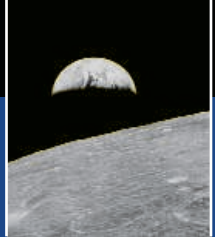
The land/sea diversity disparity
1318



Mining NASA's "lost" data
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and an electricity shutoff added to the damage, says Miguel Allende, who heads a cell genomics center in the building.

Researchers rushed to their labs the morning after the quake to slosh through chemical-laced water and salvage cell cultures and other frozen samples and reagents. But many materials were lost, Allende says.

About half of the biology department's 40 or so research groups suffered losses from the quake, says department chair Ana Preller. "The big problem is equipment," Preller says. Her preliminary estimate is $600,000 in losses. The quake also shifted and may have damaged a cyclotron in the physics department.

Allende and other faculty members have sent some students to colleagues' labs for now. Colleagues abroad have also offered to take in students from Concepción and Santiago. "It's taken 11 years to get where I am now. Doing science here is very hard. It's discouraging. But maybe it will be an opportunity to do some new things," Allende says.

–JOCELYN KAISER AND ANTONIO REGALADO

PHARMACOLOGY

The Puzzling Rise and Fall of a Dark-Horse Alzheimer's Drug

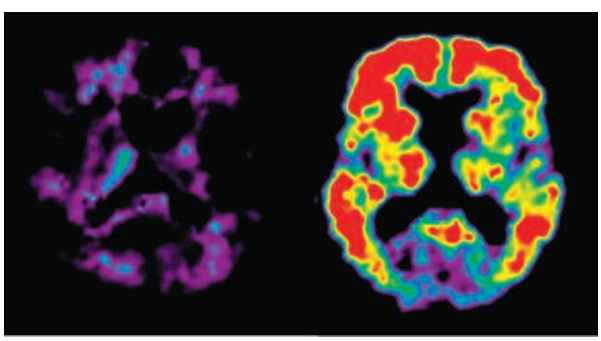
The announcement last week that a closely watched phase III clinical trial for Alzheimer's disease had failed to show a significant effect deals yet another demoralizing blow to patients, families, and caregivers. It may also mark the beginning of the end to one of the most unusual stories in Alzheimer's drug development.

The trial involved a drug called Dimebon, which catapulted into the limelight with a spectacularly successful trial published in *The Lancet* in 2008. "It looked better than anything we'd ever seen before," says Samuel Gandy, an Alzheimer's researcher at Mount Sinai School of Medicine in New York City.

Dimebon was an unlikely Alzheimer's drug. An antihistamine introduced in Russia in 1983, it turned up in a screen for potential Alzheimer's drugs led by scientists at the Institute of Physiologically Active Compounds in Chernogolovka, Russia. In follow-up experiments, the drug improved the performance of memory-impaired rats, and a pilot study with 14 Russian Alzheimer's patients showed encouraging results, published in a 2001 paper in the *Annals of the New York Academy of Sciences*.

Based on those findings, one of the Russian scientists, Sergey Bachurin, came to the United States to seek investors and partners in developing the drug. Bachurin persuaded San Francisco–based biotech entrepreneur David Hung to establish a company, called Medivation, and reportedly exchanged the rights to the drug for equity in the company. With initial support from private investors, Medivation recruited several top experts to design a larger clinical trial. The experts included Paul Aisen, a neurologist at the University of California, San Diego, who oversees government-sponsored clinical trials as director of the Alzheimer's Disease Cooperative Study; Rachelle Doody of Baylor College of Medicine in Houston, Texas; and Mary Sano of Mount Sinai.

The results were remarkable: The 2008 *Lancet* study, a double-blind, placebo-controlled trial, reported that 89 people with mild to moderate Alzheimer's disease who took Dimebon showed significant improvements in memory and cognition, as well as the ability to carry out the activities of daily life. The effects far surpassed those of any Alzheimer's drug on the market or in development, and Hung says several pharmaceutical companies bid to purchase the rights to Dimebon. Pfizer won, paying $225 million.



Bad news. A recent trial dims hopes that Dimebon will be an effective treatment for Alzheimer's disease, which loads the brain with amyloid plaques (*right*).

The *Lancet* findings struck many researchers as too good to be true, says Rudolph Tanzi, an Alzheimer's researcher at Harvard University. "Nobody could figure out what an antihistamine does" to fight Alzheimer's disease, says Sam Sisodia of the University of Chicago in Illinois. Several ideas have been floated, Sisodia says, but supporting evidence is scant. Still, he and others say they were willing to suspend their disbelief, largely because of the involvement of Aisen, Doody, and Sano. "If you had to pick the five best trialists in the world, they would be three of them," Gandy says.

But the new trial, despite a design almost identical to that of the *Lancet* study, yielded dramatically different results. It enrolled 598 patients with mild to moderate Alzheimer's. This time, however, there were no significant differences between the Dimebon and placebo groups. "It's hugely disappointing," says Aisen. He says he's at a loss to explain the discrepancy, although he notes that it's not unheard of for a drug to have both positive and negative trials before winning approval. Gandy, however, says, "I'm not sure that there has ever been such a night-and-day difference in replicate trials that turned out to be biological variation." Medivation and Pfizer are poring over the data in search of an explanation, says Hung, who declined to discuss their leading hypotheses. For now, the companies will continue with three other Dimebon trials already under way for Alzheimer's disease, in addition to one for Huntington's disease.

But to some, Dimebon is starting to look like a dark horse whose race is run. "I don't think that the drug is dead and buried today, but we need to get some clarity or good news soon," Gandy says.

–GREG MILLER

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