Newfound gene linked to several cancers

Investigators have found a single gene whose inactivation may contribute to several deadly cancers, including those of the brain, breast, prostate, kidney, and skin.

The discovery was made by two teams of researchers working independently. One was studying a rare, lethal brain tumor; the other was investigating the most common form of breast cancer.

Yet their work carried them to precisely the same place—a large section of missing DNA on one of two copies of chromosome 10 in patients' malignant cells. Researchers have found that this deletion ordinarily contains a guardian gene that appears to keep cells from turning cancerous.

When the gene on one copy of chromosome 10 is damaged or absent, the intact gene on the other chromosome is also silenced, for reasons not yet understood.

The newly discovered gene, named MMAC1 or PTEN, is one of the first to be implicated in brain cancer—in this instance, an uncommon killer known as glioblastoma multiforme. The gene may well play a role in many of the 5,000 to 6,000 deaths from this cancer that occur in the United States each year, says Peter A. Steck of the University of Texas Brain Tumor Center in Houston, whose team reports its findings in the April NATURE GENETICS.

The same gene also appears to go awry in some of the 147,000 cases of nonfamilial breast cancer diagnosed in the United States annually, report Ramon Parsons of Columbia University's College of Physicians and Surgeons in New York and his colleagues in the March 28 SCIENCE. Two other breast cancer genes have been linked to hereditary cases of the cancer, which account for about 20 percent of those diagnosed each year (SN: 9/24/94, p. 197; 12/23&30/95, p. 420).

Having identified the gene in studies of brain and breast cancers, both teams began looking for a link with other cancers. They found mutations of the gene in melanoma and in cancers of the prostate and kidney, but the mutations occurred most often in people with brain tumors.

"It's a promising discovery that may lead to an understanding of a new pathway involved in cancer," Parsons says.

Researchers say that insights arising from this research may lead to the rapid detection and treatment of many cancers.

One potential application is a test for prostate cancer that would enable doctors to identify the 10 percent of men who need rapid, aggressive treatment among the 244,000 newly diagnosed each year.

Discovery of the gene is "fascinating from many perspectives," says Bert Vogelstein of the Johns Hopkins Medical Institutions in Baltimore. "It is involved in a couple of tumor types about which very little is known, particularly prostate and brain.

"From the data so far, it appears to be a major player in several different tumor types—and major ones at that. The next step will be to show exactly how broad its involvement is."

Investigators say the gene, when functioning properly, appears to be a potent tumor suppressor. Unlike many other anticancer genes, this one doesn't immediately stop abnormal cells from replicating. Instead, it seems to serve as a failsafe measure that acts once cells have begun their wild, uncontrolled growth. The timing of its action suggests that the gene acts as a sort of brake, preventing budding tumors from turning malignant.

"We think the gene may determine whether a cancer is going to be benign or malignant," Steck says.

In the brain, breast, and other tissues, the gene appears to halt cell growth when a cell comes in contact with other cells. Researchers suspect the gene functions by producing an enzyme that removes phosphate molecules from other proteins. This step appears to be the first one in a signaling cascade that stops the cell from growing. —*S. Sternberg*

Florida manatees' future: Grim or golden?

In 1996, biologists counted 2,600 manatees lolling in the coastal waters of Florida—a record number. They also counted a record number of carcasses: 415, including about 150 poisoned after the bloom of a toxin-producing marine microbe, or red tide, last spring.

This year, after the mild winter and fewer reported carcasses, researchers expected to find an even bigger population. Instead, the aerial count of the endangered animals dropped to 2,229.

The difficulties of counting the elusive manatees have prompted biologists to use computer models to fashion a picture of the population's dynamics. One such model, described in the April CONSERVATION BIOLOGY, is the first to project the animals' future in the long haul. If birth and death rates and other conditions hold steady, the population should remain stable over the 1,000-year time frame of the model. Just a 10 percent increase in the usual death rate of about 150 per year, however, could gradually eliminate manatees in the United States.

That translates into only about one additional death per year in each of 13 key counties in the state, says zoologist Thomas J. O'Shea of the Biological Resources Division of the U.S. Geological Survey in Fort Collins, Colo. At that rate, "the cumulative impact could be extinction." O'Shea developed the analysis with Miriam Marmontel and Stephen R. Humphrey of the University of Florida in Gainesville.

They used data on the age and reproductive status of about 1,200 carcasses recovered between 1976 and 1991. The model then generated a pattern of growth for the population. By altering birth or death rates and factoring in hard-to-predict events like hurricanes or red tides, the researchers projected what might happen to the manatees under a variety of conditions.

"There's a certain amount of guesswork involved," says biologist Chip Deutsch of USGS' manatee research program in Gainesville. More important than the model's absolute numbers or dates, he says, is its identification of the factors that have the biggest effect on the direction of the population changes. Death rates among adults turn out to drive the changes, and accidents involving motorboats or other waterway contraptions account for about half of these deaths.

Despite the uncertainties in predicting natural catastrophes, one thing is clear about the Florida manatees' future. They will be jostled by an increasing population of people and boats. The problem of collisions with manatees "is only going to get worse," says Deutsch. The quality of the manatees' habitat will undoubtedly be at risk as well.

O'Shea notes that the manatees can survive, provided motorboat speed limits and other conservation efforts in the key counties stay in place and are enforced. —*C. Mlot*

Florida's manatee, a close relative of the elephant, faces no predators except the motorboat.