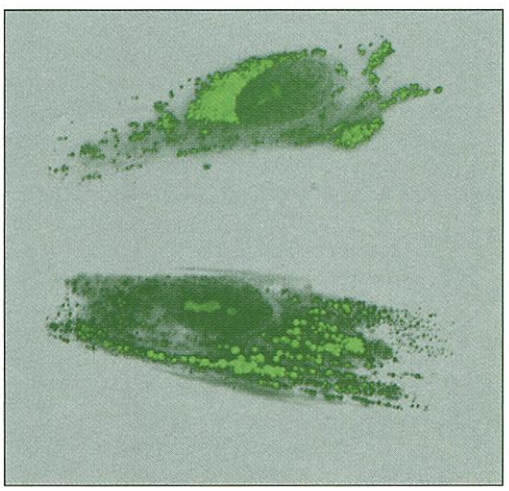
the function of the normal NPC1 protein.

On page 2298, Peter Lobel of the Robert Wood Johnson Medical School in Piscataway, New Jersey, and his colleagues report that a previously identified gene that encodes a cholesterol-binding protein called HE1 is actually NPC2. And on page 2295, a team at Mount Sinai School of Medicine in New York City describes an unexpected function for NPC1. Work by Yiannis Ioannou, Joanna Davies, and Fannie Chen suggests that it is a permease that can transport lipids such as fatty acids, but apparently not cholesterol, across membranes.

The new work should help fill a major gap in current understanding of cholesterol transport in the cell. Researchers know how cholesterol gets into the lysosomes. And they know a great deal about what happens after the lipid reaches the ER. But, says cholesterol expert Joseph Goldstein of the University of Texas Southwestern Medical Center in Dallas, "the black box is that we never knew how it gets out of the lysosome" and into the ER—a critical step, given the severe pathology that results when it's blocked.



Cholesterol depots. In this human cell, shown from two angles, the green color marks the lysosomes, which are loaded with the dye acriflavine.

CREDITS (TOP TO BOTTOM): J. P. DAVIES, F. W. CHEN, Y. IOANNOU; L. N. SANCHEZ/LANL

Because mutations in the two NPC proteins can produce that blockage, researchers suspect that in their normal form they play a role in transporting cholesterol from the lysosomes to the ER. The current work does not yet explain how they do that, but it may open the door to finding the answer. "It's the beginning of a whole new way of looking at the trafficking of cholesterol in the cell," says Goldstein.

The NIH team spent years searching for the *NPC1* gene, first mapping its location on chromosome 18 and then sorting through the DNA there until they found a gene mutated in NPC1 patients. By contrast, Lobel and his colleagues discovered NPC2 while looking for proteins that might be defective in the broader class of so-called lysosomal storage diseases. When they came upon HE1, its cholesterol-binding ability and its lysosomal location raised the possibility that it might be involved in NPC. It was. "We lucked out," says Lobel.

Using antibodies to the protein, the New Jersey team found that it is present in normal skin cells but not in skin cells from NPC2 patients. The researchers also found that adding the normal protein to cells derived from NPC2 patients reduced the cells' lysosomal cholesterol content. "When you add [the protein] back, it restores function," Lobel says. Cinching the case, sequencing studies showed that the gene from NPC2 patients, but not from controls, carries mutations that inactivate it.

Still unclear is exactly how NPC2 contributes to cholesterol transport out of the lysosomes, or how its role meshes with the newly discovered function of NPC1. Researchers had expected the NPC1 protein, which is located in lysosomal membranes, to be a cholesterol transporter, but that's not what Ioannou's team found. Instead, it resembles a family of bacterial permeases that transport various substances, including fatty acids, through the bacterial cell membrane. "Based on this structural homology, we reasoned that NPC1 is the first eukaryotic member of this family," Ioannou says.

To test whether it is a permease, the researchers exposed both normal and NPC1 cells to the fluorescent dye acriflavine—one of the molecules transported by the bacterial permeases. The dye ended up in the lysosomes of both cell types. When Ioannou and colleagues then removed acriflavine from the cell culture fluid, the lysosomes of the normal cells gradually lost the dye, while those of the NPC1 cells didn't. This indicates that the normal cells, but not the mutant ones, have a pump for transporting acriflavine out of their lysosomes.

More direct evidence that NPC1 functions as permease came when the researchers engineered cells of the bacterium *Escherichia coli* to make the protein. They found that NPC1 production greatly increased the bacterial cells' uptake of acriflavine and also of oleic acid, a long-chained fatty acid. It did not transport cholesterol, however, leaving unclear how it moves the lipid out of the lysosomes. As Ioannou says, "we have a lot to do in dissecting the functions of these proteins."

But now that both have been isolated, researchers expect that the contents of the "black box" will be revealed. "It is likely," Pentchev says, "that these contributions will … raise our scientific understanding of one of the critical issues in cellular cholesterol metabolism."

–JEAN MARX

ScienceScope

Doing Well by Doing Good? National Science Foundation (NSF) director Rita Colwell is gearing up for a big increase in public outreach that she hopes will also benefit the agency's bottom line. An advisory panel headed by PR honcho Frank Mankiewicz last week called for at least doubling the agency's $2.5 million public affairs budget as part of a major campaign to inform the public about the scientific underpinnings of today's economy. "NSF needs to be the place that the scientific media calls" on any breaking science story, Mankiewicz told the National Science Board, NSF's overseer. Such one-stop shopping would not only improve public understanding of science but also raise NSF's profile, said several panelists, who asserted that other agencies—in particular NASA—do a much better job of publicizing discoveries they have funded.

Board members embraced the panel's message, as did Colwell. "If I understand you correctly," said John White, chancellor of the University of Arkansas, "a $15 million increase in the agency's PR budget could give us a chance to increase NSF's budget by $15 billion ... a pretty good rate of return." One sour note: For all its visibility, NASA's budget has stalled in recent years, while NSF's has grown steadily.

Voicing Support A troop of arms-control experts is planning to ride to the aid of the Department of Energy's embattled national laboratories. The new U.S. Committee for the National Laboratories, announced this week, hopes to help the labs restore their reputation as guardians of national security in the wake of a string of espionage and mismanagement scandals.

"The labs have been subject to a lot of attacks, and not enough people are coming to their defense," says national security consultant Bill Courtney of DynMeridian in Alexandria, Virginia, one of the organizers of the committee. In contrast, he notes, flocks of outside supporters rally to the Pentagon's side in times of need.

Courtney says the nonprofit group—led for the time being by attorney and former government arms-control expert Thomas Graham—has been blessed by lab officials and expects to raise funds from corporations, foundations, and individual members. Among its first tasks, he says, will be "to acquaint people with some of the good things the labs are doing."

insects are much looser than those for insects meant to attack plant pests; the latter require data on the host range of candidate species.

But Robert Pemberton, a U.S. Department of Agriculture research entomologist in Fort Lauderdale, Florida, says the tide is beginning to shift. Biocontrol policies are now being talked about, he says: "We're having a lot of meetings between the biological control community and ecologists."

–MARI N. JENSEN

Mari N. Jensen is a science writer in Tucson, Arizona.

MICROBIOLOGY

Fighting Bacterial Fire With Bacterial Fire

Smearing bacteria on open sores seems like the worst approach to preventing infection. But work presented last week at the annual meeting of the American Society for Cell Biology in San Francisco suggests that applying a harmless bacterium or its products to surgical wounds may thwart infections by the dangerous pathogen *Staphylococcus aureus*, a major cause of hospital-acquired infections and one that grows more threatening as the incidence of antibiotic resistance rises.

Although physicians have previously pitted one bacterium against another to prevent infections of the intestinal and genitourinary tracts—say, eating yogurt with live cultures to combat diarrhea—this is the first attempt to use a friendly microbe to prevent infection of surgical wounds, say experts. "The idea is certainly unique and probably feasible," says microbiologist William Costerton of Montana State University in Bozeman.

The bacterium, known as *Lactobacillus fermentum*, seems to exert at least part of its protective effects by secreting a protein that prevents *S. aureus* from binding to its target cells, reported Jeffrey Howard, Gregor Reid, and colleagues at the University of Western Ontario in London, Ontario. If so, says Richard Novick, a microbiologist at New York University School of Medicine, researchers will have to reevaluate their thinking about how such bacterial interference works. Conventional wisdom attributes the infection-fighting effects to bacteria-killing toxins, says Novick. But "here's a beautiful example of bacterial interference that's caused by a substance that probably blocks colonization or adherence by the other bacteria."

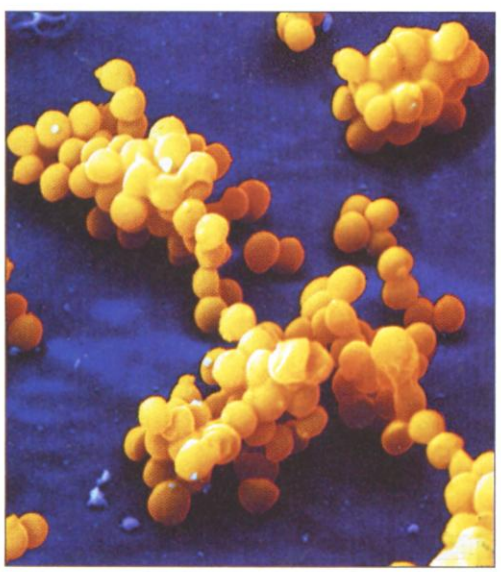
The current work extends previous experiments in which Reid and his colleagues showed that substances secreted by *Lactobacillus* inhibit the binding of *S. aureus* to synthetic surfaces such as polystyrene. Perhaps, the researchers reasoned, *Lactobacillus* or the material it secretes could also keep *S. aureus* from setting up shop in animal tissues.

To test this idea, they placed small pieces of silicone under the skin of rats to mimic a surgical implant and then added *S. aureus*. As expected, serious infections emerged at the wound sites within 3 days. But adding live *Lactobacillus* during the surgery protected the animals. None of the nine rats that received the largest doses of the beneficial bacteria developed infections, compared with five of nine controls. The secreted material worked, too. It reduced the incidence of infection by approximately 90% compared to controls.

The researchers next tried to nail down the molecules responsible for the beneficial effects by analyzing the mixture *Lactobacillus* discharges. One active component turned out to be a protein that Reid had previously found blocks microbial adherence to polystyrene. Follow-up experiments established that this protein alone hampers the ability of *S. aureus* to cause wound infections in rats.

The protein may work by outcompeting *S. aureus* for the pathogen's binding sites in tissue. *S. aureus* gains a foothold in the body by grabbing a protein called collagen, and the *Lactobacillus* protein also binds this host protein. Although the researchers have not yet established that its protective effects are due to this binding, others in the field are excited that the team is homing in on the molecular details of bacterial interference. "It's the first instance that I know of where modern biochemistry and genetics has been used to study bacterial interference," says Costerton.

He suggests that bacterial interference may have advantages over conventional antibiotics, which wipe out good

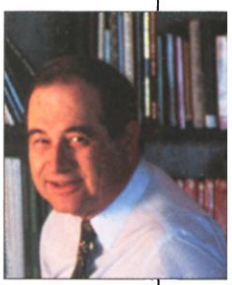


CREDITS: (TOP TO BOTTOM) RICK KOZAK; OLIVER MECKES/OTTAWA/PHOTO RESEARCHERS

No way in? Infections by *S. aureus* bacteria like these may be prevented by blocking their attachment to host cells with a *Lactobacillus* product.

ScienceScope

Going Home After 2 years at the helm of U.S. science policy, White House science adviser Neal Lane, 62, will head back to academe when the Clinton Administration ends next month. The physicist said last week that he will return to Rice University in Houston, Texas, as its first ever professor without portfolio, able to teach in any department. Lane was Rice's provost in 1993 when recruited to head the National Science Foundation. He moved to the White House in 1998, where he cemented a reputation as a genial politico who preferred to work outside the spotlight.



Top Quark After more than two rudderless years, France's National Institute of Nuclear and Particle Physics (IN2P3) finally has a new captain. On 15 December, the French government named Jean-Jacques Aubert, the institute's scientific director, as head. The IN2P3 had been without a chief since October 1998, when former chief Claude Detraz went to the CERN physics center near Geneva.

Aubert, a physicist from Marseilles, came to national attention 2 years ago when he wrote a report for former research minister Claude Allègre proposing that the IN2P3 merge with the French Atomic Energy Commission's institute for nuclear and particle physics, called DAPNIA (*Science*, 23 April 1999, p. 569). But this controversial idea—which many physicists feared would make the IN2P3 subservient to the commission's research priorities—now appears dead in the water, sources tell *Science*. In fact, some researchers doubt that Aubert's appointment will make much of a difference at all to the chronically underfunded IN2P3. Says one physicist, who asked to remain anonymous: "It just means business as usual."

Genome Gift A record-breaking grant aims to put Indiana University (IU) on the genomics map. The Lilly Endowment of Indianapolis last week announced a $105 million gift to jump-start the Indiana Genomics Initiative, which will focus on genomics, bioinformatics, and bioethics. The grant—the largest ever given by the charity and the richest ever won by IU—will help the school add 75 investigators over the next 3 years. The cash will help "attract a stellar array of intellectual talent," predicts Lilly president N. Clay Robbins.

Contributors: Jeffrey Mervis, David Malakoff, Michael Balter