# Study finds genes behind alcohol sensitivity in fruit flies

October 31 2007

Some fruit flies can drink others under the table. Now, scientists at North Carolina State University have a few more genetic clues behind why some flies are more sensitive to alcohol than others. And the results might lead to more knowledge about alcoholism in humans.

After genetically modifying fruit flies to be either extremely sensitive or extremely resistant to alcohol – lightweights or lushes – the NC State scientists found that a number of fruit fly genes undergo changes when sensitivity to alcohol changes.

A number of these genes, the researchers report, are similar to genes found in humans, suggesting that they may be good targets to study human predisposal to alcoholism.

The research is published in the November edition of *Genome Biology*, which is available online at http://genomebiology.com.

The research team – Dr. Tatiana Morozova, a post-doctoral researcher in zoology; Dr. Trudy Mackay, William Neal Reynolds Professor of Genetics; and Dr. Robert Anholt, professor of zoology and genetics – used a unique approach in the study.

Rather than examining gene changes after exposure to alcohol and the development of tolerance to it, the NC State study first artificially selected flies for alcohol sensitivity – creating the lushes and the lightweights – and then, in a "whole-genome" approach, examined the

entire genome, or set of all genes, to find genes that had consistent changes in expression as a response to the artificial selection.

"We wanted to find the genetic factors that changed when flies became more sensitive or more resistant to alcohol, knowing that genes that undergo changes are potential candidate genes for mediating sensitivity," Anholt said.

In the study, flies were exposed to alcohol vapors in a so-called inebriometer, a long vertical tube filled with a number of slanted platforms onto which the flies can cling. As flies became inebriated, they fell from platform to platform until they became so intoxicated that they fell to the bottom of the tube, where they were collected.

"When you expose flies to alcohol, they go through the tube at a rate more or less determined by their genetic background," Mackay said.

By mating the most extreme lightweights with other extreme lightweights for 25 generations and mating extreme lushes with other extreme lushes for 25 generations, the researchers created both "lightweight" flies that needed just a minute or two of exposure to fall to the bottom of the inebriometer and fly "lushes" that finally reached the tube's bottom after a "bender" of about 18 minutes.

More than 1,500 genes changed in testing, the study showed. Tests of 35 especially promising candidate genes showed 32 genes affecting alcohol sensitivity. Seventy-two percent of these 32 genes have human counterparts, the researchers said.

Some of these changed genes are involved in one of the metabolic pathways that converts alcohol into fat, and have not been previously studied for a correlation to alcohol sensitivity, the researchers added.

Finding relevant genes, Mackay says, could some day lead to devising a drug for people with higher genetic risk factors for alcoholism.

Source: North Carolina State University