

Potential novel genetic pathway for alcoholism

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A novel mutation found in a mouse gene might provide new insights into the genetic roots of alcoholism in humans, according to a study led by researchers at the Ernest Gallo Clinic and Research Center and the University of California, San Francisco. The study is published August 12th in the open-access journal *PLoS Genetics*.

The mutation, which the researchers have named Lightweight, is in the mouse version of a gene called *unc-79*. Previous studies in worms and flies have shown that *unc-79* is associated with altered sensitivity to a variety of anesthetics, including alcohol. The mutant mice are more sensitive to alcohol than their normal, wild-type littermates, and voluntarily consume more alcohol than normal mice when offered the choice between alcohol and water.

Lead author Dr. David Speca says that the name Lightweight refers to the observation that when *unc-79* mutant mice were injected with high doses of alcohol "they were knocked out for far longer than normal mice."

The function of *unc-79* is not well understood, says Speca, but he notes that experiments by other researchers suggest it may interact with a particular neuron channel (a complex of proteins essential to nerve cell function), named NALCN, to influence neuronal responses to alcohol. Although this study did not demonstrate an interaction with this channel in Lightweight mice, Speca says that follow-up experiments in the roundworm *Caenorhabditis elegans* showed that the NALCN channel

influences responses to alcohol, "suggesting that this response may be conserved from worms to mice to humans."

Studies of human twins have suggested that there is a [genetic component](#) to alcoholism, but, according to Specca, it is likely that there are multiple genes that contribute to the disease, each with its own effect, making it difficult to identify the causative factors. The question now, he says, is whether *unc-79* and the NALCN neuron channel turn out to be associated with altered responses to [alcohol](#) in humans.

"Nobody has ever studied these genes in humans before," notes Specca. "There's a chance that it's part of a new and relatively unexplored biochemical pathway that may tell us something about human susceptibility to alcoholism."

More information: Specca DJ, Chihara D, Ashique AM, Bowers MS, Pierce-Shimomura JT, et al. (2010) Conserved Role of *unc-79* in Ethanol Responses in Lightweight Mutant Mice. PLoS Genet 6(8): e1001057. [doi:10.1371/journal.pgen.1001057](https://doi.org/10.1371/journal.pgen.1001057)

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