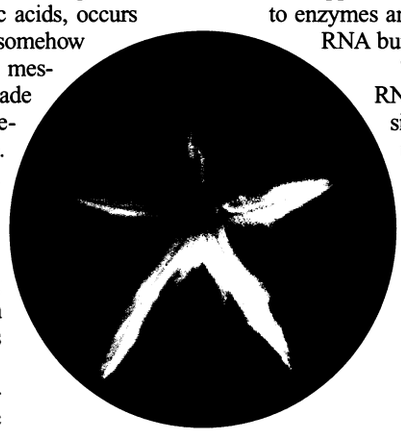
research using monkeys to study sensory perception, "would probably be totally destroyed" if the strike encompassed them, he says. Adds Lourival Possani, a biochemist at the biotechnology institute in Cuernavaca, 100 kilometers from Mexico City, "If they shut down the research, it's going to be a disaster for the entire country."–**JOCELYN KAISER**

MOLECULAR BIOLOGY

Candidate 'Gene Silencers' Found

Sometimes genes don't add up. About a decade ago, researchers added additional copies of pigment genes to petunias, hoping to darken their purple flowers. Instead, the petals turned white. Biologists now know that in many organisms, including plants, worms, and flies, adding an extra dose of a gene can have the paradoxical effect of slashing that gene's expression. This phenomenon, which goes by the name posttranscriptional gene silencing (PTGS) and helps organisms defend themselves against viral and other foreign nucleic acids, occurs because the added gene somehow causes destruction of the messenger RNA (mRNA) made by both it and the corresponding cellular gene. As a result, production of the gene's protein product shuts down. Now, researchers may have found the tracking system that homes in on the mRNA and triggers its destruction.



Quiet zone. Silenced pigment genes created the white stripes of this petunia.

Because gene silencing targets specific mRNAs, many people have thought that so-called antisense RNA—RNA with a nucleotide sequence complementary to the gene's mRNA—might be involved, possibly as a tag that marks the mRNA for degradation. They have been unable to identify those antisense RNAs or any other nucleic acid involved in silencing, however. But on page 950, molecular geneticists Andrew Hamilton and David Baulcombe of the John Innes Centre in Norwich, U.K., report that they have come up with a likely prospect: short RNA snippets, 25 nucleotides long, that match the gene being silenced.

"This could be just what we're looking for. It's the first good candidate for RNA molecules that have a role in PTGS," says Richard Jorgensen, a molecular geneticist at the University of Arizona, Tucson. The work should "lead to a much more mechanistic understanding of the process than we currently have."

Baulcombe and Hamilton, a postdoc in Baulcombe's lab, suspected that previous workers had failed to find antisense RNAs in silencing because the molecules were so small that they were running through the analytical gels too quickly for researchers to detect them. For the new search, Hamilton first added a gene that encodes a plant enzyme, called ACO, to each of five tomato plant lines. In two of them, the added gene led to the silencing of the endogenous *ACO* gene as indicated by the disappearance of its RNA.

The researchers extracted nucleic acids from the plant leaves, enriched the cellular mixtures for low–molecular-weight molecules, and separated the components using a gel system designed to retain small molecules. Hamilton then probed the nucleic acids with a piece of radioactive RNA that specifically binds to antisense ACO sequences. This probe picked up a 25-nucleotide molecule from the two lines where the gene was silenced but not from the three others. The researchers proved that the molecule was in fact RNA by showing that it disappeared from samples subjected to enzymes and chemicals that destroy RNA but not DNA.

To see whether similar RNAs would turn up in other silencing examples, Hamilton added a nucleic acid containing green fluorescent protein sequences to a leaf of a tobacco-related plant that already had a gene for GFP engineered into all its cells. A gene introduced in one place in an organism can silence the corresponding RNA at distant locations, and, in keeping with that, by several weeks later the GFP fluorescence had disappeared throughout the plant. Again, the team detected 25-nucleotide GFP antisense RNA in tissues exhibiting PTGS but not in control plants. The researchers analyzed several other examples of PTGS and in all cases they found a 25-nucleotide antisense RNA specific for the silenced gene.

The findings don't distinguish whether these antisense molecules cause silencing or are byproducts of it. If they're the cause, they may be made by an enzyme called RNA-dependent RNA polymerase (RdRP), which copies one RNA from another, creating antisense fragments. Researchers note, for example, that RdRP levels in plant cells rise upon viral infection, when gene silencing takes place. Alternatively, the 25-nucleotide RNAs may be debris left by an enzyme that chews RNA down to precisely that size. Either way, the existence of such uniform-sized RNAs provides insight into silencing, says Phillip Sharp, a biochemist at the Massachusetts Institute of Technology: "That's really remarkable. ... There's a very precise biochemical mechanism in there."

Besides pinning down what the RNAs are doing and how they are made, researchers would like to use them to enter the natural world of PTGS. Beyond acting as a defense against foreign nucleic acids, the normal role of PTGS is largely a mystery. "Can we find these 25-nucleotide RNAs in plants that don't contain any foreign DNA at all?" asks Baulcombe. "If so, what are they specific for? That will give us ideas about the processes they control."

And of course, scientists wonder whether the findings in plants apply to other organisms. "I can guarantee there will be a lot of flies and worms ground up" to look for a small RNA, Sharp says.

–**EVELYN STRAUSS**

NEUROBIOLOGY

Fetal Cells Help Parkinson's Patients

MIAMI BEACH, FLORIDA—A controversial therapy that involves injecting fetal cells into the brains of Parkinson's patients can slow down the progression of the disease, according to the first double-blind, placebo-controlled clinical study of the procedure. The study, presented here on 24 October at the Society for Neuroscience's annual meeting, shows that the fetal cells can produce a critical neurotransmitter, reducing patients' tremors and paralysis.

Parkinson's disease is marked by the death of brain cells that make the neurotransmitter dopamine. Since the 1980s, researchers have been developing a technique to substitute those brain cells with fetal cells destined to produce dopamine. In 1994, a team led by Curt Freed of the University of Colorado, Denver, received the first grant from the National Institutes of Health for a double-blind, placebo-controlled study of fetal cell transplants in human patients.

Forty patients with advanced Parkinson's disease underwent an operation in which a long needle was inserted through the forehead in four places, under local anesthesia. In half of the patients, the needles delivered small amounts of brain tissue—derived from four 7- to 8-week-old embryos—to the putamen, one of the brain areas affected by Parkinson's. The other patients constituted a control group. For them, the operation was a sham; nothing was injected into their brains.

One year after the operation, the control group hadn't improved. But the fetal tissue seemed to have taken hold in the patients who received a transplant: Positron emission to-

CREDIT: R. JORGENSEN

mography scans showed a 20% or better increase in dopamine activity in the putamen in more than two-thirds of the treated patients. Patients aged 60 or younger showed a marked reduction in Parkinson's symptoms, while older patients improved only slightly compared to the controls. Even after 36 months, the transplant group was doing better than the controls, Freed reported at the meeting.

The results of the trial are "modest, but [it was] very well done," says Roy Bakay, a neurosurgeon at Emory University in Atlanta. "It's the first study, and there are going to be advances in technology that will be exponential." New techniques to help fetal cells survive the transplant, for example, should lead to more dramatic clinical benefits, he predicts. Bakay adds that if the few human trials still under way also show no placebo effect from a sham operation, he hopes the Food and Drug Administration will remove one ethical objection to such research by allowing researchers to pit one treatment against another. "Maybe after a few of these studies, we shouldn't have to do sham operations anymore," he says. **–LAURA HELMUTH**

Researchers Plan Free Global Preprint Archive

While the National Institutes of Health (NIH) moves ahead with plans to create a free database of biological publications, a group of research librarians and information experts is trying to concoct something more far-reaching. The leaders—who are following the model of the Los Alamos National Laboratory (LANL) physics archive—met last week in Santa Fe, New Mexico, to begin working out the framework for a "universal preprint archive" that would include papers from all disciplines. By November, according to spokesperson Herbert Van de Sompel of the University of Ghent in Belgium, the group hopes to release a set of indexing protocols that would permit authors to deposit their work at participating sites and readers to retrieve the full text at no cost.

Van de Sompel, an expert on digital libraries, teamed up with Paul Ginsparg, founder of the LANL archive, and LANL research library director Rick Luce to organize last week's meeting. In attendance were more than 20 information specialists representing a variety of institutions, from Harvard University and the Massachusetts Institute of Technology to NASA and the U.S. Library of Congress. All support the idea of making scientific papers freely accessible to the public, although individual participants differ on specifics, such as how to handle non–peer-reviewed material.

The group aims to encourage the growth of preprint repositories such as the Los Alamos archive and knit them together with a set of protocols. Ginsparg's project at LANL began in 1991 as an archive for physics. Now it contains more than 100,000 papers on math, physics, and computer science. Ginsparg declined to discuss the new project in detail but said, "The hope is ... [to] catalyze real progress in new scholarly publishing models over the next 5 to 10 years" (see vole.lanl.gov/ups).

Several groups have already established preprint archives in their own disciplines, some of which have grown rapidly. For example, economists have organized several repositories in a site called Research Papers in Economics, coordinated by Thomas Krichel of the University of Surrey, U.K. (netec.mimas.ac.uk/RePEc). And Stevan Harnad of the University of Southampton, U.K., oversees CogPrints, a collection of papers in cognitive science, psychology, neurology, linguistics, and related fields (cogprints.soton.ac.uk). Last week's meeting was aimed at stimulating other grass-roots efforts.

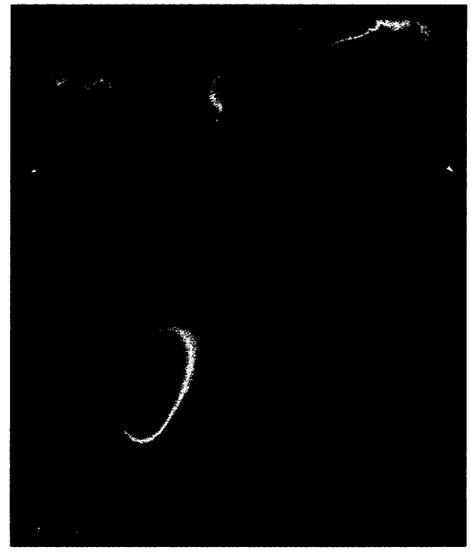
Van de Sompel says they "managed to agree on some important technical matters that will enable the creation of cross-archive end-user services," which are now being worked out in detail. The format is likely to follow a model described in a draft "Santa Fe Agreement" released earlier this month by Krichel. This draft, which lacks the indexing tags agreed upon last week, establishes a process by which archives and data providers can affiliate with the group. For example, it requires unanimous consent for changes and declares that the objective is "open and cooperative" sharing of data.

The Santa Fe effort differs in tone from NIH's PubMed Central: It's more radical. At present, the latter is gearing up to be a distributor of traditional peer-reviewed articles. But the Santa Fe archivists are focused on another type of scholarly discourse, one in which editors, peer reviewers, and paper will be optional. **–ELIOT MARSHALL**

First Glimpse of a Cosmic Funnel

Astronomers have caught their first-ever glimpse of the funnel that channels a fountain of subatomic particles, erupting from the center of a galaxy, into a narrow stream thousands of light-years long. The radio images, published in the 27 October issue of *Nature*, hint that a sheath of twisted magnetic fields focuses the particle stream.

Many galaxies have turbulent hearts that emit powerful beams of radio-emitting plasma like this one, which streaks from the center of M87, a galaxy 50 million light-years from Earth. Resembling spotlights at a Hollywood movie premier, such beams are probably generated as matter plunges into a supermassive black hole at the center of the galaxy. Magnetic fields churned up by the swirling, superheated matter presumably squeeze the material into a beam, but astronomers had been unable to locate the focusing "lens." The main problem is that the postulated lens must lie very close to the black hole itself, and it takes a radio telescope the size of Earth to see detail that fine at the center of a distant galaxy.



CREDIT: NRAO

Jet propulsion. New VLBA image of the core region of M87. Earlier radio images of the galaxy at larger scales are shown above.

Fortunately, a team of radio astronomers led by Bill Junor at the University of New Mexico, Albuquerque, had access to just such a telescope: the Very Long Baseline Array (VLBA). Consisting of 16 electronically linked radio dishes extending from Hawaii to Italy, the VLBA imitates the resolving power of a single telescope with a 10,000-kilometer-wide dish. "It is a wonderful instrument," says Junor.

Junor's image of M87 shows a 60-degree plasma cone a few hundredths of a light-year long emerging from the center of M87. Because this cone feeds directly into the 1000-light-year-long, 6-degree-wide jet seen in older images, Junor's team concludes that something is squeezing the plasma into a tight stream. "We want to invoke magnetic fields to wrap the jet," says Junor, but testing that theory with computer models "is a horrendously complicated problem." Maybe so, but astronomer Meg Urry of the Space Telescope Science Institute in Baltimore says, "these observations are an important first step" to understanding the focusing mechanism. **–MARK SINCELL**

Mark Sincell is a science writer in Houston.