UNIVERSITY OF ROCHESTER

Researcher Sues After School Spent His Grant

Robert Ader, a prominent neuropsychologist at the University of Rochester in New York, won a $200,000 research grant from Philip Morris Companies Inc. in 1989. He didn't need the money at the time, so he left it in an endowment fund for future use. But he later discovered that his department chair, without his knowledge, had spent the funds to renovate his lab. In January, after a long battle to get the money back, he sued. A judge rejected the suit last month on grounds that the statute of limitations on such complaints had run out, but Ader says he plans to appeal.

Missing money. Robert Ader hopes to get back research money used to renovate his University of Rochester lab.

The case is drawing national attention. Martin Snyder, an official at the American Association of University Professors, which is weighing whether to support Ader's legal campaign, calls it "a very, very curious situation. ... I haven't encountered anything quite like this, and no one else has, either."

Ader, the George L. Engel professor of psychosocial medicine, has been at Rochester since 1957. He is known for his pioneering rodent experiments on the interaction between the nervous and immune systems that spawned the field of psychoneuroimmunology.

His work was already well funded by public and private agencies when the money from Philip Morris—a general grant to support his research, with no strings attached and no reporting requirements—came in. So he left it untouched in his department's endowment account. For several years, he received regular interest statements indicating a growing balance, according to his lawyer, Alexander Geiger.

But the money in fact wasn't there. When a new department chair arrived in 1996 and began going through the books, Ader was told that the money had been spent to renovate his lab. He says university administrators had promised to refurbish his lab when he was named head of the Division of Behavioral and Psychosocial Medicine in 1982, but he was never told his own research funds would pay for the work.

After 4 years of memos and meetings with the then-dean of the School of Medicine and Dentistry, Ader says he was finally told his complaints were groundless because the $200,000 had been used for his research program, as Philip Morris intended. Ader won the backing of the University Committee on Tenure and Privileges, but the university president decided that the committee had no jurisdiction over the matter. After further futile appeals, Ader went to court asking the university to turn over $600,000—the grant award plus accrued interest—for his research.

University spokesperson Teri d'Agostino says that using the grant money to pay for Ader's lab was appropriate because "the funding source had placed no restriction on the use of these funds," and they "were used exclusively for Dr. Ader's program." She says that the school has no explanation for the financial statements, and that only the former chair, now deceased, knew what they were. However, she agrees that Ader should have been kept better informed about what was going on.

In court, the university did not argue the merits of the case but convinced the judge that Ader's complaint was invalidated by a 4-month statute of limitations on review of disputed grievances with government bodies. Geiger says the court has misinterpreted the law, because the last letter from university officials was sent in October, only 3 months before the suit was filed.

Ader is keeping up the attack. "It's disheartening to find, after 40 years in academia, that there are university officials who will resort to patently deceptive practices," he says. Nicholas Cohen, a longtime collaborator and a member of the Committee on Tenure and Privileges, says the group "argued [in vain] that it was indeed faculty privilege not to have money taken from them." The committee plans to recommend the establishment of some channel to handle grievances against the administration, he adds, such as the appointment of a mediator.

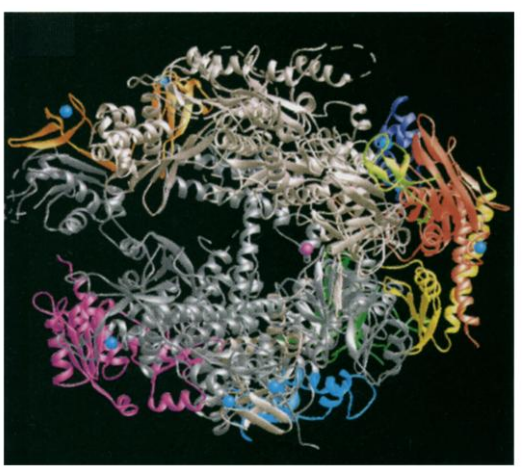
–CONSTANCE HOLDEN

X-RAY CRYSTALLOGRAPHY

Transcription Enzyme Structure Solved

If any enzyme does the cell's heavy lifting, it's RNA polymerase II. Its job: getting the synthesis of all the proteins in higher cells under way by copying their genes into RNAs, and doing it at just the right time and in just the right amounts. As such, pol II, as the enzyme is called, is the heart of the machinery that controls everything that cells do—from differentiating into all the tissues of a developing embryo to responding to everyday stresses. Now, cell biologists can get their best look yet at just how the pol II enzyme of yeast and, by implication, of other higher organisms performs its critical role.

In two papers published online today by *Science* (www.sciencexpress.org), Roger Kornberg's group at Stanford University School of Medicine describes the atomic structure of the yeast enzyme; a slightly lower resolution structure captures yeast pol II in the act of transcribing a piece of DNA into RNA. Cell biologist E. Peter Gei-



Jaws of life. This ribbon image of pol II shows the opening to the enzyme's active site. The colors mark the different protein subunits of pol II.

CREDITS: (LEFT TO RIGHT) COURTESY OF ROBERT ADER/UNIVERSITY OF ROCHESTER MEDICAL CENTER; P. CRAMER *ET AL.*

duschek of the University of California, San Diego, describes the achievement as "extraordinary." Not only does it give cell biologists their first clear view of yeast pol II in action, but it also opens the door to seeing exactly how the enzyme interacts with the many other proteins that regulate its activity. And that, adds Geiduschek, will "transform the analysis of transcription and transcription mechanisms in a fundamental way."

Kornberg and his colleagues have been on the path to the pol II structure for nearly 20 years. The first 10, he recalls, were devoted to isolating the myriad proteins involved in gene transcription. During that time, his team and others found that the pol II machinery of higher organisms is very large. The enzyme alone contains 12 different proteins bound together in a complex that has a molecular weight of about 500,000.

That, combined with the fact that the enzyme is present in cells in very low concentrations, meant that determining the enzyme's three-dimensional structure by x-ray crystallography would be extremely difficult. But by early last year, the Kornberg team, including postdocs Patrick Cramer and Averell Gnatt, the lead authors on the current papers, had determined the structure of a complex containing 10 of the enzyme's 12 proteins to a resolution of about 3.5 angstroms—good enough to see the backbones of the protein chains but not of the side chains of the individual amino acids (*Science*, 28 April 2000, p. 640). (The other two proteins, which aren't needed for RNA elongation, kept pol II from crystallizing.)

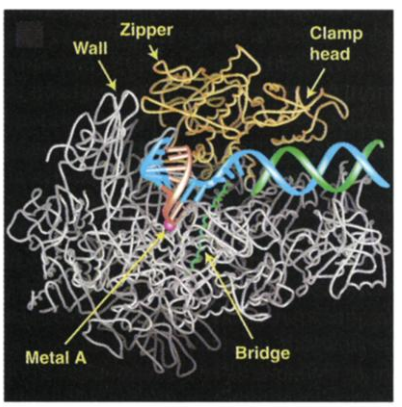
In the current work, the team has solved the pol II structure to a resolution of 2.8 angstroms. Now, Cramer says, "we can see where every amino acid goes." The new structure largely confirms what the earlier one had suggested. For example, the enzyme has a pair of "jaws" that enable it to attach to the DNA to be copied. And because the growing RNA chain is enclosed within pol II's active site, the bottom of the enzyme has a large pore through which the nucleotide building blocks of RNA can enter.

These features are quite similar to those seen in the only other multisubunit RNA polymerase whose structure has been determined, the enzyme from the bacterium *Thermus aquaticus*. Seth Darst, a former Kornberg postdoc now at New York City's Rockefeller University, and his colleagues solved that structure. And even though the bacterial enzyme is less complicated than yeast pol II, having just five subunits rather than 12, Darst says, "the central cores of the structures are identical. ... These enzymes are highly conserved." However, they vary around the periphery, which carries important contact points for regulatory proteins. Researchers will now be able to see those of the yeast enzyme clearly.

And the structure of human pol II should be very similar. Kornberg notes that 53% of the amino acids in the yeast and human enzymes are the same and that the identical amino acids are distributed similarly throughout the proteins of the two enzymes. "To all intents and purposes, the structures are the same," Kornberg says.

Once they had nailed down pol II itself, Kornberg's team was able to take the next step: solving the structure of the enzyme in a complex with DNA and an elongating piece of RNA. The researchers couldn't have done that with last year's lower resolution structure, Cramer says. But with the new one, "the elongation complex [structure] just pops out."

Among other things, that structure provides an answer to a long-standing puzzle in gene transcription. When pol II transcribes a gene, it has to latch onto the DNA and then move long distances—sometimes millions of nucleotides—without falling off. But when it reaches the end of the gene, it needs to let go. What this second structure shows, Kornberg says, is that one segment of the enzyme forms a "clamp," which is open in the free enzyme but swings shut once RNA synthesis begins and the active site contains a DNA-RNA hybrid. RNA synthesis stops at the gene's termination site, however, and with no hybrid there, the clamp swings open, releasing the enzyme.



In the loop. The pol II "clamp" (orange) holds onto the DNA while it's being transcribed into RNA (red).

CREDIT: A. L. GNATT *ET AL.*

Although researchers are thrilled by the new work, Geiduschek and others point out that "this is really more of a beginning, rather than an end, to the story." The next big step is solving the structure of pol II complexed to the many transcription factors and other proteins that regulate gene transcription. Then, "people can really begin to understand how those factors interact with the polymerase. That will have a huge impact on the field," says Robert Landick of the University of Wisconsin, Madison.

ScienceScope

Dioxin Dilemma The Environmental Protection Agency (EPA) is facing a tough decision over whether to back away from calling dioxin a human carcinogen. In a 13 March draft summary to EPA chief Christine Whitman, a subpanel of EPA's Scientific Advisory Board approved a long-debated draft report that includes the classification (*Science*, 10 November, p. 1071). But the group slammed some of the agency's conclusions. In particular, "most" members of the 21-person panel disagreed with the label.

EPA scientists are hoping for a stronger endorsement from the full science board, due to meet next month. And they vow to resist pressure from industry to downgrade dioxin's dangers. "We're sticking by our guns," says one, noting that the National Institutes of Health and other bodies agree that dioxin causes cancer. But some observers—including *The Washington Post* last week—say Whitman may put the report on ice and order more study.

IT Anyone? It's spring in Canada, and multimillion-dollar national science initiatives are popping up like crocuses. The latest to bloom is a $325 million, 5-year proposal from industry to rejuvenate university information technology departments through research in microelectronics, photonics, and other fields. The initiative, which would be run by a nonprofit entity dubbed eMPOWR Canada, hopes to follow the path taken by a national genomics initiative (*Science*, 13 April, p. 186). Although advocates say it would triple the estimated 350 faculty members in the field, produce skilled workers, and lead to marketable products, the proposal is only one of several that the government is being asked to weigh to bolster academic research.

Get-Out-of-Jail-Free Card Geologist Martin Pickford may no longer have to worry about being thrown into a Nairobi jail. Last year, Pickford, a geologist at the Collège de France in Paris who studies human evolution, was arrested by Kenyan authorities and imprisoned for 5 days on charges of fossil hunting without a permit. The charges are linked to a paleontology turf war between Pickford's research group and rivals (*Science*, 13 April, p. 198).

Pickford insists that he had a valid permit, and the charges weren't prosecuted. But just to be safe, the Community Museums of Kenya (CMK)—which sponsors Pickford—has procured him a new license that is good for the entire country through April 2004. Addy Kaaria, head of Kenya's permitting department, confirms that Pickford can now work "with no problem."

The structural work may have practical implications as well. If researchers can find differences between the way human pol II and its bacterial and fungal counterparts interact with either DNA or associated proteins, they may be able to find antibiotics that work by specifically inhibiting pathogen polymerases. Another possibility is to look for drugs that prevent transcription factors involved in stimulating cell growth from binding to pol II, as these may be potential targets for cancer therapy.

Meanwhile, the members of Kornberg's team can pride themselves on a feat that was judged impossible just a few years ago. "Until a relatively short time ago," Geiduschek says, "pol II was regarded as beyond contemporary reach." **–JEAN MARX**

ECOLOGY

Birds Weigh Risk Before Protecting Their Young

As every parent knows, what's best for the children may not always be best for the parents, be it a movie choice or where to spend hard-earned money. Feathered parents can face an even starker decision: whether to trade their progeny's survival for their own.

And cold-hearted though it may seem, birds are sometimes willing to sacrifice their young to save themselves so they can breed again. New work, reported on page 494, clearly shows that breeding birds factor in both the number of their young and their own likelihood of surviving when deciding whether to risk delivering food to the nest in the presence of a predator. This behavior even varies according to what type of threat a specific predator poses. "Birds have the cognitive ability to react [differently] to certain kinds of predators," says Jeffrey Brawn, a population ecologist with the Illinois Natural History Survey in Champaign.

The work, by Cameron Ghalambor, now at the University of California, Riverside, and his colleague Thomas Martin at the U.S. Geological Survey in Missoula, Montana, probed a long-suspected difference between birds in the Northern Hemisphere and their counterparts in the tropics and the Southern Hemisphere: Northern birds tend to lay more eggs than do similar species in the South.

For these studies, Ghalambor and Martin first analyzed preexisting data on number of young and adult survival of some 182 species, comparing birds from Europe and North America with those from New Zealand, Australia, and South Africa. They also probed these characteristics in more detail in two bird populations on opposite sides of the Equator, in Arizona and in Argentina. "I've never seen comparisons over such a broad geographic area," comments Amy Krist, an evolutionary biologist at the University of Hawaii, Hilo.

Both the preexisting data and those from the Argentina and Arizona sites confirmed the disparity in the number of eggs laid per season between northern and southern populations. Ghalambor argues that the difference may be explained by the fact that northern birds sometimes live just one season, so they "invest more in reproduction" by laying more eggs the one chance they have.

Ghalambor and Martin then tested whether that investment also results in differences in the risks northern and southern populations run to protect either themselves or their young. They looked at the parents' willingness to return to the nest to feed their chicks when confronted with a predator. The researchers compared five Argentinian species—a flycatcher, a thrush, a wren, a sparrow, and a warbler—to their closest relatives in Arizona.

Parenting strategies. Although similar in many ways, these two robin species from Arizona (*left*) and Argentina (*above*) differ in the amount of risk they will take for their young.

For each species, they tested the parents' reactions to recordings of calls from a hawk, which attacks adults; a jay, which attacks chicks; or a nonthreatening stuffed tanager. They attempted to test each bird call on each set of parents and observed them for 90 minutes both before and after. All told, they made 175 presentations to 61 nests.

As expected, birds from both hemispheres reduced their food deliveries when they heard and saw either the hawk or the jay. "It's been known for a while that birds avoid going to nests when they know they are being watched," says Robert Ricklefs, an ecologist at the University of Missouri, St. Louis. But there were some intriguing differences.

Take the house wren. The wrens in Arizona averaged 5.8 chicks per nest, while their southern counterparts averaged just 3.7. The jay, which attacks chicks, spooked the Arizona wrens more than those in Argentina, inciting a greater reduction in feeding. In contrast, the Argentinian birds were less concerned about leading the jay to their nests but were more leery of the hawk, very quickly abandoning feeding their chicks to protect themselves.

"There is a trade-off between survival and reproduction," explains Ghalambor, in which the northern birds that are unlikely to survive the winter have put all their eggs in one nest, so to speak, and do everything they can to care for those eggs. Southern birds hedge their reproductive potential, producing fewer eggs at one time but breeding more than once. Hence, they value their own survival more than that of their chicks.

Biologists have long thought that some traits evolve to compensate for other traits that might compromise an organism's reproductive potential, says Brawn. Yet demonstrating how characteristics such as nest size and risk-taking behavior vary in different environments to contribute to the species' survival has been tough. Ghalambor and Martin, says Brawn, have corroborated "one of the central principles of life history theory."

–ELIZABETH PENNISI

MICROARRAYS

Data Standards On the Horizon

Microarrays offer researchers a tantalizing way to reap the bounty of genome sequencing—if the torrent of data they generate can be managed properly. In an effort to tame the flood, a group of scientists is almost ready to propose standards for describing and sharing microarray data. Even so, researchers and journal editors are not very far along in figuring out how to enforce them.

Microarray data won't reach their potential until researchers can compare their own results with those of experiments in other

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