

## 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.

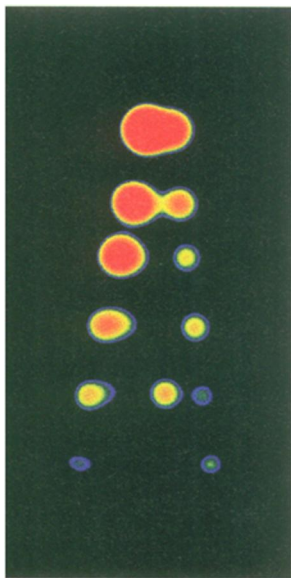
In about half, they found no p16 genes at all, while another 14 contained a mutated p16 gene. They compared these genetic sequences with DNA taken from the original tumor and determined that these alterations in the p16 were real, not artifacts, they say. —E. Pennisi

## 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.

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 ejection

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



Mirabel, Rodriguez/Nature

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.

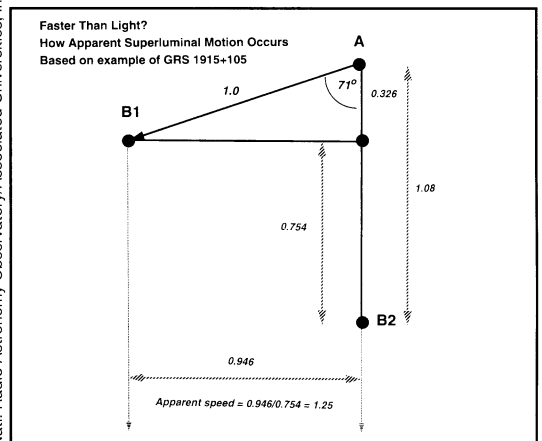
Using the Very Large Array radio telescope near Socorro, N.M., the researchers detected blobs of gas streaming in

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.

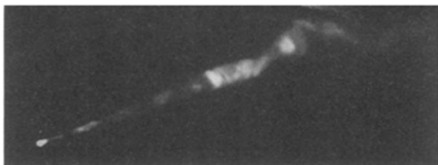
opposite directions from a compact core that coincides with the X-ray source. Tracking the material approaching Earth, they found it appears to move at 1.25 times the speed of light.

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.



A jet of gas streams from the center of the galaxy M87. Gas that lies about 900 light-years from the galaxy's center gives the illusion of moving at 2.5 times the speed of light.

light to the distant observer, even though nothing moves that fast in the object's own frame of reference. After correcting for this relativistic effect, Mirabel and Rodriguez calculate that the blobs in their study actually move at 92 percent of the speed of light.

John A. Biretta of the Space Telescope Science Institute in Baltimore cautions that the researchers haven't pinned down the distance to the object ejecting the gas, thought to be a neutron star or black hole that steals matter from a less-dense companion. If this binary star lies much closer to Earth than the 40,000 light-years they estimate, the blobs would still be cruising, but not at a superluminal speed, he says.

Nonetheless, Biretta adds, the new study may shed light on the dynamics of larger and more distant systems that also spew matter at high speed. Last June, at a meeting of the American Astronomical Society in Minneapolis, he and his colleagues reported their recent observations of superluminal motion in a jet of gas at the center of the galaxy M87.

— R. Cowen

## Test landfills percolate as bioreactors

On the outskirts of urban centers grow great manmade mountains of trash. Piled high, packed, and buried, these landfills — which hold 70 percent of domestic refuse — typically take years to amass and decades to decompose.

To manage the solid-waste stream responsibly, scientists seek speedier ways to break down garbage into useful components, extract energy-rich fuel, and recycle the remnants. Toward that end, Frederick G. Pohland and Robert E. Landreth, environmental engineers at, respectively, the University of Pittsburgh and the Environmental Protection Agency in Cincinnati, Ohio, describe a faster way to decompose rubbish using "landfill bioreactors."

Speaking at last week's meeting of the American Chemical Society in Washington, D.C., they explained that by recirculating leachates — the liquid brew of decomposing wastes — in a landfill, biological breakdown occurs up to 10 times faster than usual. "Normally, a landfill takes 20 to 30 years to decompose," says Pohland. "But using this method, it may only take 2 to 3 years."

Rain soaks and the sun bakes decaying rubbish, creating a great compost pile, says Pohland. Already rich in nutrients and microbes, the fermenting heap mostly requires nurturing to make methane gas, wastewater, and reclaim-

able solids. So engineers are testing landfill designs that mix wastes with leachates. Almost like an oven that bastes a roast, the new landfills use liners and collection systems whose pipes and pumps recirculate liquids and extract methane gas.

"We don't even have to add bacteria or chemicals," Pohland says. "The landfill is biologically active and nutrient rich. This process simply accelerates natural decomposition." Municipalities can later irrigate land with treated leachate waters, generate power from methane, and mine what remains for metals, plastics, and other recyclables.

Scientists are testing 20 landfill bioreactors, each site varying slightly in design, Landreth says. The EPA supports three of these sites: in Monroe County, N.Y., Gainesville, Fla., and Dover, Del. In Dover, the most advanced site, two 1-acre cells will soon give rise to a full-size 20-acre pilot site, Pohland says.

Landreth sees the possibility of "round robin" landfills serving communities and industrial parks. "Fill one up, move to the next. Fill that one up, then move to a third," Landreth says. "Keep going around, filling up sites and pumping out gas until the first one is fully cooked. Then dig up the first one, mine it for materials, and fill it again. You can go in a circle."

— R. Lipkin

## Family planning gets a shot in the arm

A controversial vaccine designed to halt pregnancy did just that with no significant side effects for a small group of women, researchers in India reported this week. The vaccine appears to prevent implantation of fertilized eggs by inducing the body to produce antibodies to human chorionic gonadotropin (hCG), a hormone critical to pregnancy, scientists say.

Birth control vaccines have been in the works for many years (SN: 6/25/88, p.407), but this is the first to undergo efficacy testing in humans, says Nancy J. Alexander, chief of the contraceptive branch at the National Institute of Child Health and Human Development in Bethesda, Md.

"There are lots of things that are really exciting about [this vaccine]," she says. It appears effective, yet when women stopped using it, they became pregnant quickly. Also, the vaccine did not disrupt menstrual cycles.

However, "there are still a lot of problems," Alexander notes. For one, women require booster shots. And the question of side effects won't become clear until many women use it. In addition, "a lot of

women feel [birth control vaccines] would have tremendous potential for abuse," Alexander says.

Some women's groups oppose development of a birth control vaccine. Among other concerns, they worry women will be vaccinated without their consent or knowledge.

The study included 148 women, age 20 to 35, with at least two children, an active sex life, and regular menstrual cycles, report G. Pran Talwar of the National Institute of Immunology in New Delhi and his colleagues. The women enrolled after "providing informed, written consent," the team notes.

In 112 of the women, the three initial shots boosted the concentration of hCG antibody in the blood to 50 nanograms per milliliter. That's enough to stop pregnancy, the study confirmed. During the first and third week of each cycle, the women had the amount of antibody to hCG measured. If this fell below 50 ng/ml, they received a booster shot, the team explains in the Aug. 30 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

The researchers stopped enrolling new participants in March 1992, and by

August 1993 only one woman who had antibody concentrations greater than 50 ng/ml had become pregnant. Eight women completed over 30 menstrual cycles without becoming pregnant; 36 had between 12 and 29 pregnancy-free cycles; and another 21 had between 6 and 11 cycles without a pregnancy.

However, 26 of the women whose antibody concentrations dropped or stayed below 50 ng/ml became pregnant. The researchers offered alternative forms of contraception for women with low antibody readings.

"Further work is necessary to make this vaccine workable as a general method for family planning," the investigators acknowledge. For example, researchers may want to modify the vaccine so that women don't need as many injections.

The vaccine, HSD, contains a key portion of the hCG molecule. This is combined with part of the luteinizing hormone found in sheep and either the tetanus or diphtheria toxin, which boost the body's immune response. The researchers also added a derivative of lipopolysaccharide, a molecule consisting of lipids and sugars, to the initial injections.

— T. Adler