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Genetic Variation in Alcohol Induced Modulation of Drosophila snoRNAs

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Alcohol abuse and alcoholism are significant public health problems. Alcohol consumption during pregnancy can result in birth defects, collectively referred to as fetal alcohol spectrum disorder (FASD). Identifying genetic factors that contribute to susceptibility to FASD in human populations is challenging, but can be approached in the Drosophila model. We used 100 inbred wild-derived lines of the *Drosophila melanogaster* Genetic Reference Panel to identify transcripts that undergo altered regulation when flies are reared continuously on ethanol. These transcripts include a large group of evolutionarily highly conserved H/ACA class snoRNAs, which undergo coordinated up- or downregulation depending on the genetic background, in females only. H/ACA class snoRNAS mediate pseudouridylation of ribosomal RNA and their alcohol-induced modulation is independent of variation in expression levels of the host genes that harbor them. Variation in expression of the non-protein coding gene *Uhg4* is correlated with variation in expression of the alcohol sensitive H/ACA array of snoRNAs, whereas variation in expression of *Cyclin E*, previously implicated as a central hub gene in a genetic network associated with variation in viability and development time upon alcohol exposure, is correlated with variation in expression of the host genes. Both *CycE* and *Uhg4* are prominently expressed in ovaries. Our observations suggest that modulation of host gene expression mediated via a *CycE* pathway and H/ACA snoRNA expression mediated via a *Uhg4* pathway regulates ribosome biogenesis as an adaptive mechanism to chronic alcohol exposure and may represent a Drosophila model for FASD. (supported by AA016560 and DA041613)