Licentious *Listeria.* *Listeria* (green) makes use of the host cell's degradation machinery.

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listeriolysin gene with that of one of its relatives, perfringolysin O (PFO), which is used with horrific success by the gangrene-causing *Clostridium perfringens*. He found that, unlike listeriolysin, the introduced PFO was toxic and destroyed the host cell.

To figure out what gives listeriolysin its unique abilities, Decatur, who is a postdoc in Portnoy's lab, compared its amino acid sequence with that of PFO. The sequences were quite similar except at the amino end, where listeriolysin turned out to have 27 extra amino acids. Portnoy and Decatur then made a strain of *Listeria* in which they modified the listeriolysin gene to make a protein lacking this extra bit of sequence. In tissue culture experiments, the altered *Listeria* was more toxic to macrophages than was its normal counterpart. Next, the Berkeley scientists altered the PFO gene so that its protein would have this 27–amino acid tag, then replaced the listeriolysin gene with the hybrid. With its new appendage, PFO was considerably less toxic; in fact, it acted much like listeriolysin.

To nail down the identity of this tag, Decatur and Portnoy combed the databases looking for anything resembling this stretch of amino acids. To their delight, they found it is a dead ringer for a sequence often found at the ends of proteins in yeast and multicellular organisms, including humans. In many organisms, these so-called PEST sequences are the starting points for protein-protein interactions, often targeting specific proteins for degradation by other proteins. Finding such a PEST sequence in *Listeria* was "surprising," to say the least, notes Nicholas Davis, a molecular biologist at Wayne State University in Detroit, because bacteria normally aren't equipped with the protein-degrading machinery it triggers.

Instead, the *Listeria* PEST sequence apparently prompts the protein-degrading machinery of the bacteria's host macrophages to obliterate the pore-forming protein once it has done its job, suggests Patrick Berche, a microbiologist at the Necker Hospital in Paris, whose team has similar, as yet unpublished, results. The PEST-like sequence could be a "very important" adaptation for the parasite, he adds. *Listeria* must make pore-forming proteins to escape being killed in the phagosome. Most likely, the PEST tag ensures that once freed from the vacuoles, the proteins are destroyed or disabled before they make gaping holes in the cell membrane, killing the cell and wrecking *Listeria*'s temporary safe house. "This mechanism, protein breakdown, is a good solution" to the problem of turning off the protein very quickly before it can damage the cell, says Decatur. By contrast, shutting down its gene might not reduce the amount of listeriolysin in the cell for several hours.

Work on listeriolysin and its relatives has reinforced the critical role these pore-forming proteins play in a pathogen's toxicity. Increasingly, says Portnoy, understanding pathogenesis is becoming a "question of how these proteins are modified and regulated." Yale microbiologist Craig Roy agrees: "There are spatial and temporal constraints" that pathogens evolve to get the most of the host before harming it. And for *Listeria*, it took just a small innovation to trick its host into helping control one of its more pathogenic proteins. **–ELIZABETH PENNISI**

SOLAR SYSTEM EXPLORATION

A More Cautious NASA Sets Plans for Mars

Twice burned by mission failures last year, NASA managers last week unveiled a new 15-year blueprint for Mars exploration. The revamped strategy allows for doing more science, but at a slower pace, while delaying a sample return until well into the next decade.

"Mars has a tendency to surprise us," NASA space science chief Ed Weiler said dryly at a 26 October press conference in Washington, D.C. The 1999 loss of two craft—the Mars Climate Orbiter and Polar Lander—and the new evidence of recent water on the planet are only the latest surprises. To cope with both scientific and technical uncertainties, a NASA team has developed a two-pronged approach using orbiting spacecraft followed by surface rovers. This strategy will take longer, but agency managers are betting that its flexibility will benefit researchers eager to explore the climate, geology, and possible signs of extinct or existing life on the planet. Although the less aggressive schedule has led to some grumbling within the scientific community, many researchers seem relieved with what they say is a more realistic plan.

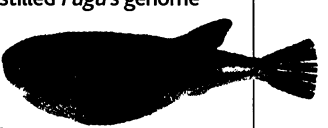
NASA's original plan relied on favorable orbital mechanics to send out fleets of or-

ScienceScope

Taking the Pledge? About 150 scientists—including prominent biologists—have so far signed an open letter calling on journal publishers to support an "online public library" that would give everyone free access to biomedical and life sciences articles that are at least 6 months old. Pat Brown of Stanford University and Harold Varmus, president of the Memorial Sloan-Kettering Cancer Center in New York City, are prime movers behind the letter, due to be delivered next May. The campaign faces a barrier, though: Private publishers haven't agreed to give the material away.

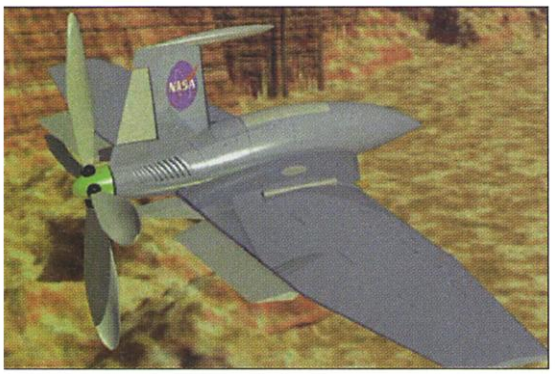
To "encourage" publishers to donate, those signing the letter pledge to sever ties after September 2001 with journals that don't cooperate. "We will publish in, edit or review for, and personally subscribe to, only ... journals that have agreed to grant unrestricted free distribution rights to any and all original research reports ... within 6 months" of publication." (See www.publiclibraryofscience.org/index.shtml) Publishers are still weighing their response.

Fishy Genomes Hungering to sequence a genome a bit more substantial than those of the dozen microbes it is finishing this month, the U.S. Department of Energy's (DOE's) Joint Genome Institute (JGI) in Walnut Creek, California, has announced it will turn next to the puffer fish, *Fugu rubripes* (below). Known best as a Japanese delicacy with potentially lethal consequences if not prepared correctly, *Fugu* has earned acclaim among biologists because it has far less genetic material than most other vertebrates. Humans have 3 billion bases, the building blocks of DNA, while zebrafish have 1.8 billion; evolution has distilled *Fugu*'s genome down to a mere 400 million. "Unlike zebrafish, [the puffer] probably hasn't undergone considerable gene duplication," says Randall Moon of the University of Washington School of Medicine in Seattle.



Even so, "this will be [DOE's] single largest project," says Trevor Hawkins, JGI's deputy director. He expects to have 95% of the sequence completed by March 2001—putting *Fugu* sequencing ahead of efforts to decode the genomes of the zebrafish and *Tetraodon*, a freshwater puffer. *Fugu* enthusiast Sydney Brenner of the Molecular Sciences Institute in Berkeley, California, and colleagues elsewhere will then put on the finishing touches.

Contributors: David Malakoff, Michael Balter, Eliot Marshall, Elizabeth Pennisi



Soaring plans. This plane would skim the surface of Mars later this decade under one NASA scenario.

biters and rovers every 2 years over an 8-year period. But that schedule left little margin for error, and the twin 1999 failures raised questions about the soundness of the hardware and software to be used in future missions. The new schedule addresses that problem by alternating orbiter and rover missions. The 2001 orbiter called Odyssey will be followed in 2003 by two small rovers that will land independently. Two years later, a sophisticated reconnaissance spacecraft capable of seeing objects as small as a beach ball will be launched.

The pace of exploration will ratchet up in 2007, with the launch of an Italian communications satellite to provide much-needed data transfer capability. NASA would send a smart lander—perhaps equipped with drills to look for moisture under the surface—and a long-range rover. The plan also calls for a debut that year of a new line of explorers called Scouts that could include balloons or planes.

In 2009, a joint U.S. and Italian orbiter equipped with radar would provide more accurate mapping of the surface. A spacecraft to bring martian soil and rock samples back to Earth wouldn't be launched until 2011 or 2014—6 to 9 years later than planned. That effort would cost between $1 billion and $2 billion, and likely would be done with substantial cooperation with the French space agency CNES. Samples would be returned 2 or 3 years later.

The rationale behind the new approach, says NASA Mars exploration program scientist Jim Garvin, is to seek "the most compelling places from above, before moving to the surface." That approach will allow the agency "to change and adapt over time in response to what we find with each mission," says Scott Hubbard, NASA's Mars program director. It will also provide more data over the long haul. Most researchers seem to agree. "Under the old plan, the fear was we might not know where to get the samples [from], or that, once we got there, we wouldn't have the technology to choose" the best samples, says Steven Squyres, a Cornell University astronomer who is principal investigator of the planned 2003 rover. "This way, we will know a hell of a lot more first."

But that's cold comfort to Carl Agee, chief scientist for astromaterials at NASA's Johnson Space Center in Houston. "We'd like to see a sample return earlier rather than later," he says. "We think the sample return is the biggest payoff."

Some observers think that NASA is being too cautious. "It's a good, but limited, plan," says Louis Friedman, executive director of the Planetary Society, based in Pasadena, California. He believes that NASA would have an easier time getting sufficient funding if it linked the robotic probes to a future human mission. Weiler disagrees, saying that "the program is not driven by human exploration but by science."

Hubbard says NASA intends to spend between $400 million and $450 million annually on the effort during the next 5 years, nearly one-third more than originally planned. In return, he promises, future missions will not only deliver good science but avoid technical snafus through stronger oversight. "This is a program," he says, "not just a collection of projects." –ANDREW LAWLER

MATERIALS SCIENCE

Long-Wavelength Lasers Sniff Out New Uses

Just a few weeks after two physicists won the Nobel Prize for figuring out how to make lasers out of semiconductors (*Science*, 20 October, p. 424), researchers at Lucent Technologies' Bell Labs in Murray Hill, New Jersey, announced that they have made those lasers much more useful. A new technique permits the lasers to shine light in regions of the infrared spectrum previously inaccessible to similar devices. The advance may open the door to cheap devices to sniff explosives and other robotic sensors.

Because long wavelengths of light are absorbed by different molecules in different ways, a spectrometer that uses these new light sources would be able to detect faint whiffs of chemicals in the air. "There is a potential here to produce robot laser sensors" tunable over the appropriate region of the spectrum, says Richard Zare, a laser chemist at Stanford University. "They don't exist today."

The work, by physicist Federico Capasso and his colleagues at Bell Labs, involves quantum cascade lasers, which are made of many layers of semiconducting materials. Each of these layers is pumped full of electrons and "holes"—spaces for the electrons to nestle in. When an electron settles into a hole, it releases light, which, in turn, induces other electrons to duck into holes, which releases more light, and so forth.

The problem with these lasers is that they can't produce light very deep into the infrared region. They can only generate wavelengths of a few micrometers before running into trouble. For a semiconductor laser to work efficiently, electromagnetic waves must be confined within the "active region" where all the electrons are falling into holes, so the light can induce more electrons to find more holes. Lasers traditionally do this with dielectric waveguides, devices that work rather like fiber-optic cables. Made of materials with different refractive properties sandwiched together, they force light to bounce around inside them.

Unfortunately, the longer the wavelength, the thicker the waveguides have to be—and the harder it gets to deposit the waveguide layers on the chip. "It's fine and dandy until you get to really long wavelengths," says Capasso. "If you wanted to make a dielectric waveguide for a 20-micron laser with conventional dielectrics, you would need a prohibitively thick material, 8 to 10 microns thick."

To address the confinement problem, Capasso and his colleagues have exploited a property of electrons, called surface plasmons, that reside at the interface between a semiconductor and a conductor. Plasmons are waves of electrons that slosh back and forth when excited by, say, an incoming photon. Roughly speaking, a surface plasmon behaves like light trapped at a conductor-insulator interface. This trapping is exactly what the Bell Labs team wants; the light is trapped without the need for bulky waveguides. "You squeeze the light close to the interface," says Capasso.

By building a sandwich of conductors and semiconductors in the chip, the team ensures that the laser light creates a plasmon where the two materials meet. The plasmon

Fire at will. Although invisible, the infrared light emitted by a surface plasmon laser packs enough punch to ignite a match.

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