

Driving Thirst

SCIENTISTS IDENTIFY A GENE THAT SENDS FLIES TO THE WATER BOWL.

Camels sport humps on their backs to store it and geese fly thousands of miles in search of it. The need for water is ubiquitous, yet the underlying genes that motivate animals to seek it have remained mysterious.

Now, Kristin Scott, an HHMI early career scientist at the University of California, Berkeley, has uncovered a gene, called *pickpocket 28* (*ppk28*), that regulates fruit flies' ability to detect water and how much time they spend drinking.

Scott and her team set out to identify genes involved in taste. They first compared genes expressed in the feeding appendages of flies that lacked taste neurons with those in normal flies. When they narrowed in on ion channels that were enriched in taste tissue, they found the *ppk28* gene.

The researchers then measured the activity of neurons stimulated with taste compounds by imaging changes in a fluorescently labeled calcium-sensitive ion channel and by inserting tiny electrodes into the flies' taste-sensing bristles. They found that neurons expressing *ppk28* activated strongly when flies tasted water, but their activity diminished when flies tasted other substances, such as sugars, bitter compounds, salts, and acids.

Moreover, neurons did not respond when flies without *ppk28* drank water. And whereas normal flies drank water for about 10 sec-

onds, mutant flies sipped for only 3 seconds. When researchers reintroduced the gene into mutant flies, their taste neurons fired when they drank water, and they went on to drink it for 12 seconds.

The results indicate that both *ppk28* and taste neurons are necessary for sensing and consuming water. To confirm the role of the gene in detecting water, Scott and her team expressed *ppk28* in neurons normally activated only when flies taste something bitter. Remarkably, these neurons began firing when flies drank water. The findings were published May 6, 2010, in *Nature*.

Because the class of proteins is found in many organisms, Scott

believes *ppk28* plays a role in water consumption in other animals, perhaps even humans. In future studies, she plans to investigate how water activates ion channels and how internal drives, such as hunger and thirst, affect the detection and consumption of water and sugar.

■ -JANELLE WEAVER



A fruit fly sucks up water with its narrow feeding appendage.

IN BRIEF

ANXIOUS MICE

Turning off a gene in mice makes them anxious, skittish, and obsessive about grooming, HHMI scientists have discovered. The engineered animals could become an ideal model for studying obsessive-compulsive disorder (OCD), characterized in humans by repetitive behaviors and anxiety.

The researchers, led by HHMI investigator Shahin Ruffieux of Weill Cornell Medical College, weren't originally studying OCD. They set out to find genes involved in the interplay between blood stem cells and blood vessel cells. Their hunt led them to a gene called *slitrk5*, which is expressed in blood stem cells and vascular cells but is most active in the brain.

To probe *slitrk5*'s function, the researchers engineered mice without the gene. While the mice appeared normal at birth, after three months they exhibited signs of anxiety: they avoided open and high spaces, preferring corners and enclosed areas. Moreover, the altered mice jumped at any touch and had bald patches on their faces from persistent grooming, which was relieved with Prozac, a standard drug used to treat patients with OCD.

Ruffieux and his collaborators found that *slitrk5*-deficient mice have structural defects in the striatum, a brain region associated with a decrease in the number of glutamate receptors. These unique abnormalities are strikingly similar to those found in the brains of people with OCD. The results were published in the May 2010 issue of *Nature Medicine*. They hope further research will illuminate just how the gene relates to the extreme behaviors and may give scientists hints about the molecular causes of OCD in humans.

COMPLEX CAUSES OF DIABETES

It's not just genes, diet, and exercise but perhaps also environmental pollutants and vitamins that are associated with a person's risk of type 2 diabetes, according to a new study. Led by Atul Butte, an HHMI physician-scientist early career awardee at the Stanford University School of Medicine, the large-scale analysis used records from the Centers for Disease Control and Prevention (CDC) to make the links.

Every two years, the CDC takes a snapshot of the nation's health, using questionnaires and blood and urine samples from individuals. They test the

samples for hundreds of pollutants, infectious agents, nutrients, and compounds, including blood sugar. High blood sugar levels signal diabetes.

Butte and his collaborators analyzed the relationship between blood sugar levels and 266 environmental factors in four sets of CDC data, spanning 1999 through 2006. They controlled for the effects of age, body mass index, gender, ethnicity, and socioeconomic status, which are already linked to type 2 diabetes.

The researchers were left with four factors that are statistically linked to one's risk for diabetes. High blood levels of polychlorinated biphenyls (PCBs)—an industrial pollutant—or heptachlor epoxide—a breakdown product of heptachlor, which was used to kill termites in the 1960s and 1970s but has since been banned for most uses—were also linked to greater chances of high blood sugar. In addition, they found a connection between high blood sugar and high levels of the most common form of vitamin E in the American diet, gamma-tocopherol. Last, they confirmed previous studies showing that high amounts of beta-carotene, a form of vitamin A, are protective against type 2