

Faulty control gene underlies retardation

A search to explain a baffling form of mental retardation exclusive to girls has led scientists to an unusual mechanism of genetic disease. The gene that goes awry is one that helps orchestrate the activity of many, if not all, of a person's genes.

The disease, called Rett syndrome, is the most common cause of severe retardation in women. It begins affecting girls when they are 12 to 18 months old, eroding speech and hand skills just as the children are learning them. Physicians diagnose thousands of cases each year, but the disease almost never recurs within a family. Epidemiologists, therefore, have doubted that Rett syndrome could be genetic. In a report in the October *NATURE GENETICS*, however, scientists pinpoint a gene as the cause.

Commenting on the find, neurologist Alan K. Percy of the University of Alabama at Birmingham says, "It's absolutely fantastic. It opens whole new avenues."

The implicated gene figures in a biological process that scientists have studied avidly but never before associated with a disease. Known as gene silencing, the process does just what its name implies. It so tightly bundles the DNA within chromosomes that gene-reading enzymes can't get to it.

Gene silencing helps orchestrate devel-

opment by preventing the bundled genes from chiming in at the wrong time. Scientists propose that defects in the gene now linked to Rett disrupt this process. They would have expected such a disruption to prove fatal, and the new study suggests that indeed is the case—but just for male fetuses.

The gene, called *MECP2*, resides on the X chromosome. Boys have just one X, so in a male embryo, a faulty *MECP2* gene would cause the genes under its control to go unsilenced in every cell.

According to Huda Y. Zoghbi of the Howard Hughes Medical Institute at Baylor College of Medicine in Houston, male embryos probably die in the womb. That would explain, she says, why boys are missing from the epidemiologists' rolls. Zoghbi codirected the recent study with Uta Francke of Stanford University.

Girls with Rett syndrome have a defective *MECP2* gene on one of their two X chromosomes and a sound gene on the other. Because every cell in a girl's body consults only one X, and picks which one at random, half her cells are ruled by the healthy silencing gene and half by the faulty copy.

Scientists are still puzzling over how girls with Rett survive at all. Defects in *MECP2* must not unleash genes to the extent biolo-

gists had expected, say Huntington F. Willard of Case Western Reserve University in Cleveland and Brian D. Hendrich of the University of Edinburgh in a commentary accompanying the report. One possibility is that only a few *MECP2*-regulated genes are freed to shout out. Another is that many genes are not silenced but are only whispering instead of blaring out of turn.

A treatment for Rett is not likely to emerge until researchers learn more, Zoghbi says. Meanwhile, says Francke, parents will benefit from the ability to screen girls for *MECP2* defects. It now takes 4 to 5 years to diagnose Rett. During that time, parents don't know whether other children that they conceive will be at high risk for the condition. A diagnosis of Rett rules against this possibility because 99.5 percent of cases arise spontaneously, says Francke.

The link between Rett and gene regulation suggests a pattern. In a study reported in August, scientists at U.S. and French laboratories showed a connection between Coffin-Lowry syndrome, another form of mental retardation, and chromosome changes related to silencing.

Because nerve cells must make myriad interconnections during development, scientists regard the brain as particularly vulnerable to disruptions as an organism grows. Francke predicts that future research will link other neurological disorders to defective gene silencing. —O. Baker

NASA loses Mars Climate Orbiter

Mars has swallowed another spacecraft.

NASA's Mars Climate Orbiter, intended as the Red Planet's first weather satellite, appears to have burned up or been torn apart just as it entered Martian orbit on Sept. 23. The satellite was to have served as a radio relay for its sister craft, Mars Polar Lander, expected to touch down on Dec. 3.

An unexplained navigation error sent the \$125 million Orbiter about 100 kilometers lower than planned into the Martian atmosphere. At that altitude, only about 57 km above the planet's surface, mechanical stresses and heat from atmospheric friction would have destroyed it, says project scientist Richard W. Zurek of NASA's Jet Propulsion Laboratory in Pasadena, Calif. Scientists calculate that the craft could not have survived at any altitude lower than 85 km.

Over the past 2 decades, several Mars-bound Russian and U.S. spacecraft have perished, notably NASA's \$1 billion Mars Observer (SN: 8/28/93, p. 134). Ironically, Mars Climate Orbiter carried a duplicate of one of Observer's instruments, an infrared radiometer designed to measure the distribution of temperature, pressure, dust, and water

vapor in the Martian atmosphere.

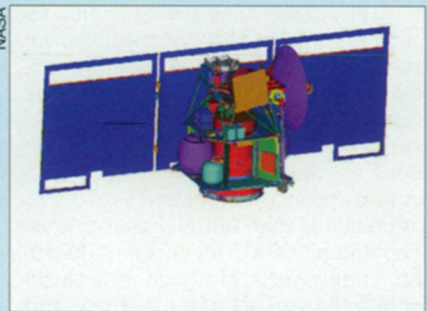
The craft would have broadcast daily weather images and data for an entire Martian year—687 days. Gathering that information could now be delayed for a decade, because Mars missions for the next several years have a different agenda: to collect samples from the Red Planet and bring them to Earth (SN: 4/25/98, p. 265).

Of more immediate concern is that the Mars Polar Lander, which will dig about a meter into Martian ice and dust near the south pole to look for evidence of recent climate changes, will have to rely on other means to communicate with Earth. Zurek says that Lander will likely use Mars Global Surveyor, which has orbited the Red Planet since 1997, to relay much of its data. That will reduce the time that Surveyor has to conduct its own mission, imaging the planet and mapping Mars' gravity.

Alternatively, Lander can communicate directly with Earth but so slowly that it couldn't broadcast all its planned observations. Zurek adds that it's unclear whether Lander, powered by the limited sunlight near the south pole, will have enough energy to send signals to Earth and carry out its full complement of Martian studies.

For the first few days of Lander's 3-month mission, the craft may have no other way to communicate. During that time, Surveyor's relay link is likely to be occupied by two small probes that have hitched a ride on Lander and will independently punch into the Martian soil.

Several space-policy analysts told *SCIENCE NEWS* that the loss of Mars Climate Orbiter, as well as two other NASA setbacks—the degradation of detectors on the Chandra X-ray Observatory and wiring problems on the space shuttle—don't seem to have altered the debate over the agency's budget. The House has proposed to cut \$1 billion from the agency's appropriation for next year, but a Senate proposal would fund the agency at the current level. —R. Cowen



Mars Climate Orbiter with its solar panels.