Alcohol-Loving Mice Spur Gene Search

Mice bred to exhibit various degrees of preference for drinking alcohol may, by virtue of their scientifically controlled couplings, help scientists identify genes that contribute to alcoholism. Which genes influence an animal's imbibing seems to depend on the animal's sex.

Two groups of genes show links to excessive alcohol consumption in the offspring of these mice, assert Lee M. Silver, a molecular biologist at Princeton University, and his colleagues. A particular chromosome 2 region, when inherited from either parent, appears to promote alcohol drinking in males, the researchers contend; a specific variation of a portion of chromosome 11 inherited from the father boosts alcohol use in females.

Both chromosome segments contain genes of known function that may correspond to human genes and could plausibly contribute to alcoholism, though not causing it on their own, Silver's group asserts in the June NATURE GENETICS.

Studies conducted by other investigators have uncovered statistical links between extreme alcohol preference in mice and the same portion of chromosome 2 tagged in the new data, as well as segments of chromosomes 3 and 9.

"Silver's study has more statistical rigor than any prior work," asserts John C. Crabbe, a behavioral geneticist at the Veterans Affairs Medical Center in Portland, Ore. "But I'm not sure how to relate its findings to the existing scientific literature."

The Princeton researchers began with 234 mice bred to exhibit one of three conditions if given access to both an alcohol solution and pure water—avoidance of alcohol, moderate intake of alcohol, or consistent preference for alcohol.

The moderate alcohol drinkers, a hybrid strain that had been produced by breeding heavy alcohol consumers with alcohol avoiders, possess naturally occurring genes that inhibit both extremes, the scientists theorize.

They then bred 262 mice by mating hybrid fathers with alcohol-preferring mothers and bred 73 mice by mating hybrid mothers with alcohol-favoring fathers.

Male offspring that drank excessive amounts of alcohol displayed a signature chromosome 2 segment more frequently than other mice, regardless of which parent engaged in heavy drinking, the investigators contend. This segment contains a cluster of seven genes that help regulate sodium activity in the brain and that may contribute to an alcohol preference, they argue.

Female offspring that favored alcohol had a unique chromosome 11 region more often than other mice, a trait they inherited from fathers that drank large amounts of alcohol, Silver's team says. A gene that inhibits the action of the neurotransmitter serotonin lies in this part of chromosome 11. Previous research has linked low serotonin concentrations to increased alcohol consumption.

Researchers have not yet located the exact genes in mice that influence alcohol drinking, asserts David Goldman, a neurogeneticist at the National Institute on Alcohol Abuse and Alcoholism in Rockville, Md., in an accompanying comment. Human genes equivalent to those that operate in alcohol-favoring mice may not exist, he adds. Intensive study of the human genes that regulate serotonin activity will be required for insight into alcoholism and other psychiatric disorders, in Goldman's view.

Rodent research still offers a promising starting point, according to Crabbe. In his earlier studies of female mice, he found a link between elevated alcohol use and a chromosome 9 region bearing a gene that regulates certain serotonin receptors in the brain. This statistical relation is significant but relatively weak, Crabbe says.

"It would be nice to find specific genes with powerful effects on alcohol drinking," Crabbe remarks. "But it's likely that many genes have moderate effects on this behavior."

Other independent research on the same strains of mice studied by Silver's group has linked a chromosome 10 area to morphine preference. Alcohol and morphine preference may be genetically distinct traits in these mice, according to the Princeton group. *—B. Bower*

Freezing water droplets to novel icy peaks

A water droplet rests on a frigid aluminum plate. As it freezes rapidly from the bottom up, the droplet undergoes a subtle change in shape, bulging slightly upward. By the time the droplet turns completely to ice, a distinctive cusp protrudes from its top surface.

When Stephen H. Davis of Northwestern University in Evanston, Ill., first asked his colleagues the question of what would happen as a water droplet freezes, he suspected that its shape would change, perhaps because water expands as it turns to ice.

"We did get this very peculiar shape—a sharp point instead of a rounded top," Davis says. The explanation of this unexpected shape, however, turned out to involve the angles between solid, liquid, and air at the interface where all three meet, which moves as the water freezes.

Understanding this effect may prove useful for modeling what happens when materials confined by surface tension rather than the walls of a container solidify on Earth—or in space under microgravity conditions. Containerless solidification is an important technique for producing ultrapure materials.

Davis, M. Grae Worster of the University of Cambridge in England, and Daniel M. Anderson, now at the National Institute of Standards and Technology in Gaithersburg, Md., report their findings in the June JOURNAL OF CRYSTAL GROWTH.

The researchers used 35-microliter droplets of distilled water, freezing them from below at a range of plate temperatures. Freezing times were typically about 40 seconds, providing insufficient time for

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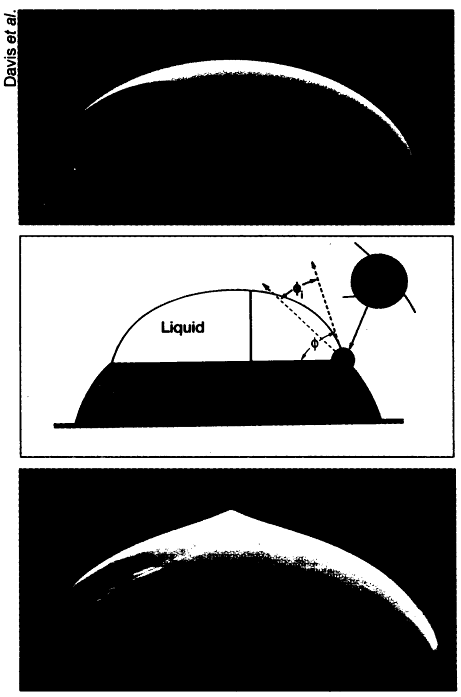

A water droplet at room temperature rests on an aluminum plate (top). The cold plate causes the droplet to freeze from the bottom up, producing a solidification front that advances upward. In the middle illustration, the inset shows a magnified view of the solid-liquid-air interface at the droplet's edge. The difference (ϕ_l) between the contact angles of the liquid (ϕ) and the solid lead to the formation of a cusp on the top surface of the frozen droplet (bottom).