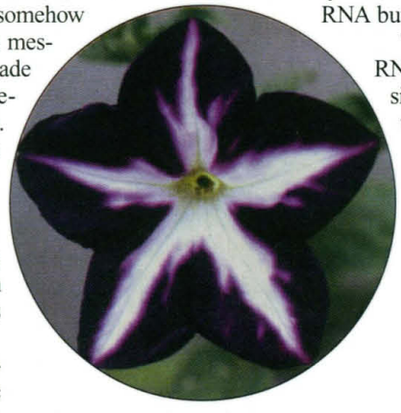
research using monkeys to study sensory perception, "would probably be totally destroyed" if the strike encompassed them, he says. Adds Lourival Possani, a biochemist at the biotechnology institute in Cuernavaca, 100 kilometers from Mexico City, "If they shut down the research, it's going to be a disaster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

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