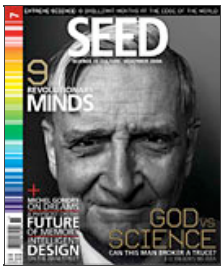

If You Can Read This, You May Be An Addict

The Self-Perpetuating Cycle of Smoking and Drinking

A False Tolerance for Red Bull

On the Fly

A Genetic Basis for Alcoholism

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by **VIRGINIA HUGHES** • Posted November 1, 2006 01:18 AM

Give them a little booze, and fruit flies get rowdy. After too much alcohol, they'll stagger and, eventually, pass out. But for a select few flies, alcohol's effects are much weaker. Now, scientists have identified the genetic mutation responsible for this difference.

The new fruit fly research, published with a corroborating mouse study in the Oct. 6 issue of the journal *Cell*, may pave the way for the future development of drug targets to treat human addictions.

"These two papers implicate a whole new pathway in the behavioral response to alcohol," said Adrian Rothenfluh, lead author of the fruit fly study and a neuroscientist at the University of California, San Francisco. These gene families have already been studied in connection to cancer and cardiovascular disease, "and now we might want to look at them in the context of addictions," he said.

Rothenfluh's team tested flies' resistance to alcohol by placing them in transparent tubes, passing ethanol vapor over the tubes, and videotaping the reactions. After five to 10 minutes of alcohol exposure, the flies typically became hyperactive. But after another 10 minutes of exposure, Rothenfluh said, the alcohol "reaches a level they can't take anymore, and they start falling on their backs."

But when Rothenfluh did the same behavioral test on one strain of genetically engineered flies, it took much longer—about 30 minutes—before they keeled over.

Finding these alcohol-resistant mutants was especially intriguing, Rothenfluh says, because human studies spanning decades have shown that people who have a higher resistance to their first drinks are more likely to become alcoholics.

"Flies are much more like humans than we ever thought before," Rothenfluh said.

The geneticists analyzed the mutant flies' DNA and found a key mutation—dubbed *white rabbit*—that disrupted the function of a family of genes known to be involved in regulating the actin cytoskeleton—a protein scaffold that allows cells to move.

In the related mouse study, researchers found that mice lacking a gene called *Eps8*—also known to be involved in actin function—were resistant to the intoxicating effects

of alcohol injected into them.

Still, human alcoholism has both environmental and genetic components. Children who are sexually abused or exposed to other physical trauma are much more likely to become alcoholics. And women, especially, start drinking heavily in response to stress.

Moreover, the genetic component of human alcoholism involves many genes, each having a small effect, said Mary-Anne Enoch, a scientist at the Laboratory of Neurogenetics at the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

"In humans we're looking at hundreds of genes interacting with each other," she said. "No one gene is going to stick out."

An interesting future experiment, Enoch said, would be to see if these mutated flies and mice have different alcohol withdrawal behaviors. One of the aims of human addiction research is to find drugs to protect people from the neurotoxic, or neuron-killing, effects of withdrawal.

"At the moment," she said, "there are a few drugs out there, but they're primitive."

Though the animal studies are helpful, David Goldman, chief of the NIAAA neurogenetics lab, said he would rather focus on human genetic studies.

"The findings point to molecules and genes that should be studied in other organisms, including the human," he said in an email.

Plus, he added jokingly, "I'm hoping that one day the genes we discover that influence human behavior will help us to address the behavioral maladies of the fruit fly."

Mutant Fruit Flies Have Genetic Resistance to Alcohol, written by Virginia Hughes, posted on November 1, 2006 01:18 AM, is in the category Plants & Animals.