Champaign, is intended to fund tabletop experiments to test the feasibility of treating nuclear waste using low electric fields and thin metallic films to produce "low-energy nuclear reactions." It's one of 45 awards, chosen from among 308 proposals and announced in May, for studies into everything from lightweight reactors to new radioactive waste cleanup technologies.

In an abstract (neri.ne.doe.gov/awardlist.html), Miley noted that preliminary experiments in which nickel, palladium, and titanium films were "highly loaded with protons" and then energized with electricity had produced reactions that appeared to transmute radioactive elements into safer byproducts and produce "excess energy." The approach, he told *Science*, "was motivated by a swimming electron theory," which suggests that high electron densities on the films can aid nuclear reactions. Further trials, he wrote, were needed to nail down "this breakthrough science." In particular, he requested funds to refine materials and to perform analyses designed to make sure the byproducts were produced by the reactions and not by accidental contamination.

The project's apparent similarity to controversial cold fusion experiments—which have unsuccessfully sought to use electrochemical reactions to spark energy-producing nuclear fusion at room temperature—raised eyebrows both within and outside DOE. An official at DOE's Germantown, Maryland, office first raised questions about the project in early June, according to NERI program manager John Herczeg. DOE officials decided that Miley's proposal should have been handled by the agency's Office of Science, which arranged reviews of NERI's basic research proposals, and not by the Office of Nuclear Energy, which oversaw the program's engineering grants. In late June, nuclear office chief Bill Magwood asked the science office to look at the grant, for which funds had not been disbursed. That office is recruiting three reviewers, who are expected to issue their opinion next month.

One group, however, says DOE should act immediately. "The credibility of DOE will be irreparably damaged unless funding for this cold fusion proposal is immediately withdrawn," Edwin Lyman, scientific director of the Nuclear Control Institute, a Washington-based arms control group, wrote in a 6 July letter to Energy Secretary Bill Richardson. The award, he told *Science*, "raises questions about the adequacy of DOE's peer review ... the whole [NERI] project needs to be looked at under a microscope." DOE officials, however, say that Miley's grant is the only NERI award scheduled for further scrutiny.

Miley says the turnabout "came as a complete shock." The proposal "is speculative but based on extensive experimental data," he says. And although his work has been identified as cold fusion, he say it is "radically different—we have trouble getting the cold fusion people to understand what we are doing." The difference, he says, is that whereas cold fusion experiments focus on fusing deuterium atoms, his work involves proton-metal reactions. He is also worried about the fate of three graduate students in his lab if DOE rescinds the award.

The flap could also jeopardize NERI's future. Despite backing from White House advisory panels and several well-placed lawmakers—including Senate Budget Committee chair Pete Domenici (R–NM)—DOE has had trouble building political support for its nuclear energy science budget, which Congress zeroed out in 1997 due to concerns about quality and other issues. NERI's commitment to peer review helped reverse the tide last year, and program officials were hoping for a $6 million increase to $25 million next year. But "the idea that DOE is spending money on questionable science could renew the doubts," says one Senate aide. Whether or not the grant is canceled, he says, the episode "will prompt a lot of questions."

–DAVID MALAKOFF

CIRCADIAN RHYTHMS

CRY's Clock Role Differs in Mice, Flies

A clock would be useless without a way to set it, and that's certainly true for the circadian clock that controls our daily biological rhythms. Several research teams reported last fall that the light-absorbing protein cryptochrome (CRY) seems to fill that role in plants and flies, synchronizing the clock to the 24-hour light-dark cycle. But research in mice raised the possibility that, in mammals, CRY might be a cog in the clockworks itself rather than the light receptor. Now two papers, one in this issue of *Science* and the other in this week's *Cell*, show how CRY interacts with the mouse and fly clocks, confirming that its roles in the two clocks are quite distinct.

Seat of action. Most of the cryptochrome (green) in a fruit fly cell exposed to light is in the nucleus. The cube shows the cell stained for cryptochrome alone (green), for a nuclear protein (red), and on the top face, the overlap of the two.

CREDIT: PALOMA MAS AND STEVE KAY

In flies, Steve Kay's team at The Scripps Research Institute in La Jolla, California, reports on page 553, light triggers CRY to reset the clock by interacting directly with a clock protein called TIMELESS. But in mice, Steven Reppert of Harvard Medical School in Boston and his colleagues report in *Cell*, CRY is part of a group of proteins that make up the central clock mechanism and may not be a light receptor at all. "This is a clear difference between flies and mammals," says clock researcher Joseph Takahashi of Northwestern University in Evanston, Illinois. And that, Takahashi points out, has become a recurring theme in animal clocks, which use the same cast of proteins but often in different roles.

At the core of the fly's clock are two proteins, PERIOD (PER) and TIMELESS (TIM), whose levels rise and then fall over the course of a day. This oscillation is caused by a feedback loop in which PER and TIM accumulate, then team up to turn off their own genes. That causes PER and TIM levels to drop until they can no longer repress their genes, and the cycle starts again. Light can reset the clock by turning the genes on prematurely, and 3 years ago clock researchers found that it does this by inactivating TIM.

How that happens was a mystery until last fall, when Jeff Hall and Michael Rosbash of Brandeis University in Waltham, Massachusetts, along with Kay, found that light can't inactivate TIM in flies with a mutant *cry* gene (*Science*, 27 November 1998, p. 1628). That meant CRY is part of the light-resetting pathway, possibly the light receptor itself. But it didn't explain how CRY affects TIM.

Now Kay's team has provided that explanation. They began with cultured fruit fly cells engineered to make PER and TIM but not CRY. The cells don't have a running clock, but the researchers follow PER and TIM activity in the cells by measuring their repression of a gene that contains the same control region as the *tim* gene. Light has no effect on that repression, so the researchers decided to add CRY to the system, Kay says, to see if that

would "at least partially reconstitute the photoreception events." It did: Adding CRY and exposing the system to light put an end to the gene repression by PER and TIM.

To see what protein CRY was acting on, the researchers then used antibodies to pull CRY from the cells. It emerged as part of a protein complex with TIM. That suggested, but did not prove, that CRY acts directly on TIM. Proof came when Kay teamed up with Charles Weitz at Harvard Medical School. Weitz's team performed a test called the two-hybrid assay, which uses yeast cells designed to turn blue when two foreign proteins—CRY and TIM in this case—bind to each other. The yeast test confirmed that CRY does directly bind TIM, and what's more, the pairing requires light. That shows that "cryptochrome actually is a photoreceptor that directly touches TIMELESS and sequesters it," pulling it out of action and thus resetting the fruit fly clock, says clock researcher Paul Hardin of the University of Houston in Texas.

As it turns out, things work differently in mice. Last fall, a team led by Aziz Sancar of the University of North Carolina, Chapel Hill, reported that mice missing one of their two *cry* genes have clocks with abnormal light responses. That suggested that CRY is a circadian photoreceptor. But the clocks of those mice also ran abnormally in the dark, convincing some researchers that CRY is a central component, rather than a light sensor, in the mouse clock. That idea got a boost in April, when Jan Hoeijmakers's team at Erasmus University in Rotterdam, Netherlands, showed that mice missing both *cry* genes have no clock at all (*Science,* 16 April, p. 421).

That report spurred Reppert to look at CRY's clock function in mice. The mouse clock, like the fly's, depends on a protein feedback loop, but in mice the PER proteins seem to enter the nucleus and shut off their genes without help from TIM. When Reppert's team tried to reconstitute the clock by putting active *per* genes into cultured fibroblast cells, however, the PER proteins did not move completely into the nucleus, nor did they completely shut off the genes. "Our cell culture assay was missing something," says Reppert.

When Kazuhiko Kume, a visiting scientist from the University of Tokyo, tried putting CRY into the cells, they were "blown away" by the result, Reppert recalls. CRY was the missing element: The gene inhibition that had been partial now was complete. In subsequent experiments, the team showed that CRY forms a protein complex with PER and helps it move into the nucleus, where CRY and PER turn off not only the *per* genes but the *cry* genes as well. The fact that CRY is "required to get the repression you need in the feedback loop" pegs it as a central clock component, says clock researcher Carla Green of the University of Virginia, Charlottesville.

CRY's shift in roles from a stimulator of gene expression in the fly to a repressor in mice is a fascinating evolutionary twist, says clock researcher Michael Young of The Rockefeller University in New York City. In the same evolutionary span, the protein seems to have lost its role as a photoreceptor as well, a function it maintains in organisms as diverse as plants and flies. It is too soon, Takahashi says, to say for certain that CRY is not, in addition to being part of the clockworks, also a photoreceptor for mammalian clocks, but "right now all the evidence suggests that it's not."

–MARCIA BARINAGA

KOREA

Faculty Protest Proposed Reform

SEOUL—Street protests by thousands of university professors have led the Korean government to modify an ambitious plan to enhance research and strengthen graduate education. Although officials say the changes are minor, some supporters of the government's plan worry that the modifications will severely undermine its goals.

The plan, announced this spring and called Brain Korea 21 (*Science*, 18 June, p. 1902), calls for spending $1.2 billion over 7 years on a handful of strategic fields, including biotechnology and materials science, as well as the traditional disciplines of biology, chemistry, and physics. The money would go to universities that have pledged to break down departmental barriers and reduce cronyism, as well as up-and-coming regional institutions. Some grants are targeted for newly formed groups from consortia of institutions that agree to cut the number of undergraduate students, expand their graduate programs, diversify admissions criteria, and establish a performance-based pay system for professors.

But last month in Pusan, 1000 university professors, mostly from the humanities and social sciences, carried signs and chanted slogans declaring that the reform—and the increased funding—bypasses their fields and could actually increase the concentration of resources at elite schools. On 8 July the protest was repeated in Seoul with double the number of disaffected faculty.

That pressure has led the government to open the door to proposals from outside the natural sciences and to scrap a plan to adopt a performance-based pay system. A typical professor at a national university with 2 decades of experience earns just under $3000 a month (private universities pay about 50% more), and some saw the proposed merit system simply as a way to reduce their pay. Officials at the Ministry of Education, which designed BK21, say that the natural sciences component is going ahead on schedule.

The concessions may have resulted from the weak position of a politically troubled government hit by several recent scandals. "The program is good for the universities. ... But the simple story is that the government is politically unable to do it," says Chung Sung Chul, director of the Science and Technology Policy Institute in Seoul. An editorial in the English-language *Korea Herald* says that eliminating the proposed merit-pay system invalidates the plan, which takes aim at "the poor research records of professors and a closed recruitment system." Without those changes, the newspaper says, "the BK21 is simply a waste of tax money."

Research rumble. Korean professors demonstrate in Seoul against government plans for higher education.

CREDIT: HUR YOUNG HAN/*CHOSUN ILBO*

Most scientists still back the plan, however, because it promises strong support for high-quality research. Last week Lim Jeong Bin, a biology professor at Seoul National University, was preparing his group to meet a 20 July deadline for BK21 applications. He remains optimistic that the plan will not unravel. "I think the protests will subside," he says, and the government will move ahead.

–MICHAEL BAKER

Michael Baker writes from Seoul.