Gene mutation in worms key to alcohol tolerance

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Scientists used the nematode worm as a model to look at the role genes play in alcohol tolerance.

(PhysOrg.com) -- The work follows a study carried out by Oregon Health and Science University, which suggested a link between a gene mutation in mice and tolerance to alcohol. Researchers at Liverpool have investigated this in worms, looking specifically at the role the gene plays in communication between cells in the nervous system.

This gene specifies the ways in which amino acids arrange themselves into a protein called UNC-18 – or Munc18-1 in humans, an essential

component of the nervous system. Researchers found that a naturally occurring change in this gene can result in a change in the nature of one of the amino acids, which then alters communication between cells in the nervous system. As a result of these changes the nervous system becomes less sensitive to the effects of alcohol, allowing the body to consume more.

Professor Bob Burgoyne, Head of the University's School of Biomedical Sciences, explains: "Alcohol consumption can affect the nervous system in a number of ways. Low concentrations of alcohol can make the body more alert, but high concentrations can also reduce its activity, resulting in motor dysfunction and a lack of coordination. Some people, however, are more susceptible to these effects than others, but it has never been fully understood why this is.

"We used the nematode worm as a model to look at the role genes play in alcohol tolerance because all of the worm's genome has been characterised and we can therefore identify its genes easily. The gene we looked at corresponds to a gene in humans that performs the same function in the nervous system. Mutations in genes can occur naturally without any known cause and will persist if they are not particularly harmful."

Dr Jeff Barclay, co-author of the research, added: "We investigated alterations in amino acids in two genetically identical worms. One carried a mutation that was exactly the same as the genetic change our American colleagues found in mice and the other carried a different change within the same gene. Both these mutations altered the way communicate occurs between cells in the nervous system. The mutations reduce the negative behavioural effects of alcohol and so more can be consumed before the body starts to react badly to it.

"Now that we have shown the link between the gene and alcohol

tolerance in worms, it is possible to search the human gene to see if there are any spontaneous changes that could help identify individuals with a predisposition to alcoholism."

The research is published in *Molecular Biology of the Cell.*

Provided by University of Liverpool