

Gene for Manic Depression?

A decade-long study of the genetically and culturally isolated Amish population in southern Pennsylvania has yielded the first evidence that there is a gene somewhere along the tip of a specific chromosome that predisposes its bearers to manic depression, and possibly to severe depression without mania. Genetic studies of other populations indicate, however, that there is no single "manic-depression gene."

The critical gene among the Amish is in the area near the short end of chromosome 11, report psychiatrist Janice A. Egeland of the University of Miami (Fla.) School of Medicine and her colleagues based at the Massachusetts Institute of Technology and Yale University. Although the DNA sequence of the gene, which determines its physiological and biochemical functions, has not been established, the gene is dominant, say the researchers in the Feb. 25 NATURE. Its inheritance from either parent renders a person susceptible to manic depression.

"The real challenge now will be to find an assay that will identify the specific gene [involved in manic depression]," notes molecular biologist Daniela S. Gerhard, a participant in the project who is now at Washington University in St. Louis.

Egeland and her associates have had little success in pinning down a chromosome position for such a gene in the past, but recent advances in recombinant DNA techniques permitted the identification of two genes at the tip of chromosome 11 that appear together only among Amish family members with a psychiatric "mood disorder."

The study focused on three Amish families with mood disorders spread through three generations. Of the 81 family members, 14 had some form of manic depression, 5 had severe depression and 62 had no psychiatric symptoms.

DNA samples were isolated from blood

samples and the investigators located areas at the tip of chromosome 11 containing one gene responsible for the production of insulin and another, called *Ha-ras-1* (*HRAS1*), that produces a protein believed to be involved in benign forms of cancer. DNA-cutting enzymes were used to slice into these two sites so that genetic forms or mutations of each gene could be identified.

In the two oldest Amish generations under study, specific forms of insulin and *HRAS1* appeared in combination only among those with a mood disorder. In the third generation, the same pattern occurred among those with psychiatric symptoms, as well as among some symptom-free individuals. Since manic depression often is not noticeable until sometime between 15 and 35 years of age, the researchers say the latter group may be at risk for developing the illness later.

A computer program was then used to determine the probability of the two markers appearing at the same chromosome position as the proposed gene predisposing individuals to manic depression. Based on the estimate that 85 percent of those in the sample who

inherited the gene would develop the disorder, this assumption was statistically confirmed. The exact location of the proposed gene appears to be closer to the *HRAS1* position.

It is not known whether chromosome 11 markers will appear in Amish families with mood disorders that do not include manic depression, acknowledge the researchers. Theoretically, the ability to tag at-risk individuals through DNA analysis could lead to studies of life events that might trigger the genetic predisposition. For now, the scientists are considering possible molecular mechanisms of manic depression, such as a defect in a chromosome 11 gene involved in formation of the neurotransmitter dopamine.

Suspicious that one gene does not underlie all cases of manic depression are supported by two other studies in the same issue of NATURE. DNA analysis by European researchers of families in Iceland with several generations of mood disorders and a similar analysis of non-Amish families in the United States, reported by scientists at the National Institute of Mental Health, found no evidence of a gene predisposing to manic depression at the end of chromosome 11.

"This isn't surprising," says Gerhard. "Manic depression occurs among 1 percent of the population and I wouldn't expect it to be a one-gene disease."

— B. Bower

Biological warfare research under fire

The Department of Defense (DOD) and its growing efforts in biological-warfare research may have hit a snag last week, when the federal agency agreed to submit its collection of biological warfare research programs to far-reaching environmental impact studies. Agreement to conduct the studies, which are expected to take nearly two years to complete, settles a lawsuit brought against the agency last September by an environmental action group based in Washington, D.C.

The Foundation of Economic Trends claimed in its suit that the government was violating the National Environmental Policy Act by not assessing the biological warfare program's effect on the environment. The compromise accepted by both parties last week does not ascribe guilt to DOD; it also allows research to continue during the impact studies.

Nonetheless, foundation president Jeremy Rifkin sees the decision — sanctioned by a federal judge — as "one of the broadest victories in history" under the national policy act. "It means DOD is going to have to be held accountable to the public for its entire [biological warfare] program," he said in an interview. In 1985, Rifkin's group used a similar lawsuit to halt construction of a high-containment laboratory in Utah that had been proposed by the Army (SN: 6/8/85,

p.359).

The agreement came two days after a biological warfare symposium at the annual meeting of the American Association for the Advancement of Science. At the Chicago meeting, David L. Huxsoll of the Army's Medical Research Institute of Infectious Diseases (MRIID) in Fort Detrick, Md., heard charges from symposium attendants that even the development of *defensive* biological weapons adversely affects foreign relations, and that classified research on such weapons is being conducted at some of the program's participating labs.

The DOD program — which involves nearly 20 government labs and more than 100 universities and private groups, but is the primary responsibility of the Army — has an annual budget of about \$60 million. Prior to military stockpiling, vaccines and other "defensive" biological weapons are tested in a group of human volunteers at MRIID and then field-tested, according to Huxsoll. He said field-testing for two new vaccines recently began, using volunteers in Argentina and the People's Republic of China. He added that the Army already has sufficient stores of vaccines against tularemia and Venezuelan equine encephalitis to protect both the regular and reserve armed forces. — D.D. Edwards

Nearby supernova

Astronomers at the Cerro Tololo Interamerican Observatory at La Serena, Chile, discovered a supernova in the Large Magellanic Cloud on the morning of Feb. 24. This is the nearest known supernova to us in almost 400 years and apparently the first in that time to be visible to the naked eye. From the Southern Hemisphere, it should be the brightest star in the sky. It will not be visible from most of the Northern Hemisphere. □