dean for 7 years. "I think it reaffirms the university's goal of maintaining Yale medical school as among the very most research-intensive national institutions."

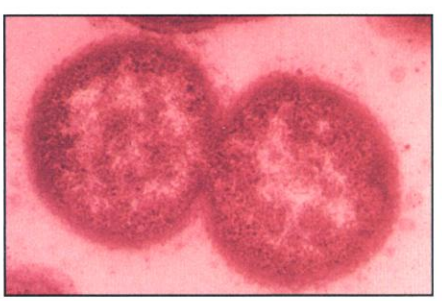
The investment comes at a time when many university medical centers are suffering from rising costs and reduced clinical income, says the Association of American Medical Colleges. But Rosenberg says that because Yale has been so successful in winning research grants, it hasn't needed to rely heavily on clinical income.

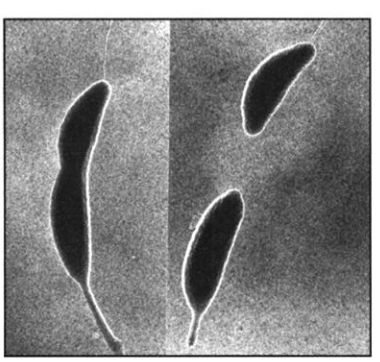
–CONSTANCE HOLDEN

MICROBIAL GENOMICS

Culling Genes Early Yields Rich Harvest

CHANTILLY, VIRGINIA—A team of human sequencers using high-powered computers has just finished assembling the entire genetic sequence of the common bacterium *Caulobacter crescentus*. The feat, announced at a meeting* on microbial genomes held here last month, marked another important milestone in the burgeoning business of gene sequencing. But the real news was that even before the sequence was completed, another team had scoured the emerging data and found several hundred new genes involved in the bacterium's cell cycle.





Preview of coming attractions. Microbial genomes are yielding their secrets even before they are complete: *B. anthracis (above)*, *N. meningitidis (right)*, and *C. crescentus*, stalked and mobile stages *(below)*.

That accomplishment underscored an important take-home message from the meeting: Sequence data don't have to be perfect, or even finished, to be extremely useful. Indeed, another team reported that it has used early sequence data to identify targets for a vaccine against a pathogen that causes meningitis. And researchers studying the microbe that causes anthrax said they will soon start analyzing gene expression even though these genes are still buried in tiny pieces of unconnected sequence data. "It's amazing how fast [the genome data have] been put to use," raves microbial genomicist Siv Andersson of the University of Uppsala, Sweden. "People should be looking at genomes long before they are done," adds Janine Maddock, a microbiologist at the University of Michigan, Ann Arbor.

Take the case of *C. crescentus*, a bacterium that thrives in aquatic environments that lack sufficient nutrients for most other lifeforms. This makes the bug a potential candidate for cleaning up pollution. But microbiologists are fond of it for another reason as well: Because it goes through distinct morphological stages, it is useful for understanding differentiation in prokaryotic organisms (those without a cell nucleus).

Typically, *C. crescentus* has a whiplike appendage called a flagellum that it uses for swimming. But when it's time to reproduce, *C. crescentus* jettisons its flagellum, replacing it with a short stalk that anchors the tiny cell to a nearby surface. The DNA then replicates and the stalked cell divides asymmetrically, pinching off a new, mobile "swarmer" cell. These characteristic "stalked" and "swarmer" stages enable microbiologists to associate genetic changes with distinct stages of the cell cycle.

The Institute for Genomic Research (TIGR) in Rockville, Maryland, has been sequencing the organism's 4-million-base genome, which is about the same size as that of *Escherichia coli*. At the meeting, William Nierman reported that TIGR had just finished putting the pieces of the sequenced genome together. But a team at Stanford University headed by Lucy Shapiro, in cooperation with TIGR, began working with these data about 9 months ago, long before they were assembled—in fact, they were still in 700 separate pieces.

The group scanned the early sequence with gene-finding programs, culling about 3000 tentative genes, team member Michael Laub reported at the meeting. They spotted DNA from each gene onto a glass slide and used this microarray to monitor the RNA transcribed from each gene at 15-minute intervals over *C. crescentus*'s life cycle.

Their initial results indicate that the organism alters the activity of 462 genes—some 400 of which are newly recognized to change—over the course of the cell cycle, says Laub. "They found genes they never would have thought of looking for," notes Andersson. Laub and his colleagues expected to see changes in the expression of the genes that make the flagellum, for instance. But they can't explain why 107 genes related to energy use and metabolism are altered as well. Laub speculates that metabolic requirements change depending on where the organism is in its life cycle. "The array data are leading us in new directions," he notes.

Other microbiologists at the meeting were impressed not just with the Stanford team's data but that they were able to garner them at all with a microarray. Microarrays are still tricky to use, and bacterial RNA is much harder to work with than, say, yeast or human. "This is the first successful microbial cell cycle experiment that's ever been done," says Maddock. Moreover, it demonstrates that microbial RNA can readily be put to use in these global expression studies, adds Frank Rosensweig, an evolutionary biologist at the University of Florida, Gainesville. "I regard this as a real breakthrough paper."

Microarrays aren't the only way to make use of preliminary sequence. For the past 2 years, TIGR researchers have been working with E. Richard Moxon, a microbiologist at the University of Oxford, to sequence a strain of *Neisseria meningitidis*. Early in the sequencing process, Moxon and TIGR's partner, Chiron Corp. of Siena, Italy, began analyzing those DNA fragments to look for proteins that might be new vaccine candidates. Rino Rappuoli and his team at Chiron used computer programs to identify DNA sequences likely to code for proteins found on the surface of the bacterium. The researchers then inserted these genes into bacteria, isolated the proteins produced, and injected the proteins into mice that were later exposed to the pathogen. Rappuoli reported at the meeting that, of some 600 proteins the computer identified, 350 were successfully produced in bacteria, and 25 of those induced a protective immune response in the mice—some strong enough to warrant further investigation.

Other global expression studies will start soon on the anthrax genome. Even though the entire sequence may not be complete un-

CREDITS: J. MADDOCK/UNIVERSITY OF MICHIGAN

* The Fourth Annual Conference on Microbial Genomes, 12 to 15 February.

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

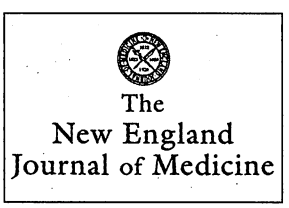
The New England Journal of Medicine (*NEJM*), which prides itself on having the toughest conflict-of-interest guidelines for authors in scientific publishing, has been forced to admit that it has been regularly breaching those standards. Whereas some researchers say that the missteps show that such strict 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."

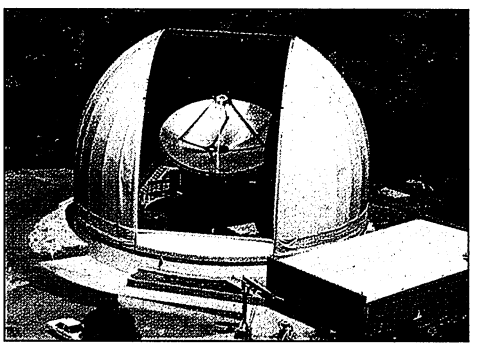
–CONSTANCE HOLDEN

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