Gene for Most Common Cancer Found

As a fruit fly embryo matures, the activity of a gene called *patched* helps guide its development. Two research groups now report that the human counterpart of *patched* is the crucial gene that goes awry in basal cell carcinoma, the most common of all human cancers.

This skin cancer strikes an estimated 750,000 people a year in the United States. Unlike most other cancers, it rarely kills because it seldom invades other parts of the body. Still, if not caught early and removed surgically, basal cell carcinoma can cause severe disfigurement.

Investigators suggest that the newly discovered gene is the cancer's "gatekeeper," the initial gene that must be mutated for disease to occur.

As a result of the discovery, "there will be a topical cream that cures basal cell carcinoma" in 5 to 10 years, predicts Allen E. Bale of the Yale University School of Medicine. Bale heads an international team of researchers that reports the finding in the June 14 CELL.

In addition to skin cancer, mutations in the human version of *patched* result in basal cell nevus syndrome, a rare condition in which affected individuals suffer various cancers, including, often, hundreds of basal cell carcinomas, and developmental defects such as fused ribs, extra digits, spina bifida, and oversized heads. Among the deadliest outcomes of the syndrome—also called Gorlin syndrome—is medulloblastoma, a brain cancer in children.

Discovery of the new gene is "incredibly significant in terms of understanding the pathogenesis of basal cell nevus syndrome and basal cell carcinomas in general," comments Bert Vogelstein of the Johns Hopkins Medical Institutions in Baltimore.

A second group has isolated the same cancer gene. Headed by Matthew P. Scott of the Howard Hughes Medical Institute at Stanford University and Ervin H. Epstein Jr. of the University of California, San Francisco, this team describes its work in the June 14 SCIENCE.

Scott has been studying *patched* in fruit flies for more than a decade. Using *patched*'s DNA sequence, his group recently identified a similar human gene. They found it on an area of chromosome 9 long thought to hold the gene responsible for basal cell nevus syndrome. Scott's team then joined forces with Epstein's group, which was looking for the gene behind the syndrome.

"We're working on the most common human cancer at one end of the bay, and 30 miles away someone is working on [fruit flies]—and it turns out we're working on exactly the same gene," marvels Epstein.

Working independently, Bale's group had also found *patched*'s human counterpart while examining genes from the same region of chromosome 9.

To determine whether the new gene causes the syndrome, both sets of researchers studied the DNA of afflicted families and found that affected members have mutations in the gene, whereas unaffected members do not.

Both groups also identified several mutations in the gene when they examined tumor cells from basal cell carcinoma patients not afflicted with basal cell nevus syndrome. One mutation is an alteration often generated by ultraviolet light, supporting the charge that exposure to the sun can trigger skin cancer, says Epstein.

Investigators believe that to trigger basal cell carcinomas and other cancers, flaws must occur in each of a cell's two copies of the newly discovered gene.

Basal cell nevus syndrome, however, seems to result when only one copy of the gene is defective. Developmental abnormalities would occur because cells in the embryo make only half the normal amount of the gene's protein. Moreover, having one faulty copy of the gene would predispose people with the syndrome to cancer: A mutation in the one normal copy would be all that's needed to trigger tumor formation.

Though its exact role remains unclear, *patched*'s protein sits in the outer membrane of a cell and may help turn genes off by transferring signals from outside the cell into the nucleus, where genes reside. In embryonic fruit flies, *patched* counteracts the growth-promoting activity of a gene called *hedgehog*.

The linking of *patched* to basal cell carcinoma is one of several instances recently in which a gene involved in fruit fly development has been tied to human cancer. "This is one of the most exciting aspects of the work. We're seeing a merging of the people studying development and the people studying tumorigenesis," says Michael Dean of the Frederick (Md.) Cancer Research and Development Center and a coauthor of the CELL report.

— J. Travis.

Running gaze catches on with fielders

When major league baseball outfielder Ken Griffey Jr. streaks toward a fly ball hit by a batter on an opposing team, he does not know precisely where the horsehide will land. But with the help of a surprisingly simple guideline that even Little Leaguers may employ for tracking moving objects, the perennial all-star reaches an opportune spot at which to snag the sphere.

That, at least, is the implication of a new study conducted by two British psychologists, Peter McLeod of Oxford University and Zoltan Dienes of Sussex University in Brighton.

In any sport in which a ball must be intercepted, a successful fielder runs at a speed that maintains a relatively constant angle of gaze toward an oncoming projectile between 0° (looking straight ahead) and 90° (looking straight up) throughout its flight, the researchers contend. If that angle reaches either 0° or 90°, the ball will be missed, except for rare instances in which a heroically outstretched hand or leg saves the day.

"The [formula] fielders use to intercept the ball is one that ensures they arrive at the right place at the right time but does not tell them where or when that is," McLeod and Dienes assert. "It would not be surprising if children who are learning to catch discovered the importance of [the angle of gaze]."

The scientists videotaped six skillful ball handlers—one professional and four amateur cricket players and one professional soccer player—as they ran backward or forward to catch a hard white ball shot toward them by a machine placed about 150 feet away. The machine discharged balls at each of two angles and at varying speeds, so the fielders did not know whether the projectile would land in front of or behind them.

When fielders had a short distance to run or more time to get to a ball lofted higher into the air, they did not simply run to the place where the ball would land and wait, the researchers report in the June JOURNAL OF EXPERIMENTAL PSYCHOLOGY: HUMAN PERCEPTION AND PERFORMANCE. Instead, they ran more slowly, at a speed that maintained a consistent angle of gaze between 0° and 90°, according to McLeod and Dienes.

This finding suggests that fielders focus on the relationship between themselves and the ball, rather than predicting where the ball will land, argues psychologist Michael K. McBeath of Kent State University in Kent, Ohio. Fielders also tend to position themselves so that a moving ball's path follows an apparently straight line (SN: 5/13/95, p. 297).

— B. Bower