P16's cancer role debated and verified

Barely four months ago, biologists heralded the discovery of a new tumor suppressor gene, called p16, that influenced cell growth and replication and played a key role in the development of several cancers (SN: 4/23/94, p.262).

In mid-July, a team at the University of Southern California in Los Angeles challenged the significance of p16 in tumors. In the earlier studies, researchers had found the frequent occurrence of p16 mutations or deletions by examining the genetic makeup of cells removed from human tumors and grown in the laboratory.

But few alterations exist in fresh tumor tissue, Charles H. Spruck III, Mirella Gonzalez-Zulueta, and their colleagues reported in the July 21 NATURE. They looked for p16 mutations in 31 bladder tumors and in 13 groups of malignant bladder cells cultured in the laboratory.

The p16 mutations occurred three times more often in the lab-grown cells, suggesting the seeming prevalence of p16 mutations or deletions in cancer may have arisen as an artifact of the type of cells studied, they suggested.

Now, three new reports in the September NATURE GENETICS help put this controversy to rest. Two strongly implicate p16: one in a lethal skin cancer, malignant melanoma, and one in pancreatic tumors. The third study, also of p16's role in melanoma, was more equivocal, but nonetheless argues in favor of p16's involvement in some melanomas.

"The data are different than what's been done before," says Nicholas C. Dracopoli of the National Center for Human Genome Research in Bethesda, Md. "[The results] are much more positive."

In about 10 percent of melanomas, the skin cancer runs in families. Dracopoli, in studying some of these families, has found that some, but not all, lack p16 genes or possess mutated versions. About 75 percent of the cells taken from 18 families contained aberrations of this gene, Dracopoli says.

He and his colleagues detected eight different versions of the gene, each with a single nucleotide substitution. Six of these seemed to increase the risk of cancer, and three showed up in more than one family, the group reports.

Independently, a second team of geneticists took a close look at chromosome 9 in other melanoma-prone families. Alexander Kamb of Myriad Genetics Inc. in Salt Lake City and his coworkers examined that chromosome in eight U.S. and five Dutch families suspected of harboring p16 mutations.

Even though the mutations had seemed located on this chromosome at the site of the p16 gene, this analysis did not confirm that most of the genetic changes had really occurred within the p16 gene, Kamb says. Only three U.S. families had a nucleotide substitution in the active part of the p16 gene; the rest did not. One of those substitutions tends to occur naturally as an alternative version or polymorphism of the p16 gene, leaving just two with possible links to cancer.

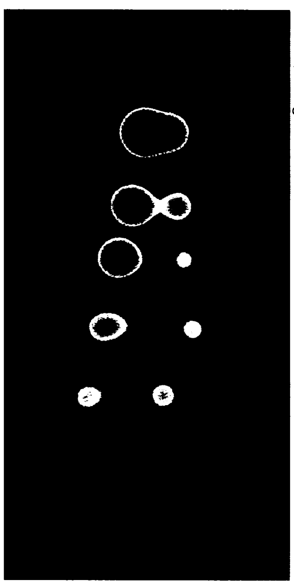
However those two substitutions also showed up in families studied by Dracopoli, notes Brandon Wainwright from the University of Queensland in St. Lucia, Australia. And the third NATURE GENETICS report clearly links changes in p16 to pancreatic cancer, he adds.

In that study, Scott E. Kern and his colleagues at the Johns Hopkins Medical Institutions in Baltimore implanted cells from 27 human pancreatic tumors into specially bred mice. They then analyzed the genetic makeup of cells from new tumors that developed in these mice.

In about half, they found no p16 genes at all, while another 14 contained a mutated p16 gene. They compared these genetic sequences with DNA taken from the original tumor and determined that these alterations in the p16 were real, not artifacts, they say. —*E. Pennisi*

Grand illusion: Moving faster than light

Giant blobs of gas racing faster than light across the sky? Sounds like the stuff of science fiction, but astronomers have known for years that the hearts of distant galaxies can eject material so violently that the matter seems to travel several times the speed of light. Now scientists have for the first time detected the same phenomenon in our own galaxy.



Mirabel, Rodriguez/NATURE

Radio images show gas blobs separating from the high-energy source GRS 1915+105. Red denotes highest radio intensity, blue the lowest.

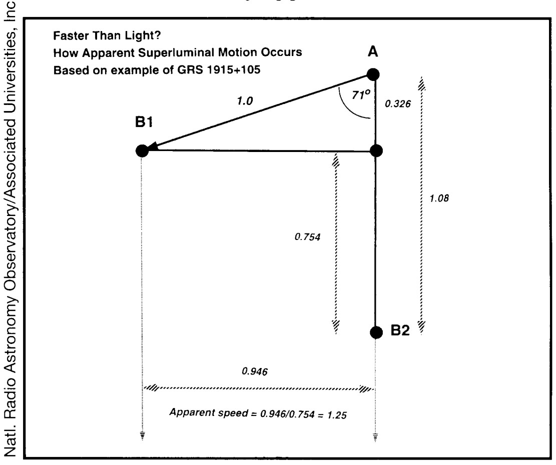
Because the newly found gas lies no farther than 40,000 light-years from Earth, this system "may offer the best opportunity to gain a general understanding of relativistic ejections seen elsewhere in the universe," the codiscoverers write in the Sept. 1 NATURE.

I. Felix Mirabel of the Centre d'Etudes de Saclay in Gif-sur-Yvette, France, and Luis F. Rodriguez of the National Autonomous University of Mexico in Mexico City began their study by monitoring an intriguing source of X-rays. At its most luminous, this intermittent source, dubbed GRS 1915+105, ranks among the brightest X-ray emitters in the Milky Way.

Using the Very Large Array radio telescope near Socorro, N.M., the researchers detected blobs of gas streaming in opposite directions from a compact core that coincides with the X-ray source. Tracking the material approaching Earth, they found it appears to move at 1.25 times the speed of light.

According to the theory of special relativity, nothing travels faster than light. But the theory also offers an explanation for the illusion that objects moving nearly that fast exceed this cosmic speed limit.

Tracking such a speedy object, a distant observer sees the motion occur over a shorter time than that measured by an observer sitting on the object. Thus, the motion may appear faster than



Natl. Radio Astronomy Observatory/Associated Universities, Inc.

Gas blob starts at A, moving 71° from the line of sight of a terrestrial observer (B2). Moving at 92 percent of the speed of light, the blob travels to B1, a distance of 1 light-year. The light that the blob emitted at A travels 1.08 light-years in the same time. Because the blob moves so rapidly, the light it emits at B1 arrives at the observer only 0.754 years later than the light it emitted at A. Thus, the blob appears to have traveled 0.946 light-years across the sky in 0.754 years, or 125 percent of the speed of light.

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