

that are already approved and under construction (*Science*, 30 April, p. 734). "We're very disappointed, because we've been leading this field and now we're on hold while our rivals move ahead," Weekes says.

There is a chance, however, that astronomers may be able to proceed with VERITAS—possibly even at Mount Hopkins. Weekes says he hopes to discuss with the Forest Service the feasibility of two alternative sites in the vicinity of the present Whipple base camp. Although both sites suffer from rougher ground and greater exposure to transient light, they retain most of the cost savings of the original plan. Another possible site in Mexico would be considerably less accessible, he notes.

Even better, both of the Arizona alternatives lie more than a mile from the sweat lodge. Smithsonian officials hope that distance will allow Trevor Weekes's high-energy view of the universe to coexist with Cayce Boone's more traditional one. —MARK MURO  
Mark Muro writes from Tucson, Arizona.

## CANCER RESEARCH

### A New Way to Combat Therapy Side Effects

For decades, physicians have been treating cancer with chemotherapy and radiation, and for decades, the side effects have been brutal. Because the treatments damage healthy tissues even as they kill tumor cells, patients develop anemia, infections, vomiting, diarrhea, and other problems. These side effects can be so severe that they prevent patients from receiving effective treatment. Now, by capitalizing on their knowledge of a powerful tumor suppressor gene, researchers may have found a better way to ease side effects in some patients.

On page 1733, a team led by Andrei Gudkov of the University of Illinois, Chicago, reports that it has identified a novel compound that protects mice against side effects induced by radiation and allows them to withstand what would otherwise be lethal radiation doses. Other known compounds that help protect healthy tissue from cancer therapies have only limited effects, for example, helping restore the bone marrow's ability to make red blood cells. But because of its unusual mechanism of action, the new compound, a small organic chemical called pifithrin- $\alpha$  (PFT $\alpha$ ), may protect all vulnerable tissues.

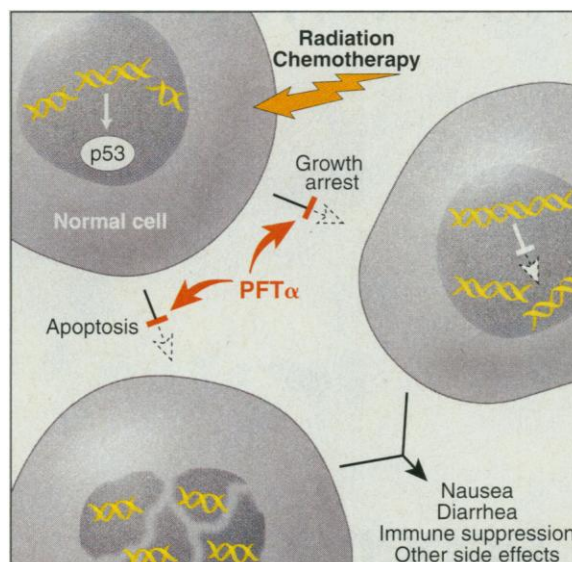
PFT $\alpha$  works by blocking a

protein called p53. When cells are poisoned by chemotherapeutic drugs or barraged by radiation, p53 spurs them either to commit suicide or to go into growth arrest. People whose tumors contain an active p53 gene won't be eligible for the drug, because it could help their tumors fight the therapy, too. But in about 50% of all human cancers, the p53 gene is inactivated, and PFT $\alpha$  could help people with such tumors endure higher, possibly life-saving doses of radiation or chemotherapeutic drugs. It's a "beautiful" paper, says molecular biologist Scott Lowe of Cold Spring Harbor Laboratory in New York. "A lot of people are going to say, 'Gee, why didn't I think of that?'"

To come up with their drug, Gudkov's team reversed conventional thinking about the p53 gene. Loss or inactivation of the gene is thought to be one of the genetic changes leading to cancer, presumably because it contributes to loss of growth control in tumors. That's led researchers to try to restore p53 to the tumors lacking a functional copy. But earlier results had shown that the protein also mediates the side effects of cancer therapy. For example, the healthy tissues of p53-deficient mice suffered less damage from gamma irradiation than the healthy tissues of normal mice.

That meant that blocking p53 could potentially prevent side effects—but only if it could be done without triggering the formation of additional tumors. Many researchers doubted that was possible, but Gudkov says he gambled that a drug that blocks p53 "temporarily and reversibly" would do the trick. But first the researchers had to find such a compound. None was available, he says, "because nobody was ever interested in suppressing p53."

Because p53 turns on cell-suicide genes,



**Defense line.** By interfering with p53's ability to induce apoptosis and growth arrest, PFT $\alpha$  may protect cells against cancer therapy side effects.

## ScienceScope

**Teachers and Researchers: Unite!** A new Russian initiative aims to bridge the gulf between universities and the nation's science strongholds, the institutes of the Russian Academy of Sciences (RAS). Russia's Ministry of Education and the U.S. Civilian Research and Development Foundation (CRDF) announced last week that three regions each will receive \$1 million to create centers that bring university and RAS researchers together.

The RAS's 325-odd institutes have long been the preferred workplace for Russia's top scientists, as they can work unfettered by teaching demands. But last year, in a bid to improve science teaching, the Education Ministry and CRDF hatched a plan to create joint RAS-university centers that would be funded by U.S. foundations and Russian sources (*Science*, 29 May 1998, p. 1336).

From 80 proposals emerged three winners: Far Eastern State University in Vladivostok, whose center will focus on marine life; Krasnoyarsk State University in Siberia, which will develop techniques for environmental remediation; and three universities in the Rostov region, which will study earthquake safety and pollutant monitoring. Another four centers are expected to be announced next May.

In Flux Nuclear scientists have given a lukewarm endorsement to efforts to restart the Fast Flux Test Facility, a controversial research reactor that has been idle since 1993. The American Nuclear Society (ANS) is applauding last month's decision by Energy Secretary Bill Richardson to study a restart, but says it will only back the move if the reactor doesn't drain funds from other nuclear research projects.

On 18 August, Richardson decided to move ahead with an environmental study of using the mothballed reactor in Hanford, Washington, for everything from fusion research to medical isotope production (*Science*, 20 August, p. 1191). But critics have opposed such plans, contending that the reactor's potential for generating radioactive waste overshadows any possible benefits.

ANS president Andrew Kadak has a different worry: that the restart's estimated \$400 million cost could siphon funds from DOE accounts that support university reactors and research. But he says the group will withhold final judgment until next year, when the restart study is expected to be completed.

**Contributors:** David Malakoff, Alexander Hellems, Richard Stone

the team devised a cultured cell system they could use to screen rapidly for compounds that block this activation. Several dozen of the 10,000 synthetic chemicals so tested had the desired effect, and about one-fifth of these were not toxic to cultured cells. One member of this group—PFT $\alpha$ —looked particularly promising. It blocked apoptosis triggered by radiation as well as by four chemotherapeutic drugs, and it also inhibited growth arrest induced by radiation. But it had no effect on the responses of p53-deficient cells—an indication that it works as postulated. “That satisfied us a lot, because it was what we expected,” Gudkov says.

The Gudkov team went on to test PFT $\alpha$  in mice barraged with a near-lethal dose of gamma radiation. “Amazingly,” he says, “a single injection rescued [normal] mice completely” from a radiation dose that usually kills 60% of the animals, while having no effect on p53-deficient animals. What’s more, the treated mice have survived more than 8 months—about half the normal mouse lifespan—and none have developed any tumors.

The group has begun testing PFT $\alpha$  to see if it also protects mice from chemotherapeutic drugs, and Gudkov says the “preliminary data are promising.” Moreover, other potential p53 inhibitors are in the pipeline. Still, before any of them can be used in the clinic, more long-term animal studies are needed to make sure that the drugs don’t induce tumor formation or have other dangerous side effects, warns medical oncologist Ronald Bukowski, director of experimental therapeutics at the Cleveland Clinic.

But if the new compounds pan out in humans, it would be great news for cancer patients. “What it means is that there may be... a selective way to decrease side effects and give optimal doses of treatment,” Bukowski says. “That’s what we’re all looking for.”

—DAN FERBER

Dan Ferber is a writer in Urbana, Illinois.

## ASTRONOMY

### Hubble Snaps Some Moving MACHOs

The name may suggest swagger, but MACHOs have been frustratingly reclusive. For the past decade, teams of astronomers across the globe have been scouring the halo of old stars that surrounds our galaxy for MACHOs (massive compact halo objects)—hypothetical objects that might make up the invisible “dark matter” pulling on the galaxy’s visible stars. The results have been tantalizing but ambiguous. Now a team of astronomers led by Rodrigo Ibata of the European Southern Observatory (ESO) in Munich, Germany, believe they have captured five candidate MACHOs on camera.

By comparing two Hubble Space Telescope images that probe the distant universe, Ibata’s team found the five objects moving very slightly in the foreground. The team believes the objects may be old white dwarf stars—dim, burned-out stars—in the halo. If the numbers can be extrapolated to the entire halo, “it would be a fair statement to say that at least part of the dark matter mystery has been solved,” says team member Harvey Richer of the University of British Columbia in Vancouver, Canada. But other astronomers caution that vast numbers of white dwarfs would create their own problems for theorists. And Ken Freeman of Mount Stromlo Observatory in Canberra, Australia, cautions: “It is not clear at this stage exactly what the MACHO objects are, so I am not sure if this is the first time that MACHOs have been imaged directly.”

Thus far, the standard technique for MACHO searching has been gravitational microlensing. Astronomers monitor stars in the Large Magellanic Cloud, a companion galaxy to the Milky Way, watching for the flicker that might indicate that the gravity of an unseen object passing between a star and Earth has slightly focused the star’s light. These efforts have detected almost 20 candidate MACHOs, and many astronomers believe MACHOs may account for a sizable chunk of the galaxy’s dark matter. But others say the lensing objects could lie outside our galaxy, in the Large Magellanic Cloud itself (*Science*, 17 July 1998, p. 332). And no one knew what MACHOs were—extremely dim stars, stray giant planets, or even small black holes.

Ibata, Richer, and Douglas Scott, also at the University of British Columbia, decided to see if they could spot MACHOs directly in a Hubble image called Deep Field North. This image, an exposure made over several days in December 1995, shows the faintest objects ever recorded by astronomers, including galaxies in the far reaches of the universe. A single image could not reveal whether any of the objects were MACHOs, but in a second image, any object orbiting in the halo of the galaxy would probably betray itself by moving across the sky.

In 1997, the group learned that Ron Gilliland of the Space Telescope Science Institute in Baltimore, Maryland, planned a second deep image of the same spot to search for

extremely distant supernova explosions. Gilliland agreed to share data from the image, made in December 1997. “I did find two supernovae,” he says, “but in the end, the search for moving objects turned out to be the more important project.” In a paper to appear later this year in *Astrophysical Journal Letters*, Ibata and his colleagues list five faint, bluish objects that changed position between December 1995 and December 1997. Two of them display a substantial proper motion (about 1/20th of an arc second in 2 years), while the other three are “right on the detection limit,” says Richer.

He and his colleagues suspect the objects are old, dim white dwarfs at a few thousand light-years’ distance. Although it is hard to extrapolate accurately from such a small population, if this number of white dwarfs were

scaled up to the whole of the galaxy, the total would be on the order of a few trillion—in good agreement with the microlensing studies. Assuming that the moving objects are white dwarfs, “the whole picture is self-consistent,” says Richer.

ESO’s Peter Quinn notes, however, that swarms of white dwarfs surrounding galaxies like our own would create astrophysical problems. If they formed in the usual way, from sunlike stars that grew old, shed their atmospheres, and then cooled, the process would have enriched the universe

with far larger amounts of elements heavier than hydrogen and helium than are seen. Ibata and his colleagues hope to confirm their proper motion measurements once Hubble has taken a third Deep Field North image next December. Other researchers have spotted what they think may be white dwarfs in a southern Deep Field image, and Ibata’s team hopes to make a second image of the same spot to see if they are halo objects.

Definitive confirmation may come from wide-angle surveys with large ground-based telescopes, says Gilliland. “If much closer members of this population are found, they could be studied spectroscopically to determine their true nature,” he says. Richer and his colleagues have their fingers crossed: “If the ground-based surveys don’t find them, our scenario is not correct,” he says.

—GOVERT SCHILLING

Govert Schilling is an astronomy writer in Utrecht, the Netherlands.



**Motion picture.** Five candidate MACHOs and their movement between 1995 and 1997 (bottom two rows).