SWI/SNF chromatin remodeling complexes are required for normal behavioral responses to acute ethanol exposure

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Alcohol Use Disorder is a significant social problem, and there is much interest in understanding relevant targets of ethanol's action. We use *C. elegans* to model the acute effects of ethanol on neuronal function to identify the molecular targets of ethanol and determine the mechanisms of the development of tolerance to those effects.

To ask if there is a role for the regulation of chromatin structure in ethanol response behaviors, we examined the role of SWI/SNF chromatin remodeling complexes in acute behavioral responses to ethanol in worms. We found that different SWI/SNF complexes regulate different components of the acute response to ethanol: SWI/SNF BAF complexes are required for the initial depressive effects of ethanol, whereas SWI/SNF PBAF complexes are required for the development of acute ethanol tolerance. Although SWI/SNF complexes play important and diverse roles in many tissues, we found that they are required in adults and in neurons for normal ethanol responses (Mathies *et al*, 2015).

We predict that SWI/SNF complexes regulate the expression of genes that are important for determining the level of acute sensitivity to ethanol and the development of acute tolerance to ethanol's effects. We have focused first on the development of tolerance to ethanol. To identify the mediators of the response to ethanol, we have performed gene expression studies in which we are comparing several strains to identify PBAF-regulated genes specifically in adult neurons. There are several over represented classes among the differentially regulated genes in our dataset. One particularly interesting group is genes that are involved in lipid metabolism, and we are currently testing a model in which lipid effects on membrane microarchitecture, and the proteins contained within, modulate the behavioral effects of ethanol. One mechanism of SWI/SNF modulation of ethanol responses may be through regulation of these lipid mediators.

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