genomes, notes Wang Guihai, director of the CAS Bureau of Life Sciences. It is the second project of the China Biological Resource Genomes Project, following a decision to sequence China's superhybrid rice (*Science*, 5 May, p. 795). Danish officials hope to use the knowledge to stimulate work in bioinformatics as well as to strengthen the country's pork industry. A better understanding of pig genomics would also promote the use of transgenic animals as sources of transplant organs, as disease models, and for the production of medical treatments. **–LI HUI**

Li Hui writes for *China Features* in Beijing.
With reporting by Lone Frank in Denmark.

ARCHAEOLOGY

New Site Suggests Anasazi Exodus

High in the cliffs of Mesa Verde in southwestern Colorado lie some of the world's most beautiful and mysterious ruins. For decades, scientists have puzzled over the fate of the people who once lived there, the Anasazi. Whereas conventional wisdom has them dying off or leaving slowly, archaeologist Stephen Lekson of the University of Colorado, Boulder, has now proposed a more dramatic and large-scale exodus to the south for at least some Anasazi. That effort, he argues, would have required a higher degree of social cohesion than has been attributed to the Anasazi culture.

Lekson's work involves pottery and masonry styles from three pueblo ruins in southern New Mexico, up to 470 kilometers from Mesa Verde. "These sites are significantly farther south than the Anasazi are supposed to have gone," says Lekson, who has been invited to present a paper on his finds at the Society for American Archaeology annual meeting next April. "Meanwhile, the size involved suggests whole villages picked up and moved as units. This is different from the usual picture of just individual families wandering off." Comments Jefferson Reid, an anthropologist at the University of Arizona in Tucson who has heard Lekson's presentations: "This is a highly plausible idea that can now be evaluated."

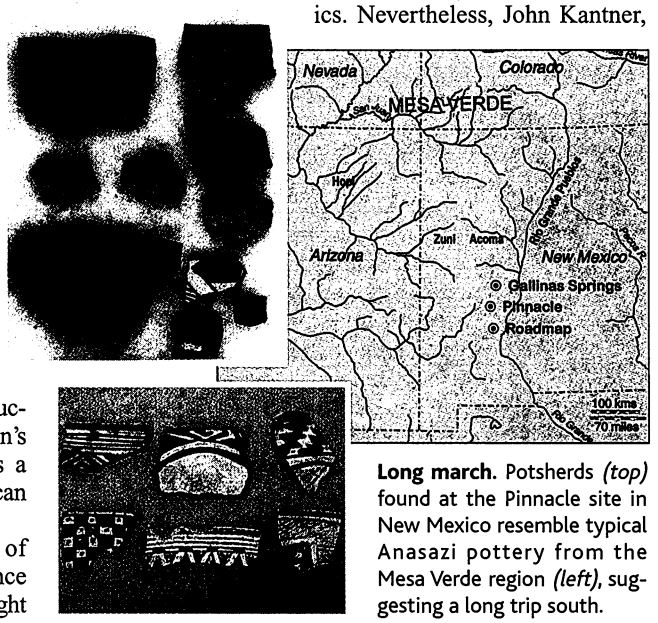
The traditional view of the Anasazi's disappearance suggests that a killer drought or large-scale political or social stresses set off a slow trickle of émigrés. Rarely are large groups imagined in motion. And rarely are the emigrants said to have moved farther than the areas that became today's pueblos in northern Arizona and New Mexico, ranging from the northern Rio Grande country in the east to the Hopi lands to the west. Lekson, in contrast, found Anasazi-like artifacts 420 kilometers south of Mesa Verde, at Pinnacle Ruin (see map), during work this summer with graduate students Brian Yunker and Curtis Nepstad-Thornberry. He says the far-south pueblo-style ruin, like two others in the region, exhibits key characteristics of Mesa Verdean culture that "stick out like a sore thumb" in their locale, he says.

Half of the pottery sherds collected at the site look very much like the Mesa Verde black-on-white style, Lekson argues. The neatly coursed masonry and layout of the multistoried room-blocks look more like the massive defensive pueblos of Mesa Verde than like the region's less organized Mogollon culture sites. And an excavated midden shows that Pinnacle's dwellers piled their trash thickly like Mesa Verdeans instead of following the local practice of spreading it thinly around habitations. Such evidence, along with the sheer size of the three southern ruins—which between them may have contained 800 rooms—"pretty strongly" argues that a sizable stream of well organized Anasazis trekked deep into southern New Mexico around 1300, Lekson says.

Several researchers who have heard Lekson's presentations are attracted to his ideas but say that more data are needed. Archaeologist Harry Shafer of Texas A&M University in College Station, for example, chided Lekson for drawing "premature" conclusions without further excavations and chemical trace analyses of the ceramics. Nevertheless, John Kantner, an archaeologist at Georgia State University in Atlanta, says that "a huge, systematic move could add another element to the picture" of greater mobility.

Lekson, for his part, says that the small amount of trash at the site suggests that his wayfarers' wanderings did not end in southern New Mexico. Moreover, the oral traditions of several pueblo peoples possibly descended from Anasazi emigrants tell of long, convoluted migrations that wended far to the south, then turned back north. "It could be these folks came here for 100 years, then headed north again," Lekson says. "Quite a trip, huh?" **–MARK MURO**

Mark Muro writes from Tucson, Arizona.



Long march. Potsherds *(top)* found at the Pinnacle site in New Mexico resemble typical Anasazi pottery from the Mesa Verde region *(left)*, suggesting a long trip south.

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MICROBIOLOGY

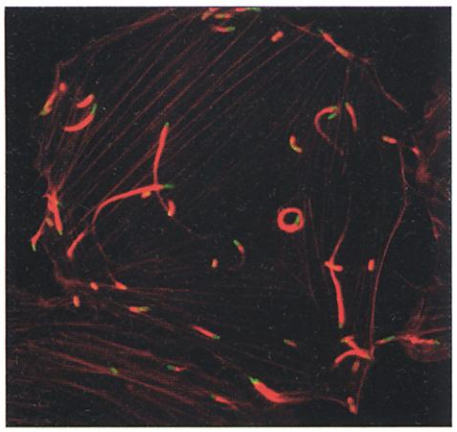
Listeria Enlists Host In Its Attack

It was just a small innovation—a 27–amino acid addition to a protein some 500 amino acids long. But that change likely made all the difference for a food-borne pathogenic bacterium called *Listeria monocytogenes*. As described on page 992 by microbiologists Amy Decatur and Daniel Portnoy of the University of California, Berkeley, this innovation enables *Listeria*, which can cause meningitis and death in people with compromised immune systems, to deploy a toxic protein without killing its host cell. As a result, the microbe remains comfortably ensconced within the cell and can avoid confronting antibodies, the immune system's foot soldiers.

Many bacterial pathogens are extracellular, frequently doing their dirty work by injecting toxins into cells. But not *Listeria*. When consumed, say, in a contaminated cheese, it enters the body and hunkers down in a nearby macrophage—even though this type of immune cell usually helps fend off infections.

As a macrophage first engulfs *Listeria*, it traps the microbe in a vacuole called a phagosome, supposedly out of harm's way and targeted for eventual destruction by the cell. But once inside, *Listeria* makes a pore-forming protein called listeriolysin O that tunnels into the phagosome membrane, dissolving it and setting the microbe free within the macrophage, where it can replicate before conquering other cells.

Microbiologists had long wondered why *Listeria*'s pore-forming protein doesn't bore through the macrophage's outer membrane as well and destroy the host cell. That's how a family of 19 related proteins deployed by extracellular pathogens usually work. Although these bore in from the outside, there seemed to be no reason why listeriolysin O couldn't punch holes in the membrane from within. Indeed, 6 years ago, Portnoy made a *Listeria* strain in which he replaced the



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

CREDIT: (TOP TO BOTTOM) J. SKOBLE/UNIVERSITY OF CALIFORNIA, BERKELEY; MRC

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