ciety, and Spain's National Geographical Institute, the observatory is in the process of being linked to a 30-meter telescope at Pico Veleta in southern Spain; together, they will form a so-called very large baseline millimeter array, a virtual telescope the size of the distance between the two observatories. The accident is expected to slow completion of this effort even further, Bremer says.

–ALEXANDER HELLEMANS

Alexander Hellemans writes from Naples, Italy.

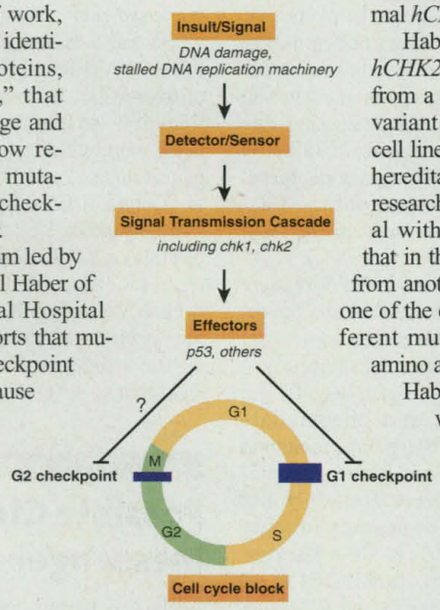
HUMAN GENETICS

Checkpoint Gene Linked To Human Cancer

As any driver knows, reliable brakes are every bit as important to safety as the gas pedal. The same can be said about cells when it comes to dividing. They have to know when to stop, say, when their chromosomes have been damaged, because if they don't the resulting mutations may propel them down the road to cancer. Over the past several years, a great deal of work, much of it in yeast, has identified a network of proteins, called "checkpoints," that helps cells sense damage and put on the brakes. Now researchers have linked mutations in one of these checkpoint proteins to cancer.

On page 2528, a team led by cancer geneticist Daniel Haber of Massachusetts General Hospital (MGH) in Boston reports that mutations in a known checkpoint gene called *hCHK2* cause some cases of Li-Fraumeni syndrome (LFS), a hereditary cancer susceptibility that leaves its patients prone to developing any of several cancers, including breast and brain cancers and certain leukemias. This is not the first gene linked to LFS. In 1990, Stephen Friend's team, also at MGH, found that inherited mutations in the well-known tumor suppressor gene *p53* can cause the condition. Subsequent work showed that *p53* mutations account for only about 75% of the cases, however. The new work provides an explanation for some, although not all, of the remaining LFS cases. And even though the number of LFS patients may be small—only about 200 families worldwide have been reported—the discovery of *hCHK2* and additional LFS defects in the future may "help [us] to understand the molecular mechanisms of tumorigenesis" reaching far beyond LFS, says Friend, who is now at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

The finger of suspicion already pointed at cell checkpoints as being important. Indeed, the p53 protein itself halts cell division in response to chromosomal damage. So Haber and his team studied several members of four LFS families that did not have *p53* mutations, looking for mutations in the human counterparts of genes previously identified in yeast as playing a major role in checkpoint control. Most such genes turned up as perfectly normal. But in one family, three LFS patients had identical mutations in one copy of the gene encoding chk2, a kinase enzyme that passes on the stop signal in damaged yeast cells by attaching phosphate tags to other proteins. The protein produced by the mutated gene would be unable to perform this function, Haber says, because part of it, including its enzymatic center, is missing. A healthy relative, in contrast, had a normal *hCHK2* gene.



Genetic quality control. Cells have "checkpoint" pathways that sense chromosomal damage and stop cells from dividing to allow time for repair. Mutations in checkpoint components, such as *p53* and *chk2*, can pave the way to cancer.

Haber's team next looked at *hCHK2* in 18 patients suffering from a related syndrome called variant LFS and in 49 cancer cell lines from a variety of nonhereditary human tumors. The researchers found one individual with a mutation similar to that in the first family. The gene from another individual and from one of the cancer cell lines had different mutations, changing one amino acid to another. Although Haber doesn't know for sure whether these "spelling errors" debilitate the kinase, he notes that his team failed to detect them in the gene from 50 healthy control individuals. "This suggests that these alterations are not simple sequence variants that are prevalent in the general population," says Haber.

The results are likely to receive a warm welcome in the cancer community. "This is great. People have been searching for mutations to explain LFS [in families with intact *p53*] for almost a decade and [have] found absolutely nothing," says Friend. But he adds that, because *hCHK2* mutations turned up in only one of the four families studied, "there is a good likelihood that [other LFS families] will have mutations in other interesting genes." Paul Russell, a yeast cell cycle expert

CREDITS: (LEFT TO RIGHT) BELL *ET AL.*/VERITAS

ScienceScope

Star-Crossed? The U.S. Forest Service has decided to take another look at a controversial plan to build the world's largest array of ground-based gamma ray telescopes near a Native American sweat lodge at the base of Arizona's Mount Hopkins.

In September, the agency rejected a request from astronomers at the Smithsonian Institution in Washington, D.C., for a permit to build the $16.6 million, seven-reflector array on public land (*Science*, 10 September, p. 1650). It said then that the 4-hectare site, which is less than 1000 meters from a multitribe steam hut, conflicted with "Indian religious practices." But at the Forest Service's invitation, the Smithsonian submitted a new plan last week.

The revised proposal uses the same site, says Trevor Weekes, principal investigator for the Whipple Observatory project, but moves the access road farther from the sweat lodge and sets the dishes closer to the ground. But those changes don't satisfy Native American groups, who object to the presence of any scientific facility so close to the sweat lodge. "[The Smithsonian] can't take no for an answer," says sweat lodge operator Cayce Boone, a Navajo, who feels "betrayed" by the Forest Service for keeping the issue alive.

In the Wind The American Meteorological Society has decided to do something about the weather—or at least what it claims is the government's relative inattention to atmospheric policy. The society has put up $400,000 to address the problem and has recruited two prominent National Science Foundation officials—former atmospheric division director Richard Greenfield and outgoing geosciences chief Robert Corell—to lead the effort from its Washington, D.C., office.

The Atmospheric Policy Program represents a "considerable investment" for the 12,000-member Boston-based organization, says executive director Ronald McPherson. The idea, he says, is to self-fund a few studies on hot topics—such as the growing commercialization of weather data—then persuade agencies and other funders to pick up the tab for future activities. Although the program won't lobby the government on legislation, Greenfield says he hopes to provide graduate students and professionals with a better understanding of atmospheric research. "I can't name anybody at the top levels of government with a strong background in atmospheric sciences," McPherson says.

flies in which the *pdf* gene has been inactivated have functional clocks but lose their rhythmic activity patterns under certain conditions, suggesting that a signal from the clock that affects activity is missing.

The finding builds on earlier hints, including one reported in *Cell* 2 weeks ago by Michael Young of The Rockefeller University in New York City and postdoc Justin Blau, who found that the clock genes regulate PDF production, as would be expected if it were an output signal from the clock. If PDF does turn out to be a bona fide output signal, says clock researcher Paul Hardin of the University of Houston, it will help researchers to "ultimately map out a pathway" from the clock to behaviors that it controls.

Rhythm centers. The red stain shows the distribution of the protein that gives rise to PDF in the fruit fly brain.

The first clues that PDF (for pigment-dispersing factor) might be involved with the clock came from its resemblance to a peptide called pigment-dispersing hormone, which drives a daily rhythm of color changes in some crustaceans. Rhythm researcher Charlotte Helfrich-Förster at the University of Tübingen in Germany provided further evidence for that idea in 1993 when she discovered that PDF is made in certain of the so-called lateral neurons of the fruit fly: clusters of neurons on each side of the fly's head where its clocks are housed. What's more, she showed in 1998 that those neurons make direct connections to the part of the fly brain that appears to control the fly's activity level, and that those connections are essential to maintain daily activity rhythms. That strongly suggested that something made by the lateral neurons acts as the messenger controlling clock activity. PDF was a good candidate, but researchers had not yet knocked out the gene to test that idea.

Then last December, Taghert and graduate student Susan Renn were studying neuropeptide expression and in their lab stocks found flies that were missing PDF. Further testing showed that the flies had a mutation in the *pdf* gene. To check out whether the mutation affects the flies' clocks, Renn and Taghert joined forces with clock researchers Hall, Michael Rosbash, and postdoc Jae Park, who were already studying *pdf* gene expression. The researchers found that the animals have working clocks; for example, in normal light-dark cycles, the flies became active in anticipation of darkness, a sure sign that their clocks were running. But in constant darkness, their activity rhythms gradually faded away over several days. Because PDF is apparently not part of the clock itself, the fading suggests that it contributes to the output signal that controls activity rhythms, says Taghert. It can't be the only signal, because flies still have activity rhythms under some conditions without it, he notes, but it seems to dominate under constant dark conditions.

If PDF is such an output signal, it must be controlled by the clock. And that appears to be so. In their *Cell* paper, Blau and Young described the discovery of a new clock gene, *vrille*, and reported that both *vrille* and another clock gene, *clock*, regulate PDF: *clock* controls the expression of the *pdf* gene in the lateral neurons, and *vrille* controls the accumulation of the PDF peptide. Surprisingly, PDF production remains level throughout the day, but it might be released rhythmically from the lateral neurons, which would explain its rhythmic effects on activity.

The data also suggest another possible function for PDF, as a signal that helps to synchronize the pair of fruit fly clocks. If the two clocks in the lateral neurons were to get out of time with each other, the fly's rhythms would disintegrate into chaos. Normally light should synchronize the clocks, but in constant darkness, they could drift apart without a backup. In that case they could show a gradual loss of rhythmicity similar to what happened in the PDF mutants kept in the dark. Helfrich-Förster found that some of the PDF-containing lateral neurons crossed to the other side of the brain, where they could act as a backup synchronizer.

Right now researchers can't tell whether PDF exerts its effects on activity patterns directly, by synchronizing the clocks, or both. Researchers might be able to resolve that issue by selectively destroying the lateral neurons that cross to the other side of the brain, but not the ones that project to the activity-controlling area. And if they could find the receptor through which PDF exerts its effects, they should be able to identify the neurons that respond to it. That would enable them to confirm that it controls daily activity rhythms

CREDIT (LEFT TO RIGHT): P. H. TAGHERT AND S. C. P. RENN; BEIJING UNIVERSITY

ScienceScope

Unsanctioned The U.S. government is scaling back sanctions imposed on 51 Indian research labs and industries after the country conducted nuclear weapons tests in May 1998. The organizations weren't allowed to receive U.S. exports, and their scientists were effectively barred from visiting U.S. labs.

The change, announced 16 December, follows a congressional directive to pare down a sanctions list of 204 Indian institutions to those "that make material contributions to weapons of mass destruction and missile programs." Indian officials see it as an effort by the Clinton Administration to nudge their country toward signing the Comprehensive Test Ban Treaty, which the U.S. Senate rejected this fall.

Both Indian and U.S. scientists are happy with the move, which will take a few months to put into effect. "It will be wonderful to have [Indian scientists] back on the team," says David Cutts, a Brown University physicist who is part of an international group upgrading one of the main particle detectors at Fermilab's Tevatron accelerator (*Science*, 21 May, p. 1259). Indian scientists built and shipped a piece for the detector but have been unable to travel to Fermilab to install it.

Double Duty Xu Zhihong, a 57-year-old plant biologist, has been named president of Beijing University. In an unusual move, Xu will also retain his position as a vice president of the Chinese Academy of Sciences (CAS) in a bid to cement links between the government and university research sectors. He succeeds physicist Chen Jai'er, who will become chair of China's funding agency for basic research, the National Natural Science Foundation.

Xu, who has spent most of his career at CAS's Shanghai Institute of Botanical Physiology, says his goals are to improve the quality of university teaching and encourage cross-disciplinary research. Researchers applaud Xu's appointment and see his dual role as a way to strengthen the sometimes tenuous relationship between CAS and universities. "Unfortunately, the two systems do not cooperate enough," says Zou Chenglu, a biophysicist at CAS's Beijing Institute of Biophysics and a CAS member.

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