congenic lines spanning most of the confidence interval. One of the congenic lines spans from 122 to 127.63 Mb while the other line spans from 127 to 127.63 Mb. The larger congenic region captures both phenotypes of elevated freezing to context and tone while the smaller congenic region captures only elevated freezing to tone suggesting the presence of two loci affecting innate and learned fear. By sequencing boundaries and looking at polymorphisms in our congenic intervals, we can gain a better sense of a region that contains genes affecting anxiety-like behavior in mice that may also contribute to pathogenic anxiety in humans.