The plan calls for Aurora to screen several hundred thousand molecules in its library over the next 5 years and identify two or three that might be candidate drugs for CF. If this approach yields some promising "hits," the CF Foundation plans to pay Aurora an additional $16.9 million to prepare the candidates for clinical trials. Carrying the drugs through to final approval, however, would require coinvestment by a major pharmaceutical company. Profits would be shared among the CF Foundation and its business partners, but the foundation would immediately plow all of its own royalties directly back into research on new therapies.

Quest. Aurora will use its blue-green fluorescent technology to screen for candidate CF drugs.

CREDIT (RIGHT): PALLAVA BAGLA

CF Foundation president Robert Beall thinks this new "virtual drug company," a hybrid profit-nonprofit venture, is unique in the pharmaceutical industry. His group decided to take the plunge into drug R&D because it didn't want to wait for manufacturers of small-molecule drugs to take an interest in CF. A decade ago when the CF gene was discovered, researchers hoped new drugs would follow close behind. The discovery yielded a wealth of information about what goes amiss in the disease, but translating those insights into therapies has been slow. The CF Foundation is involved in at least 20 collaborative projects and is now supporting clinical trials of gene therapies, using three different types of gene transfer vectors. But this is the first time it has tried to lead the discovery process itself.

Big drug companies have not been drawn to the field, Beall notes, because the number of CF patients who might buy a drug is relatively small—only about 30,000 in the United States. And he says that "when we tried to get them involved" in searching for interesting new compounds, "they didn't return our calls." So the foundation hired a consultant to vet innovative small firms; they quickly settled on Aurora. The company maintains a library of 400,000 small molecules that can be screened at high speed for medical applications. Aurora is a particularly good fit for the CF Foundation, says Beall, because it specializes in assaying proteins that permeate the cell membrane, based on a proprietary blue versus green fluorescence test developed by Roger Tsien and colleagues of the University of California, San Diego (*Science*, 2 January 1998, p. 84). CF is a disease in which chloride flow through the cell membrane is restricted.

Aurora will use cells from CF patients to test whether compounds help restore normal ion channel function, says Paul Negulescu, vice president for discovery biology. "We provide the discovery engine," he says, "and [the CF Foundation] provides an extensive and sophisticated [drug] development network." The foundation manages a clinical trial network based at eight centers around the country, coordinated by a team at the Children's Hospital of Seattle. This approach, Negulescu says, could serve as the model for "a new type of drug-discovery process" for other orphan diseases, including those that primarily affect poor nations.

Francis Collins, director of the National Human Genome Research Institute and co-discoverer of the CF gene, says "this roll-up-your sleeves partnership" between a disease advocacy group and a drug discovery company is novel. "The CF Foundation is taking an interesting step: This obviously has a high risk, but could also have a high payoff if it works." By providing early support for the discovery of new drugs, Collins says, the foundation assures that the disease "will get more attention and more cutting-edge approaches than it would otherwise."

–ELIOT MARSHALL

BIOMECHANICS

Geckos Climb by the Hairs of Their Toes

The Tokay gecko is the envy of every serious rock climber and Spiderman wannabe. This tropical lizard defies gravity, running up walls and upside down across ceilings as readily as across floors. It can hang from one toe pad—that's akin to holding oneself in midair by one fingertip. And that pad sticks to walls even in a vacuum and underwater. *Gecko gecko*'s secret: rows of tiny hairs with multiple split ends on the bottom of each pad, says Kellar Autumn, a biomechanist at Lewis and Clark College in Portland, Oregon.

While he was a postdoctoral fellow in Robert Full's lab at the University of California, Berkeley, Autumn figured out how these tiny hairs—each no taller and much more slender than the period at the end of this sentence—can be so strong. Armed with that knowledge, Autumn, Full, and

ScienceScope

Muzzled Watchdog The Indian government has stripped its Atomic Energy Regulatory Board of its role in overseeing the safety of the nation's nuclear weapons program, a move that critics fear will aggravate problems at deteriorating weapons facilities. The action, taken in April but revealed last week, will allow the Bhabha Atomic Research Center (BARC) in Mumbai, the nation's leading weapons lab, to create its own safety panel.

The shift leaves weaponeers free to set weak safety standards, critics say. "In one stroke, the safety assurance and regulation of the mostly old and dilapidated BARC facilities have been made the responsibility of those who are managing these installations," A. Gopalakrishnan, the former head of the board, told the Indian press. But R. Chidambaram (below), chair of the Atomic Energy Commission, says that India is merely following the lead of other nuclear powers in separating regulation of civilian and military plants.

Edwin Lyman of the nonprofit Nuclear Control Institute in Washington, D.C., disputes that claim: "Actually, the trend in the U.S. is in the other direction," with weapons labs coming under increasing scrutiny. He sees the Indian decision as a misstep: "I can only expect things to deteriorate under the new system."

Biocomputing Burst A push to get the National Institutes of Health (NIH) to fund more computing research is gaining ground. The agency this week announced a $10 million initiative to develop National Programs of Excellence in Biomedical Computing that will nurture a new generation of byte-savvy biologists.

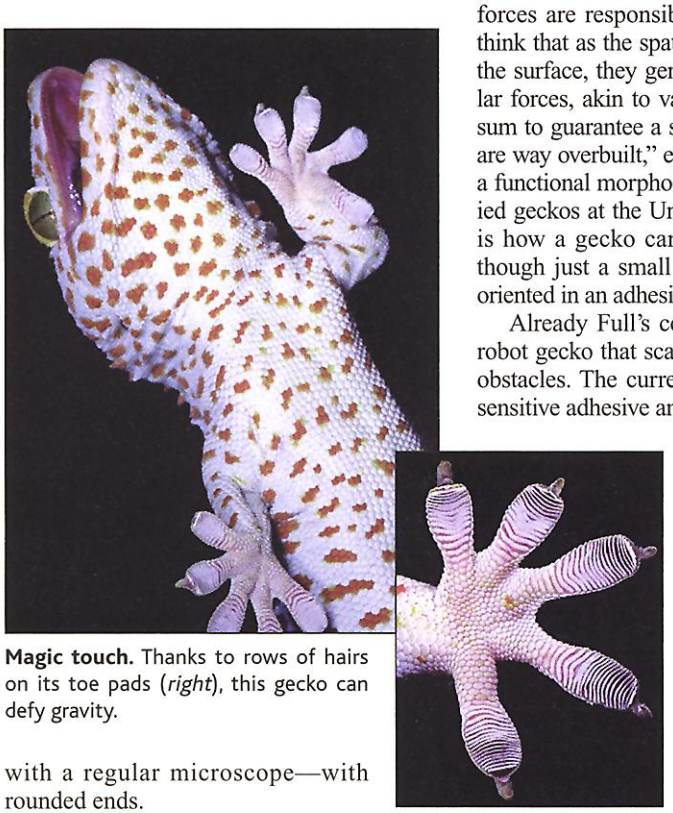
Last year, an NIH advisory panel called for creating up to 20 such centers at U.S. universities to encourage cooperation between cyberscientists and biologists and create better software and networks for manipulating the mushrooming biological data sets (*Science*, 11 June 1999, p. 1742). The new program will take a first step toward that goal by providing funds for universities to sketch out their vision of a biocomputing center and try out some pilot projects.

Contributors: Pallava Bagla and David Malakoff

their engineering colleagues hope to design synthetic "footpads" to improve the maneuverability of robots and perhaps to design an entirely new type of adhesive.

As they report in the 8 June issue of *Nature*, weak attractive forces between the 1000 or so split ends on each hair and the ceiling help the gecko grab even the smoothest surface. Such forces are typically generated when two surfaces come very close together. Simply changing the angle of the hairs, called setae, causes these forces to disappear; then the ends let go and the lizard scrambles forward with no hesitation. "It's great to look at how evolution has solved mechanical problems," marvels Bruce Jayne, a functional morphologist at the University of Cincinnati in Ohio.

Gecko toe pads are covered with rows of setae made of keratin, the same protein in human hair and bird feathers. Each seta's curved shaft ends in many hundreds of spatulae, stubby tendrils—too small to see with a regular microscope—with rounded ends.



Magic touch. Thanks to rows of hairs on its toe pads (*right*), this gecko can defy gravity.

To figure out how these hairs might help geckos hang upside down, Autumn tapped the expertise of Berkeley engineer Ronald Fearing and Stanford engineer Thomas Kenny. With the help of a microelectrical mechanical sensor, designed for use with atomic force microscopy, they were able to measure the lateral and perpendicular forces exerted by a single hair that had been removed from a gecko's foot. "The technical difficulty of measuring forces at such a small scale is really significant," points out Jayne. That Autumn and his colleagues succeeded "is really admirable."

At first the hair didn't stick well to the sensor surface. But that changed after the researchers gently pressed the hair into the surface and then began to drag it across and nearly parallel to the sensor—movements that resemble how intact setae work as the gecko puts its foot down. With that motion, "adhesion is rapidly engaged, and that's when we see fairly large forces," Autumn explains.

Previously, Berkeley's Duncan Irschick had measured the overall adhesive forces of a gecko foot. From those, Full and Autumn had calculated the contributions of individual hairs, some 500,000 of which are arrayed in sets of four in a leaflike pattern on the pads. Amazingly, recalls Autumn, "each [hair] was 10 times more adhesive than we would have predicted." One seta is strong enough to hold up an ant, and a million could support a small child.

Autumn and other researchers have ruled out that suction, glue, or even electrostatic forces are responsible. Instead, he and Full think that as the spatulae get close enough to the surface, they generate weak intermolecular forces, akin to van der Waals forces, that sum to guarantee a secure foothold. "Geckos are way overbuilt," explains Anthony Russell, a functional morphologist who has long studied geckos at the University of Calgary. That is how a gecko can cling to ceilings even though just a small fraction of its setae are oriented in an adhesive direction.

Already Full's collaborators have built a robot gecko that scales walls and walks over obstacles. The current model uses pressure-sensitive adhesive and mimics how the gecko uncurls its toes as it puts its foot down and then peels the toes to detach the setae as it walks. These motions "reduce the attachment and detachment forces to almost nothing," enabling the robot (and the gecko) to use up very little energy in the process, says Full. The next step is to outfit the robot with synthetic setae.

The researchers don't expect to find a material that they can split 1000 times, however. Instead, they hope that studies of other lizards and also of kissing bugs, which have setae with few and sometimes only one spatula, will help them design simplified setae that can be manufactured. Eventually, Full and Autumn envision an all-purpose, reusable, gecko tape—one that leaves no residue behind. But Full is not so sure that gecko gloves and climbing shoes will ever be more than a rock climber's fantasy. **–ELIZABETH PENNISI**

NEUROBIOLOGY

Trigger Found for Synapse Formation

Because the ability to form connections between nerve cells is at the heart of all brain function, neurobiologists have looked long and hard for the molecules needed to achieve such biological hardwiring. But they've had little luck in finding the matchmakers of nerve cell connections, called synapses, in the brain—until now, that is.

In today's issue of *Cell*, molecular neurobiologist Tito Serafini and colleagues at the University of California, Berkeley, report that a single protein can apparently trigger synapse formation between brain neurons isolated from mice and grown in culture. The notion that just one molecule can jump-start so critical a process "is a big breakthrough," says molecular and cellular neurobiologist Richard Scheller of Stanford University. If the finding is borne out in living animals, it could provide fresh insights into how the brain is wired during embryonic development and might eventually provide new ways to enhance or at least maintain synapse formation in the brains of patients suffering from neurodegenerative diseases such as Parkinson's or Alzheimer's.

The critical players, according to Serafini's team, are either of two sister proteins called neuroligin 1 and -2. Neurobiologists had suspected that the neuroligins might play some role at the synapse since their discovery about 5 years ago by Thomas Südhof's team at the University of Texas Southwestern Medical Center in Dallas.

At the time, the researchers were studying another set of proteins called neurexins that bind to a toxin from black widow spider venom. Because the neurexins can be produced in literally thousands of variants, investigators thought that the molecules might be involved in building the many different synaptic circuits of the brain—an idea buttressed by Südhof's finding that the proteins act like molecular glue to help cell surfaces adhere to each other. A neurexin, anchored in the surface of the transmitting cell of the synapse, would hook up to a binding partner on the cell that receives the connection, or so the thinking went.

That hypothesis led Südhof to search for candidates that bind to neurexin. In 1995, his team pulled out neuroligin 1, and shortly after that, its relatives neuroligin 2 and -3. Using antibodies, the researchers also showed that neuroligin 1 is located in the synaptic membrane of the receiving neuron. But "the missing link," says Südhof in retrospect, was showing that neuroligins can ac-

CREDITS: M. MOFFETT