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.

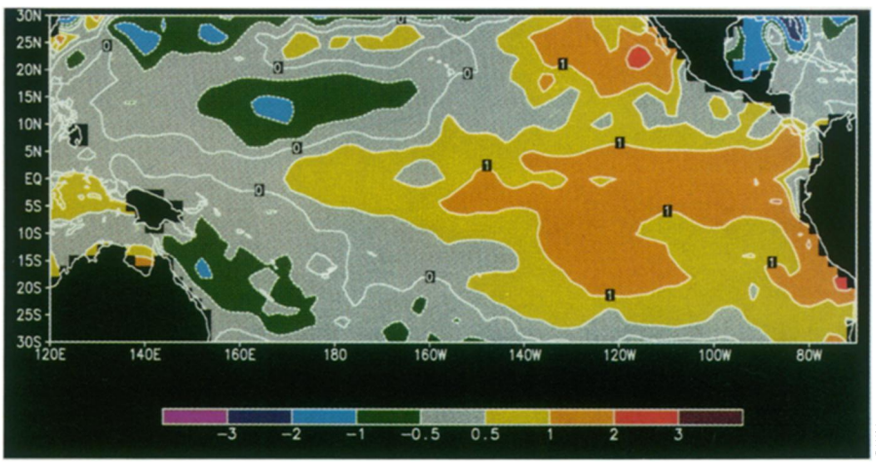
Surprisingly, 13 percent of "sporadic" colorectal tumors—tumors in people who did not report a family history of HNPCC — also showed the characteristic DNA alterations. It may be that some of those cases can be traced to a previously unrecognized inherited tendency toward colorectal cancer, Hamilton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

Americas, and even Africa.

The present warming began in mid-1991 and reached its mature phase by early 1992, bringing excessive rain to central South America, northern Mexico, and the western coast of the Gulf of Mexico. At the same time, the abnormal weather caused droughts in southeastern Africa, the Philippines, and northern Australia, according to the NMC.

By mid-1992, the El Niño had lost strength as sea surface temperatures dropped in the equatorial Pacific, leading Kousky and others to announce that the warming was nearing its end. At the same time, several experimental computer models predicted that this part of the Pacific should revert to normal temperatures or even reach cool conditions by the end of the year.

Contrary to expectations, water temperatures in the central Pacific began climbing once again in late 1992, and the warmth spread toward the South American coastline, reestablishing the El Niño, says Kousky (SN: 1/23/93, p.53). During April, observations of sea surface temperatures continued to show a large patch of warm water, both along the equator and spreading to the tropics of the northern and southern hemispheres.

The warm conditions in the central Pacific probably will persist through the middle of 1993, but the equator could cool off quickly because the pool of warm water there is thin, covering only the top surface of the ocean, says Kousky.

Moisture injected into the atmosphere by the warm water in the central Pacific played a role in the intense rains that washed California this year, Kousky says. The lingering El Niño also continued the drought in southeast Africa and will likely weaken the monsoon rains in India and Indonesia this year, he adds.

While most computer models missed the call this year, a new one under development at the NMC did make the right prediction. During the summer of 1992, the NMC ran the first real forecast on the model, which correctly called for a winter warming.

This experimental version is more complex and has better resolution than other models currently in use, but its developers say they need to test it further before they can judge its accuracy. The first prediction "was a success," says NMC meteorologist Ming Ji. "It could be luck, but it was encouraging." — *R. Monastersky*

New superconductor record

After a five-year lull with no reports of a material that could superconduct at temperatures above 127 kelvins, researchers have finally found a record breaker. The new superconductor appears to offer no resistance to electrons at 133 kelvins, a group at the Laboratorium für Festkörperphysik in Zürich, Switzerland, has announced.

"Finally, something is happening again in high-T_c [high-transition-temperature superconducting]," says Andreas Schilling, lead author of the report in the May 6 NATURE.

Unlike the previous recordholder, the new superconducting champion contains mercury instead of thallium. Schilling's team made its discovery while attempting to make a material called mercury-1201, which acts as a superconductor at temperatures of up to 94 kelvins (SN: 3/20/93, p.182). Mercury-1201 contains a single mercury and copper oxide layer per unit cell of the crystal, and its Russian discoverers hypothesized that additional layers would boost its superconducting temperature. Indeed, the Swiss team has created two- and three-layered versions of the mercury-barium-copper oxide that appear capable of superconducting at 110 and 133 kelvins, respectively.

The researchers haven't determined yet just how their synthesis differed from the originally reported method. But when they examined their product with an electron microscope, they saw clear images of the plate-like grains common to high-temperature superconductors. Within the grains, they found evidence of multiple layering. Results from measurements of magnetization and resistivity led them to conclude that the triple-layered component of their material mixture could superconduct at 133 kelvins.

Scientists are still far from finding superconductors suitable for everyday applications, though. Says Schilling, "I think this material will have the same value as thallium compounds, which means it has no practical value because it's poisonous." □

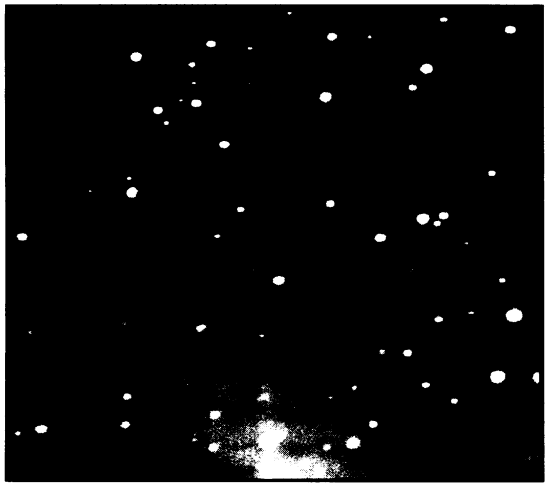
Peering into Orion nebula's stellar nursery

Astronomers have viewed with greater clarity than ever before a dust-cloaked region of starbirth in the Milky Way. The violent interactions they recorded there may shed new light on luminous knots of gas, known as Herbig-Haro objects, whose origin has been controversial ever since they were discovered in the late 1940s.

Australian astronomers David A. Allen of the Anglo-Australian Observatory in Epping and Michael G. Burton of the University of New South Wales used an infrared array to probe the interior of the dusty Orion nebula, a molecular cloud that harbors the stellar nursery nearest to Earth. They report their findings in the May 6 NATURE.

Their striking false-color images trace the high- and low-energy scenes from a startling story unfolding near the brightest star, dubbed IRc2, in Orion. Allen and Burton believe that the Herbig-Haro objects they recorded with the 3.9-meter Anglo-Australian Telescope were triggered by blobs of gas ejected from the star a mere 1,000 years earlier. Plowing into surrounding gas, the blobs ionized iron atoms, thus taking on a false-green cast. Surrounding many of these blobs are structures that resemble the bow shocks created when a boat rushes across a lake. Allen suggests that these bow shocks lack the punch to ionize iron but can excite molecular hydrogen, depicted as a red glow.

Infrared image depicts collisions in the Orion nebula. Energetic gas blobs appear green in the light of ionized iron atoms; lower-energy wakes appear red, due to the glow of molecular hydrogen.



Allen, Burton/Anglo-Australian Telescope

Other researchers say the images don't rule out alternative explanations for forming Herbig-Haro objects in Orion. C.R. O'Dell of Rice University in Houston notes that these knots might be formed when a slow-moving jet of gas from a star strikes a stationary wall of gas in the interstellar medium. Alternatively, a fast-moving jet may create knots of bright emissions as it shocks and pushes out surrounding gas. Allen says that a narrow jet could not account for the wide angular spread of the knots. However, John Dyson of the University of Manchester in England suggests that a jet wiggling like the end of a loosely held garden hose might explain the distribution.

Researchers, including Allen, agree that more than one mechanism may create Herbig-Haro objects. In any case, writes Dyson in a commentary accompanying the NATURE article, the findings "show that many [violent] surprises are in store as modern observational techniques... probe into hitherto unexplored regions of interstellar space." — *R. Cowen*