NEUROBIOLOGY

Jumbo Gene Offers Clue to Parkinson's

People with Parkinson's disease often can't keep their hands from trembling or relax their face to form a smile. For years researchers have known that these hallmark symptoms arise from the slow death of neurons in the substantia nigra, a brain region that pumps out the neurotransmitter dopamine. Now a Japanese research team appears to have uncovered a huge clue to what triggers this neuronal death.

The team, led by Nobuyoshi Shimizu of Keio University School of Medicine and Yoshikuni Mizuno of Juntendo University School of Medicine, both in Tokyo, reports in the 9 April issue of *Nature* that it has discovered a massive gene, dubbed *parkin*, whose mutated version causes a rare inherited form of parkinsonism. Although the finding won't resolve a long-running debate over whether a genetic flaw or some environmental insult is the primary culprit behind most Parkinson's cases, neurobiologists hope that it will offer a glimpse at the shadowy players involved in the molecular wreckage of a patient's brain.

The Parkin protein's structure links it to protein-degrading machinery in the cell, prompting speculations that a cell with abnormal Parkin may accumulate toxic levels of proteins. "This research is very important," says Robert Nussbaum of the National Human Genome Research Institute in Bethesda, Maryland, "because we'll want to see if a deficiency of Parkin might be occurring in nonhereditary Parkinson's disease as well," perhaps as a secondary effect of underlying disease processes.

To hunt down the new gene, Shimizu, Mizuno, and their colleagues studied Japanese families afflicted with a rare disease called autosomal recessive juvenile parkinsonism (AR-JP), the symptoms of which sometimes start in teenagers. In contrast, in common nonhereditary Parkinson's, symptoms start in people over 40.

A few years ago, the Japanese group tracked the AR-JP gene to the long arm of chromosome 6. In their latest work, they used positional cloning—a technique in which ever-finer maps of inherited mutations narrow a gene's possible location—to nab *parkin*. It turned out to be a monster gene. It has more than 500,000 nucleotides, making it the second largest known disease gene after *dystrophin*, involved in muscular dystrophy. Consistent with *parkin*'s role in AR-JP, the gene is highly active in the substantia nigra. But it may not be functional in patients with AR-JP, because large swathes are missing.

The team soon discovered that Parkin is "one of the most unique proteins ever known," says Shimizu. One portion resembles ubiquitin, a protein that, like Charon—the mythical boatman of the river Styx—ferries defective or spent proteins to proteosomes that chop them up. Defects in Parkin's ubiquitin-like section may subvert protein degradation and lead to toxic protein buildup. Parkin also has a zinc finger, a motif often found in proteins that help regulate gene expression.

The big question now is whether the discovery of *parkin* will help explain the more common nonhereditary form of Parkinson's. Researchers note that while substantia nigra cells in patients with nonhereditary Parkinson's are littered with aggregated proteins called Lewy bodies, AR-JP patients don't have Lewy bodies. Still, the dissimilarities between the diseases don't rule out an underlying connection. In nonhereditary Parkinson's, Shimizu says, "some environmental factor may be altering the form of Parkin over time."

–Mutsumi Stone

Mutsumi Stone is a correspondent for Newton Magazine *in Washington, D.C.*

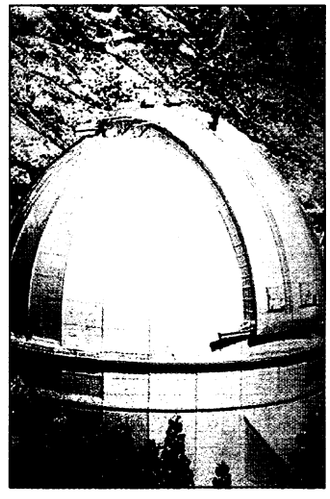
ASTRONOMY

El Niño Brings Winter of Discontent

At Kitt Peak National Observatory in Arizona, workers had to remove six trash bags full of snow from the top of the 4-meter telescope's dome in December. In Chile, heavy rains recently washed out the road to Cerro Tololo Interamerican Observatory, stranding astronomers on the mountaintop. At Apache Point Observatory in New Mexico, heavy snowfall kept domes closed for days. As El Niño watchers everywhere know, it has been no ordinary winter, and astronomers, who need clear skies and access to mountaintops, felt it more than most scientists.

True to form, El Niño—a warming of the eastern tropical Pacific—brought cloudy, wet weather to the Southwestern United States and Chile, exactly where astronomical observatories are concentrated. "Southern California, Arizona, New Mexico—these people feel it strongly," says Nate Mantua, an atmospheric scientist at the Joint Institute for the Study of Atmosphere and Ocean at the University of Washington in Seattle. "If you look at the storm tracks, they all hit here," adds astronomer Judy Cohen of the California Institute of Technology in Pasadena, which runs Mount Palomar Observatory in southern California. "We're getting dumped on."

Some observers at Palomar and Lick Observatories in California say they thought the weather wasn't much worse than in an average winter. But at Cerro Tololo in Chile, which has a reputation for clear skies, observers got to peek at the sky only 11 nights in February—half the usual number. At Kitt Peak, bad weather wiped out 40% of observing time in January, says Phillip Massey, an astronomer there. Because astronomers have to apply for telescope time 6 to 10 months in advance, it isn't always possible to reschedule a night of observing, he adds. And a makeup night may not help. "If your objects are up once a year, it can mean a year's delay."



MOUNT WILSON OBSERVATORY, PASADENA, CA

Heavy weather. Clearing snow from the dome at Mount Wilson.

Atsuko Nitta, a graduate student at the University of Texas, Austin, who is studying a variable star, had one clear night in seven when she observed in Chile last July, just after the current El Niño started. She had three clear nights out of eight in March. Because her research requires continuous observations of the star from sites around the globe, "when you don't get data you really suffer," she says. "We were counting on the data from Chile."

Winter is over and the eastern Pacific is cooling, but astronomers aren't yet in the clear. The Climate Prediction Center of the U.S. National Oceanic and Atmospheric Administration predicts unusually high rainfall through April or May in the Southwest. Chile may continue to have wetter than usual weather through July.

The clouds do have a silver lining: The same weather patterns that dumped clouds and moisture on the continental Americas bypassed Hawaii. Astronomers at the Keck Observatory, which has the largest telescopes in the world, have reported unusually dry, clear weather, with plenty of starry nights.

–Melissa Blouin

Melissa Blouin is a science writer in Arkansas.