til June 2001, TIGR's Timothy Read plans to start microarray studies in July to identify target proteins. Les Baillee, a microbiologist with the Defense Evaluation and Research Agency in Porton Down, Salisbury, United Kingdom, is eagerly awaiting the results, which he says will enable anthrax researchers to avoid laborious screening and focus directly on likely vaccine candidates. These data should be valuable, too, for researchers studying *Bacillus anthracis*'s close cousins, one of which causes food poisoning and the other of which is used to control insect infestations of crops. Says Read with obvious delight: "The sheer number of ways you can use genome data is amazing."

–ELIZABETH PENNISI

CONFLICT OF INTEREST

NEJM Admits Breaking Its Own Tough Rules

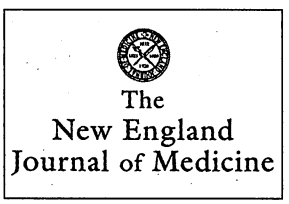
The New England Journal of Medicine (*NEJM*), which prides itself on having the toughest conflict-of-interest guidelines for authors in scientific publishing, has been forced to admit that it has been regularly breaching those standards. Whereas some researchers say that the missteps show that such strict standards are impractical, the journal's editors see them as a spur to do better.

The problem came to light last fall when the *Los Angeles Times* published two articles documenting instances in which *NEJM* review authors had financial links to drug companies that sold products they were writing about. The *NEJM* did its own review and came up with 19 rule-breaking articles covering treatments for diseases such as multiple sclerosis, breast cancer, and diabetes. In a terse apology in the 24 February issue, the editors list these as cases "in which one or more authors ... received major research support ... from relevant companies or served as consultants at the time they were invited to prepare their articles."

NEJM Editor Marcia Angell says that the mistakes were due to "poor communication and poor coordination" among editors. That's no surprise, she says, given that *NEJM* is charting new territory: "We are attempting to maintain a conflict-of-interest policy that no one else even bothers to try."

The journal makes public any information on the corporate ties of authors of research papers, and it essentially forbids writers of reviews and editorials from having any industry connections. The problem, says Angell, is that for reviews there was "a discrepancy between policy and practice. ... We permitted major [industry] research support to researchers if that support was given to the institution" rather than to the individual. That exemption was proposed by the editor of the drug therapy reviews, Alastair J. J. Wood of Vanderbilt University in Nashville, Tennessee, and the editors at the journal's Boston headquarters accepted it.

Through this generous loophole were admitted almost half of some 40 drug-therapy review articles published since 1997. Vera Price, a dermatologist at the University of California, San Francisco (UCSF), who published an article on hair-loss treatments, told editors, for example, that she had received research funds and consulting fees from a company that sells such treatments. But because the research money had gone to UCSF first, she was asked to sign a statement saying she had "no current, recent past, or planned future financial associations ... with a company that stands to gain" from products discussed in the article. Angell says the *NEJM* basic policy will remain unchanged, and no exceptions will be made for institutional funding. Authors will also be asked to submit a detailed accounting of all funding sources.



Some observers believe that *NEJM*'s policy is unrealistic. "It's almost impossible to find a very informed commentator on a medical topic who hasn't had money from the pharmaceutical industry," says Tony Delamothe, deputy editor of the *British Medical Journal*. The *BMJ* doesn't ban anyone on the basis of their funding sources, he says, but requires that all such information be divulged to readers.

But Wood and Angell think that their 10-year-old policy is the best. "To say 'caveat emptor' is not helpful to readers," says Angell. Other journals are not as conscientious on that issue, adds Wood: "We frequently see articles that we've previously rejected for conflict of interest popping up in other prestigious journals."

–CONSTANCE HOLDEN

RADIO ASTRONOMY

Budget Pressures Force Closing of Kitt Peak Dish

TUCSON, ARIZONA—Like a homeowner with limited storage space, the National Radio Astronomy Observatory (NRAO) is discarding a cherished possession to make room for a big new acquisition. But some scientists say the observatory is acting in haste, before it has worked out the financing for its new purchase and years before delivery.

Last week NRAO officials announced that they would shutter a pioneering millimeter-wavelength telescope on Kitt Peak in southern Arizona on 1 July, laying off half the 25-member staff. The observatory is building one of two prototypes for a proposed array of 64 dish antennas in the Chilean desert, a joint project with the European Southern Observatory that could cost each partner an estimated $200 million. But that project, called the Atacama Large Millimeter Array (ALMA), hasn't received any construction funds and won't come online for several years, creating a gap that many U.S. radio astronomers say will put a serious crimp in the field. "Young researchers are going to get tired of waiting for research time and go off and get grants to do something else," warns Tom Bania, a professor of astronomy at Boston University. "It doesn't make much sense [to close Kitt Peak] when you're making a big commitment to the field with ALMA."

No openings. The 12-meter millimeter telescope at Kitt Peak will be shut down on 1 July.

CREDIT: (RIGHT) NRAO/AUI

A flat budget is forcing NRAO's hand, says director Paul Vanden Bout. The observatory would receive $32.5 million in the 2001 budget request from the National Science Foundation (NSF), unchanged from the current year (*Science*, 11 February, p. 952). "We had once hoped to keep the 12-meter [dish] going until ALMA began interim operations, probably in 2005, but that hope began to fade last year," Vanden Bout says. A final decision to shut the telescope was made "in the last few weeks," he adds, and that suddenness "may have shorted discussion a little."

Indeed, the abrupt closure has disturbed many researchers. The Arizona dish, which opened in 1967, pioneered exploration of the molecular composition of the interstellar medium at millimeter wavelengths. Later, it proved ideal for studying molecular clouds, star formation, and distant galaxies, as well as the atmosphere of Mars and Venus. Used by 150 investigators a year, it is also the only U.S. millimeter-wavelength telescope run full-time as a national facility and open to all astronomers.

For that reason, Lucy Ziurys, an astrochemist at the University of Arizona in Tucson, frets that closing the telescope will

doom many research projects, noting that no other facility offers the same combination of highly sensitive and stable receivers to detect faint signals, extremely efficient data collection, and wide frequency coverage in the millimeter range. "I myself won't be able to finish five or six projects," she says.

Others worry that the closure could drive young researchers out of the field. These critics doubt that ALMA will begin even interim operations by 2005, given that NSF has requested $6 million to extend a 3-year, $26 million design and development effort for another year and won't make a bid for construction funds until 2002 at the earliest.

To be sure, the directors of at least two university facilities—the California Institute of Technology's Owens Valley Radio Observatory and the Five College Radio Observatory in Massachusetts—say they would welcome proposals from Kitt Peak researchers. The university community "may well be able to pick up much of the slack," says Anneila Sargent, president-elect of the American Astronomical Society, director of Owens Valley, and a member of the board of Associated Universities Inc., which operates NRAO for NSF. "Compromises and adaptations will be possible." But some astronomers are skeptical that university-run dishes and arrays will be able to accommodate researchers displaced from Kitt Peak. "Yes, the university facilities make time available to outside scientists, but they're not really oriented to the general user like a national observatory," says astronomer Jean Turner of the University of California, Los Angeles.

Whatever the outcome, all parties agree that the decision to close the 12-meter telescope is a sad one. "You'd like to focus on the future without letting go of the present and the past," says Vanden Bout. "Unfortunately, that couldn't happen here."

–MARK MURO

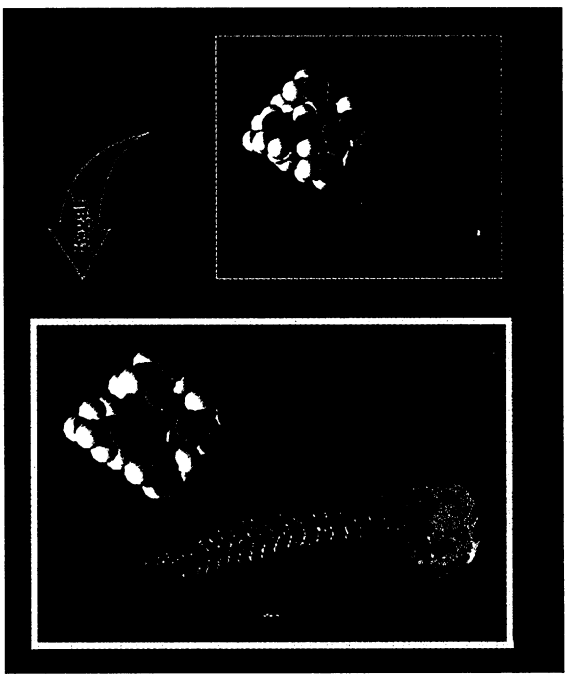
Mark Muro writes from Tucson, Arizona.

MAGNETIC RESONANCE IMAGING

Detecting Enzyme Activity in Live Animals

Thomas Meade and his colleagues at the California Institute of Technology in Pasadena have adapted a technique perhaps best known for peering inside athletes' injured knees to watch genes being turned on in living tadpoles. The researchers report in the March issue of *Nature Biotechnology* that they've used magnetic resonance imaging (MRI) to track the expression pattern of an enzyme called β-galactosidase in living *Xenopus laevis* tadpoles. They were able to see the enzyme being produced deep within the animal's head, where conventional imaging techniques can't reach without slicing through the animal.

"They can see a measurable result in a living animal," says Claude Meares, a chemist at the University of California (UC), Davis. "That's really quite exciting." What's more, the resolution—the highest so far in these types of studies—was good enough to discriminate structures as small as individual cells. Richard Harland, a developmental biologist at UC Berkeley, describes that achievement as "impressive."



Uncaged. When β-galactosidase (β-gal) opens the chemical cage surrounding gadolinium (purple), cells producing the enzyme light up in the MR image of this tadpole.

Meade's team is one of several groups using MRI to probe cellular processes deep inside living organisms (*Science*, 17 December 1999, p. 2261). The payoff could be considerable. By allowing researchers to follow the activity of specific genes in living embryos, for example, the technique should generate new insights into embryonic development. And ultimately, experts hope, it will provide more sensitive methods for diagnosing diseases such as cancer and also help physicians measure how well therapies for cancer and other diseases are working.

Typically, MRI detects perturbations induced in hydrogen atoms—particularly those in water—by an intense magnetic field. To measure the activity of β-galactosidase, Meade and his colleagues needed to find a way to amplify the signal only in those cells where the enzyme is active. They turned to gadolinium, a metal that enhances the contrast in MR images because its unpaired electrons interact with the protons in water, boosting the signal. The researchers enclosed the gadolinium in a chemical cage that normally keeps it from interacting with water, but they provided the cage with a gate, in the form of a sugar molecule, that springs open when clipped off by β-galactosidase. This exposes the gadolinium to water, thus upping the MRI signal wherever the enzyme is active.

To test the technique, Angelique Louie, a postdoc in Meade's lab, injected both of the first two cells of *Xenopus* embryos with the caged gadolinium. Then she injected DNA or messenger RNA that encodes β-galactosidase into just one of the two cells and allowed the embryos to grow into tadpoles.

The researchers generated MR images of the living animals. Then they compared these images with the patterns obtained when they killed the animals and stained them with a reagent that reveals β-galactosidase activity. Bright regions in the MR images correlated strongly with the locations of enzyme production revealed by the staining. "You can see things to a cellular level in deep tissues," says Louie.

The method holds promise for a wide variety of applications. In principle, Meade notes, the chemical properties of the gate that shields the gadolinium can be modified so that it opens in response to any of many different enzymes. In addition to creating agents that could be used to study embryonic development, researchers could, for example, devise compounds that are activated specifically in cancer cells. This might provide a technique for early detection of new tumors or those regrowing after treatment, notes Daniel Sullivan, a radiologist at the National Cancer Institute in Bethesda, Maryland. Similarly, it might someday be possible to monitor the effectiveness of gene therapy by designing the gadolinium cage so that it's opened by a therapeutic gene's product.

Researchers have a long way to go before such applications become reality, however. In order to be medically useful, the caged gadolinium would have to penetrate into the tissues of the body after it is injected into the bloodstream. The next step, Meade says, is to look at how well the compound distributes through small animals such as mice. If it doesn't, he says, he hopes to devise ways to deliver the compound efficiently, say by attaching proteins that can snake their way into cells. "The door's been cracked," Meade say. "Now it's just left to our imagination to see what we can develop."

–EVELYN STRAUS

CREDIT: A. LOUIE AND T. MEADE, *CHEMICAL & ENGINEERING NEWS*