together proposals. The prize will be $25 million a year over 4 years for each institute, and the winners must raise twice that amount from outside sources. Only the 10 University of California (UC) campuses, including the new Merced site, are eligible to host the new institutes, but collaborators can come from any university in the state.

"The bill promotes technological and scientific research and training to maintain California's leadership," says Antonio Villaraigosa, former speaker of the California assembly, who introduced the bill at the request of Governor Gray Davis. "These institutes will concentrate resources and mobilize the state's best scientists and engineers in medicine, biotechnology, telecommunications, energy, space, and agriculture."

The idea for the California Institutes for Science and Innovation grows out of the state's economic boom and a rare political alignment in which Democrats control the governor's mansion and both legislative houses. It's a departure from most other state science and technology investments, which tend to focus on short-term economic development rather than basic research. It also differs from the typical state investment in university buildings, made without regard to the potential commercial value of the research going on inside. "States spend billions of dollars on university infrastructure, but most of it is not targeted for an economic payoff," says Dan Berglund, executive director of the State Science and Technology Institute in Columbus, Ohio. Adds Robert Conn, dean of the Jacobs School of Engineering at UC San Diego (UCSD), "The commitment of the state to provide this infrastructure is extraordinary. It's bold thinking."

Conn is part of a team at UCSD and UC Irvine drafting a proposal for an institute in telecommunications and information technologies that would build on existing research efforts and local expertise. Officials have already made progress in lining up outside donations, Conn says, including a $15 million pledge from QualComm, the wireless communications giant headquartered in San Diego. In a similar vein, UC Davis, the state's agricultural campus, is proposing an institute on environmental informatics and technology to develop new production methods in agriculture and other sectors. "We want to improve the economy without damaging the environment," says Kevin Smith, Davis's vice chancellor for research.

The Los Angeles and Santa Barbara campuses are jointly proposing a nanosystems institute that would also have a heavy emphasis on developing a cadre of researchers for this emerging area. "The institute would provide core facilities that otherwise would be difficult to build or to use because we wouldn't have a critical mass of investigators," says Roberto Peccei, dean of physical sciences and interim vice chancellor for research at UCLA. "One of the products of this institute will be grad students and undergrads who will have some real understanding of cross-disciplinary fields. You can get a lot of people to work together who otherwise wouldn't."

Although the bill has yet to be approved, the UC system has asked campuses to submit their ideas by the end of this month. Experts in the relevant fields will review them for scientific and educational merit, along with the importance of the work to the state's economy, says UC official Susanne Huttner, and from that pile will come a final round of submissions in September. Any California campus, public or private, can collaborate on a proposal, and a single campus can submit more than one idea. But no university can land more than one institute.

Although the state money is intended for bricks and mortar, state officials say that the outside funding—from federal agencies, foundations, and industry—may be used for research activities and operating costs. And while three new institutes pale in comparison to the number of existing centers on California campuses, they would represent a significant part of the state's investment in basic research (see pie chart). In addition, the absolute amount is nothing to sneeze it, says Berglund: "$300 million over 4 years is a big number." –EVELYN STRAUSS

TOXICOLOGY

Dioxin Draft Sparks Controversy

Even before it is released, the U.S. Environmental Protection Agency's (EPA's) new report on dioxin is creating a furor. A draft, leaked to *The Washington Post* last week, concludes that dioxin is 10 times more likely to cause cancer than previously believed, posing a risk as high as 1 in 100 among the most exposed individuals. Some scientists immediately blasted the findings as "unbelievable," while acknowledging that they had not seen the report. Even before the leak, concern from other federal agencies about public anxiety prompted the White House to organize an interagency review of the draft, which has yet to undergo review by EPA's Science Advisory Board.

Five years ago, that same board kicked an earlier version of the dioxin reassessment back to EPA for revision, calling it scientifically flawed (*Science*, 26 May 1995, p. 1124). The 1994 assessment concluded that low levels of dioxin could be causing significant reproductive, immune, and developmental effects and retained dioxin's label as a "probable" carcinogen. After analyzing the

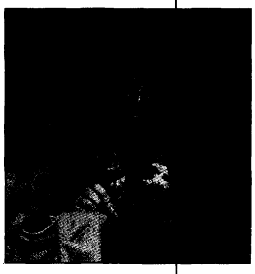
ScienceScope

Late Hit Representative James Sensenbrenner (R–WI), chair of the House Science Committee, reduced a senior National Science Foundation (NSF) official to tears last week when he banned her from testifying about science education. "Your conduct is insulting to this committee," he bellowed at a mortified Judith Sunley, NSF's chief education officer. "I'm giving you an F and excusing you for the day."

Sensenbrenner's gag order was triggered by NSF's failure to heed a committee policy requiring witnesses to submit testimony at least 24 hours in advance. The purpose, says committee spokesperson Jeff Lungren, is to give staff and members time to prepare questions. Instead, a copy of Sunley's two-page statement arrived a few minutes before the start of the 17 May hearing on H.R. 4271, a bill that would expand NSF's role in precollege science and math education (*Science*, 21 April, p. 419).

That statement, the product of negotiations between NSF and the White House, expressed support for the bill's intent but offered caveats. "Ironically, [the White House] thought our original draft was too supportive," says one NSF official. Even without NSF's verbal endorsement, the committee is expected to approve the legislation. But its chances of going any further this year are slim.

Elusive Goal A heavily touted promise to eradicate polio by the end of this year won't be met, world health officials admitted last week. Speaking at the World Health Assembly in Geneva, World Health Organization (WHO) Director-General Gro Harlem Brundtland (right) said that obstacles ranging from armed conflict to a temporary vaccine shortage will foil the organization's best efforts in sub-Saharan Africa and the Indian subcontinent, regions where the disease is still active.



Noting a current $300 million shortfall in the campaign's budget, Brundtland also urged leaders in high-risk countries to remain committed to an effort that has made considerable progress. Some 190 countries are now free of the disease, and even the Indian subcontinent reports that the number of cases plummeted from 25,711 in 1988 to 1866 last year. But Uton Muchtar Rafei, WHO regional director for Southeast Asia, warns that up to 10% of the target population remains out of reach because of a growing birthrate, a transient population, and insufficient supplies of the oral vaccine.

CREDIT: AP PHOTO/J. MCCONNICO

evidence again—including new analyses of occupational studies, according to an EPA scientist—the agency has now upped dioxin's classification to "known" carcinogen. Although dioxin levels in the environment have been steadily falling since the 1970s, once ingested, exposure continues because the pollutant bioaccumulates in body fat.

Michael Gough, a retired biologist and dioxin expert, asserts that "there is no convincing evidence" that dioxin is 10 times more potent a carcinogen. Scientists who helped write the report counter that evidence of higher potency is solid and should not be surprising: Even in 1994, EPA had recognized that dioxin has a much longer half-life in humans than in rats. What's more, the International Agency for Research on Cancer recently classified dioxin as a known carcinogen as firmer evidence has emerged from studies of workers exposed to dioxins. But even one scientist who co-authored a key chapter of the new study cautioned against reading too much into EPA's characterization of a 1-in-100 risk. "That's at the very upper edge of body burden in the United States," says Chris Portier of the National Institute of Environmental Health Sciences.

Meanwhile, EPA officials point out that the report is not final; the agency intends to release a draft for public comment in June and send it for final scientific review in September. With this inauspicious debut, the report seems sure to attract a wide audience.

–JOCELYN KAISER

MICROBIOLOGY

New Clues to How the TB Bacillus Persists

The tuberculosis bacterium has been called the world's most effective pathogen. It kills an estimated 2 million people each year and lurks in one-third of the world's population. In most, the infection remains latent, but in some it explodes in disease years to decades later. Just how this organism manages to persist silently in the body in a kind of truce with the immune system has long been a mystery —one just now beginning to be solved.

Two groups, one led by Stanford University microbiologist Stanley Falkow and the other by microbiologist William Jacobs of Albert Einstein College of Medicine in New York City, have identified genes that may be required for persistent TB infection. If so, the proteins made by the genes could be good targets for new drugs against TB, which are badly needed because the pathogen is becoming resistant to current medications. The work is "clever and exciting," says infectious disease specialist William Bishai of Johns Hopkins School of Public Health in Baltimore. "If we understand how the organism adapts and persists, we'll be much better off in terms of drug development."

For their work, which is described on page 1436, the Stanford team used an animal TB model: the infection of frogs by *Mycobacterium marinum,* a close cousin of the TB bacillus, *M. tuberculosis*. The researchers chose *M. marinum* because it grows faster than *M. tuberculosis* and is not spread through the air. But it causes latent infections in frogs, similar to those in human TB. In particular, the animals develop a pathological hallmark of persistent TB infection: clusters of immune cells called granulomas where the bacteria live for years.

Turned on. The green glow marks *M. marinum* bacteria persisting in a frog granuloma.

CREDIT: RAMAKRISHNAN *ET AL.*

To identify the genes that allow *M. marinum* to persist, Falkow, with Stanford colleagues Lalita Ramakrishnan and Nancy Federspiel, attached the gene for a green fluorescent protein to random fragments of *M. marinum*'s genome and then inserted the fragments, carried on circular pieces of DNA called plasmids, into normal strains of the bacterium. That way, if a fragment contained a gene that became active, its bacterial host would glow green, and the gene could be identified by its location on a plasmid.

Using this technique, Ramakrishnan and her colleagues found a dozen genes that *M. marinum* turns on when living inside frog granulomas but not when growing on its own. Most of them have close counterparts in *M. tuberculosis,* whose genome was sequenced in 1998. Two in particular caught the researchers' interest, because they are members of a family of genes called PE-PGRS that comprises 5% to 10% of the *M. tuberculosis* genome. These genes are blueprints for bizarre-looking proteins that contain hundreds of glycines in a row and whose functions are unknown. Intrigued, the Stanford researchers knocked out one of the PE-PGRS genes in the frog bacterium.

When they put these mutants into macrophages, the main type of immune cell in granulomas, that were maintained in lab cultures, the bacteria didn't grow at all. And they grew only poorly in frog granulomas, with the number of bacteria in the frogs reduced to 1/50 that of wild-type infections. That suggests that at least some of these PE-PGRS family members play a role in persistence. "This is the only demonstration that these genes have any function," says Eric Rubin, a microbiologist at the Harvard School of Public Health in Boston.

Others aren't convinced that the Stanford group's finding casts any light on human TB, however. Ian Orme, a TB researcher at Colorado State University in Fort Collins, thinks the frog model is a poor one, in part because *M. marinum* is relatively harmless to mammals and must be injected in "monster doses" to produce signs of infection in frogs. "I'm not arguing that frogs are people," counters Falkow. "But *marinum* and *tuberculosis* have a common ancestor, and they share a common pathogenic apparatus."

One way to settle the argument would be to knock out the PE-PGRS gene in *M. tuberculosis* itself and see whether that affects the organism's virulence. Such an effort could be greatly facilitated by a method developed by the Einstein researchers in the course of their work, which appears in the April issue of *Molecular Cell.*

Jacobs also started with a safer organism: bacillus Calmette-Guérin (BCG), used in the TB vaccine. Two years ago, he and Einstein colleagues Michael Glickman and Jeffery Cox began randomly knocking out genes in BCG looking for mutants that failed to form cords, a phenomenon in which the microbes join in long ropelike structures in culture. Because such "cording" seems to correlate with high virulence, Jacobs reasoned that pinpointing genes needed for cording might lead him to virulence genes.

The researchers found that mutations in a BCG gene that makes an enzyme called cyclopropane synthase prevent the bacteria from forming cords. They then went on to inactivate the comparable gene in *M. tuberculosis.* In the past, producing such gene knockouts took 6 months, in part because it's very hard to get gene-disrupting DNA fragments into the TB genome. But the group used a rapid new technique co-developed by Einstein's Stoyan Bardarov, which uses a TB-infecting virus to insert the fragments, and so achieved its goal in just 3 weeks.

The mutant TB strains thus obtained also failed to form cords. What's more, they were less virulent. Control animals infected with the unaltered microbe all died from the infection after about 7 months. By contrast, the mutant bacteria grew rapidly in their hosts for a few weeks, but then began to die off slowly,