tremely exciting," says neurologist Hugo Moser, who studies ALD at the Kennedy Krieger Institute at Johns Hopkins University School of Medicine in Baltimore. Neurologist Dennis Choi, of Washington University School of Medicine in St. Louis, agrees. Benzer and Min "didn't just simply create the model"; they also showed that it could identify "something that is of interest for human treatment," he says. "That is a validation."

Benzer and postdoc Min made their discovery as part of a project to find fruit fly mutations that mimic those that cause human neurodegenerative conditions. First they mutated flies with P elements, little bits of DNA that jump around the fly's genome, inactivating genes. Min then looked for mutants with shortened lifespans and examined them for signs of dying neurons. In one such mutant, one of the neural layers in the flies' eyes had an abnormal bubbly appearance, prompting the researchers—who had already named other neurodegenerative mutants after foods—to call it *bubblegum*.

When Min cloned the mutated gene, it turned out to encode a protein whose sequence suggests it is an acyl coenzyme A (CoA) synthetase, a type of enzyme that helps break down fatty acids. The involvement of that enzyme brought ALD to mind, Min recalls, because a similar enzyme is impaired in ALD. In the human disease, which is passed from mother to sons on the X chromosome, the impairment is indirect, because the primary mutation is in a gene encoding one of a class of proteins that transport substances across membranes. Researchers do not know how the transporter affects the synthetase, but the synthetase's decreased activity results in high blood levels of very long chain fatty acids (VLCFAs) in ALD patients and—also for poorly understood reasons—progressive degeneration of brain neurons. The ALD link prompted Min to see whether VLCFA levels are also high in the mutant flies, and sure enough, they were.

> **"Using the fruit fly as a model ... is extremely exciting."**
>
> —Hugo Moser

The researchers then tested whether the flies respond to Lorenzo's oil, which is a mixture of two fatty acids. In humans, the oil lowers VLCFA levels by slowing their synthesis, although so far in clinical trials it has shown little or no effect on disease progression. Benzer and Min saw something similar when they treated adult mutant flies with glyceryl trioleate oil, one of the components of Lorenzo's oil. The flies' VLCFA levels dropped, but their brains still had dying neurons. Min tried another approach, beginning treatment when the flies were larvae. When those flies grew to adulthood, says Min, "the pathology was not there."

On the face of it, that finding suggests that starting oil treatment early might ward off the neuron death. But giving the oil to humans before symptoms begin doesn't seem to have increased its effectiveness, says Moser. One reason may be that humans have a barrier that prevents easy transfer of many substances—including Lorenzo's oil—from the blood to the brain. Fruit flies lack such a barrier, and Moser says the fly results may rekindle efforts to alter Lorenzo's oil to enable it to enter the brain.

ALD and the fly condition differ in other ways as well. Not only are the mutations in different genes, but flies lack an inflammatory response, which may contribute to the human disease. And the sick fly neurons look different from the dying neurons in ALD. Although flies may be an imperfect model, there are enough similarities to expect that "we can learn a lot" from them, says biochemist Paul Watkins, who studies ALD at the Kennedy Krieger Institute.

The flies should allow researchers to quickly screen potential ALD treatments for their effects on diseased brain cells, says Choi. Compounds identified this way would not be a sure bet against the human disease, he cautions, but they "would be good starting points" for further study. Watkins adds that the mutant flies may provide insights into the molecular basis for ALD. His lab is searching for the acyl CoA synthetase that is key in ALD, and although they have found six human versions of the enzyme so far, none is abundant enough in the brain to fit the bill. The defective fly enzyme belongs to a different subfamily than the known human enzymes, and because its mutation causes neuropathology, he says, it "could be the one we're missing."

If any of these applications proves fruitful, Benzer will no doubt be pleased. He says his goal was to establish flies as a disease model that, although not perfect, would provide "hints on physiology which may or may not extrapolate to humans." And he has his sights set beyond ALD; *bubblegum*, he says, is just one of a "whole zoo" of mutant fly strains developed by his lab that suffer neural degeneration and might turn out to be useful models of other human diseases.

–MARCIA BARINAGA

ScienceScope

Down to the Summit Marine scientists are cruising toward their goal of building an observatory at the tip of a massive underwater volcano. More than two dozen researchers this week boarded a University of Washington research vessel bound for the Axial volcano, 400 kilometers off the Oregon coast. Once there, they hope to complete the second phase of the year-old U.S.–Canadian observatory project, which plans to assemble a suite of instruments focused on the geology and biology of the Juan de Fuca Ridge, where microbes and other sea life thrive around sea-floor vents of superheated water.

Last year, researchers installed the first instruments—including water chemistry and earthquake monitors—at the New Millennium Observatory (NeMO), which sits more than 1000 meters above the sea floor and 1400 meters under the surface. On this year's cruise they plan to drill rock cores and deploy new equipment at the observatory, which has no firm completion date.

Hopes for neat science are high, as NeMO rests on "the most volcanically active site" in the region, says oceanographer Stephen Hammond of the Marine Environmental Laboratory in Newport, Oregon. To follow the action, check out newport.pmel.noaa.gov/nemo.

Gene Bonanza? Germany's biggest basic research funder says the country's genome studies are lagging behind and need a big cash infusion to catch up to the United States, France, and the U.K. In a report last week, the DFG argued that the government should spend an additional $570 million over the next 5 years to put German genome research on the world map.

The report suggests that about 40% of the new funds go to studying genes identified in the human genome project, the genomes of model organisms such as the fruit fly, and ethical and legal issues. Plant and microbe studies would split another 40%, with the rest to be spent on bioinformatics, overhead, and other categories. The DFG also made a pitch for a new national committee to coordinate Germany's genome efforts.

Such ideas are likely to get a serious hearing from research minister Edelgard Bulmahn, who wants more genome research. Last month, she said her ministry will ask Parliament to double funding for Germany's part of the Human Genome Project, to about $45 million a year by 2002.

along with the traditional disciplines of physics, chemistry, and biology. At the same time, undergraduate enrollments in departments that receive government funding as part of newly formed consortia will be cut by 30% to lighten the teaching load on faculty members who will be carrying out the research. Funding will also go to beef up provincial universities and to lessen the frantic competition for entry into SNU.

Scientists working in the targeted fields see the plan as a way out of an inefficient and stale departmental system. "There is no collaboration or communication," says Lim Jeong Bin, a microbiology professor at SNU, who wants to see "real restructuring." He adds that "If [the government] doesn't do anything, the universities won't change on their own." The targeted money is intended to help Korea become a master in certain areas rather than remaining a jack of all trades, says Kim Sun Ho, assistant director of BK21 at the Ministry of Education, which is overseeing the program. "Universities have many subjects and faculties," he says, "but they lack specialization."

AIMING HIGH IN SCIENCE

Goal	1998	2005
Boost annual production of science Ph.D.s	2500	4500
Boost publication rate and international ranking*	10,000/17th	20,000/10th
Boost annual number of patent applications	7000	40,000
Reduce annual amount spent on overseas education	$700 million	$100 million savings

* As calculated by the Institute for Scientific Information.

Targeted research. Brain Korea 21 initiative hopes to raise scientific productivity in several sectors.

Success will require a break from tradition for Korean faculty, however. To qualify for a biotechnology grant, for example, 30 of SNU's 50 biology professors must join with 15 professors from another university to create a new biotechnology graduate research program. The remaining 20 SNU professors will be left to teach undergraduate courses to a smaller student body. Although Lim says that departmental barriers to such collaborations are high and that organizing such a cross-departmental group is somewhat "unpractical," he agrees that "the overall direction is right." The new rules also mandate that half of the graduate students admitted to a new program come from other universities and that universities develop a more independent system for evaluating professors.

Faculty members in fields not singled out for special attention—in particular, mathematics—are worried that students will shun their departments for other majors and that research funding will dry up. Their fears are stoked by the government's decision to increase from 270 to 2000 the number of students who are exempt from military service if they pursue Ph.D.s in strategic areas. But education ministry officials say that any discipline may compete for funding and that the money comes on top of existing funding.

Critics also say the program is skewed toward applied science, and they fear that emphasis will starve basic research. Chung laments that only 20% of the project's funding is actually flowing directly into research, with the bulk divided among undergraduate and graduate training, equipment and materials, and scientific exchanges. "Education is getting too much, and research is receiving too little," he says.

But ministry officials argue that fostering strong local research universities is in the national interest, that a larger network of high-quality institutions will improve Korean science, and that limited resources require them to set priorities. They also hope that training more graduate students locally will save money and ease the brain drain caused by students who remain abroad. "The 21st century is going to be a knowledge-based society, and we want to move with the changes," says Kim.

—MICHAEL BAKER

Michael Baker writes from Seoul.

PATENT LAW

Supreme Court Limits Scope of Appeals

The U.S. Supreme Court has limited a special federal court's power to second-guess decisions by government patent examiners. Last week's 6–3 ruling disappointed many biomedical and computer companies, who say it will make it harder to appeal patent rejections. But legal experts say it will be years before the impact is clear.

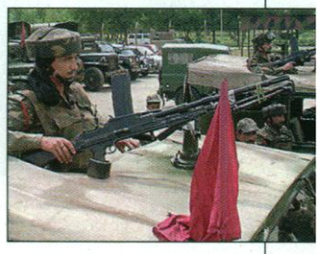
The case, *Lehman* v. *Zurko*, stems from the rejection of a patent application for cybersecurity software written by Mary Ellen Zurko, now with Iris Associates in Westford, Massachusetts, and her colleagues at the Digital Equipment Corp. (DEC). DEC—now Compaq Computer Co. of Houston, Texas—appealed the 1994 decision by the U.S. Patent and Trademark Office (PTO) to the Court of Appeals for the Federal Circuit, a panel that hears patent and other technical cases (*Science*, 27 November 1998, p. 1622).

Last May the court ruled that the denial

ScienceScope

Caught in the Crossfire Two Indian telescopes under construction in the Himalayas are the first scientific casualties in the latest battle with Pakistan over the disputed Kashmir region.

A $10 million, 2-meter optical and infrared telescope and another smaller instrument were scheduled to see first light in October at the world's highest site (4440 meters) for optical astronomy. But those plans are on hold due to fighting that erupted last month in the Kargil sector of the Himalayan state of Jammu and Kashmir. Intense shelling by Pakistani forces has blocked shipments of critical components to the remote observatory near Hanle—where the crisp, clear skies are great for astronomy.



It's not clear when peace might return. In the meantime, the Indian Institute of Astrophysics (IIA), which is building the telescopes, is preparing to reduce delays by airlifting equipment to the site. If all goes well, says IIA director Ramanath Cowsik, "there can be first light in early 2000."

By Any Other Name National Institutes of Health (NIH) director Harold Varmus is already taking plenty of flak from editors for a proposal to launch a government-backed online publishing venture (see p. 1887). Now comes another blow: Varmus's name for his brainchild, "E-Biomed," is already taken.

Last week, Mary Ann Liebert Inc., a medical publisher in Larchmont, New York, issued a press release saying that in April it applied for an International Standard Serial Number (ISSN) from the Library of Congress for a journal called *e-biomed*, which it plans to launch next year. The company has also tied up "www.e-biomed.com" and ".net" for Web sites.

That in itself doesn't mean NIH is prohibited from using E-Biomed, as an ISSN does not lock up exclusive rights to a title, according to the Library of Congress. It may not matter anyway: One editor who recently met with Varmus told *Science* that the NIH chief seems to be leaning toward broadening the journal to other life sciences, such as plant biology—so a different name might make sense.

Contributors: David Malakoff, Robert Koenig, Pallava Bagla, Jocelyn Kaiser

CREDITS: (LEFT TO RIGHT) KOREAN MINISTRY OF EDUCATION; AIJAZ RAHI/AP