Cancer Team Targets Colorectal Gene

An international team of scientists has discovered the underlying genetic basis for a common type of colorectal cancer. Their findings, along with those of another group, may provide new hope for people whose family tree is riddled with such cancers.

The researchers have homed in on the mutant gene's location on one of the 46 human chromosomes and predict they will identify the defective gene within two years.

"I'm just elated to see the gene finally discovered," comments Henry T. Lynch, the researcher who first described this type of familial colorectal cancer in the mid-1960s. Lynch is an oncologist at Creighton University School of Medicine in Omaha, Neb.

The disease, hereditary nonpolyposis colorectal cancer (HNPCC), strikes 160,000 people in the United States each year. People with a family history of HNPCC have an elevated risk of developing colorectal cancer as well as a variety of other malignancies, including cancer of the endometrium and stomach.

In the first of three reports, Bert Vogelstein of the Johns Hopkins University School of Medicine in Baltimore and Albert de la Chapelle of the University of Helsinki in Finland and their colleagues describe two large families, one from Canada and the other from New Zealand. The team started by searching for well-known cancer-causing genes in certain white cells. When that effort failed, they then began the painstaking process of combing through all the genetic material in those cells, says Stanley R. Hamilton, a Johns Hopkins pathologist who co-authored two of the reports, which appear in the May 7 SCIENCE.

"It was a fishing expedition in the true sense of the word," he says.

That hard work paid off when the team narrowed their search to a precise stretch of DNA located on chromosome 2. So far, there are no known cancer-causing genes along this region of the chromosome, Hamilton notes.

A second report by the same group hints at the molecular workings of this gene. In that study, the researchers studied samples of colorectal tumors taken from people with a family history of HNPCC as well as tissue from colorectal cancers from patients who had no such history. Most of the HNPCC tumors showed abnormalities in repeated sequences of DNA that occur on all chromosomes.

That finding suggests that the faulty gene may regulate the process of replicating or repairing DNA, speculates Hamilton. The end result appears to be the addition or subtraction of these repeated DNA sequences in otherwise normal genetic material, he says. These errors, in turn, may lead to genetic mutations known to cause colon and other types of cancer, he adds.

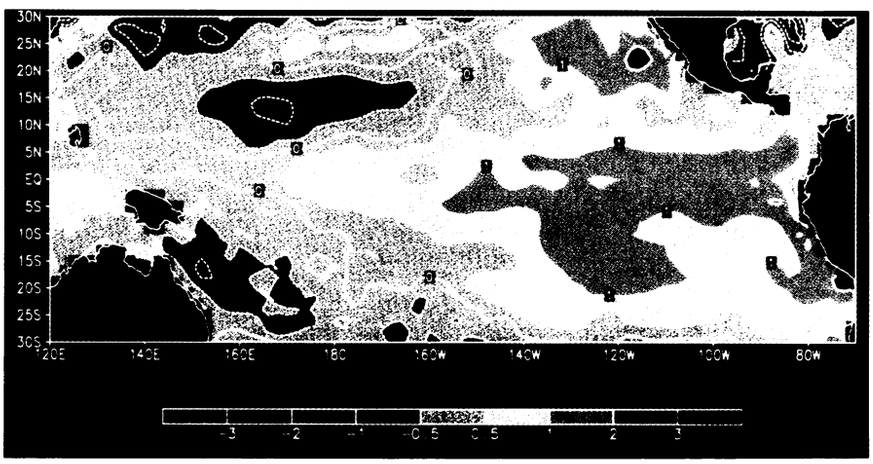
Surprisingly, 13 percent of "sporadic" colorectal tumors—tumors in people who did not report a family history of HNPCC — also showed the characteristic DNA alterations. It may be that some of those cases can be traced to a previously unrecognized inherited tendency toward colorectal cancer, Hamilton says.

In the third report, a group led by Stephen N. Thibodeau studied 87 individuals with apparently sporadic cases of colorectal cancer. The team collected tissue from 90 tumors and discovered that 28 percent showed the same alterations in the DNA-repeat sequences seen in HNPCC. That finding suggests that some individuals in the study inherited the faulty gene on chromosome 2, says Thibodeau, who is at the Mayo Clinic in Rochester, Minn. However, this gene may also play a role in some cases of sporadic colorectal cancers, in which a mutation arises after birth and is not passed on to future generations.

The researchers predict that within one to two years their findings will lead to a simple blood test that will identify people at high risk for HNPCC. In the past, physicians had to rely on a family history that suggested a risk of this familial cancer. Even when that history revealed numerous examples of colon cancer, doctors had no way of telling whether an individual patient had inherited the faulty gene, Lynch points out. Once a blood test is developed, doctors will be able to give patients a more definitive picture of their risk, he adds.

For those who don't carry the gene, the results of such a blood test would bring the relief of knowing their risk of colorectal cancer is not elevated, Lynch says. For people who do have the gene, and thus an elevated risk, doctors might suggest preventive measures, even surgical removal of the colon before it becomes cancerous, Lynch adds. In any case, once identified, such people could be monitored closely for the first signs of cancer. With early detection, there is a much greater chance that a patient can be cured, notes Hamilton. —*K.A. Fackelmann*

Defying predictions, El Niño still simmers



Above- and below-average sea surface temperatures for March 28 through April 24. Yellow and orange show large, lingering pool of warm Pacific water.

The current El Niño warming in the Pacific Ocean has surprised most human forecasters and computer models by hanging on far longer than predicted, promising continued disruptions in the typical weather patterns for many parts of the planet, according to researchers from the National Meteorological Center (NMC) in Camp Springs, Md.

Having lasted almost two years so far, this El Niño is the longest in the last 50 years. "It is an unusual event that we're seeing now," says Vernon E. Kousky, an NMC meteorologist who last week presented an update on the warming.

El Niños, which recur irregularly two to three times a decade, start when winds along the equator slacken, allowing a pool of warm water from the western Pacific to spread eastward. As sea surface temperatures climb in the central and eastern Pacific near the equator, thunderstorms develop over this part of the ocean, which normally lacks significant rainfall. This alters the storm patterns over Asia, the