report also presents a cautionary tale to the rest of the world: "BSE could have arisen anywhere and spread wherever animal protein is recycled," says Ferguson-Smith. "Other countries should ponder our experience."

–HELEN GAVAGHAN

Helen Gavaghan writes from Hebden Bridge, West Yorkshire, U.K.

GENE SEQUENCING

China, Denmark Team Up to Tackle the Pig

BEIJING—China and Denmark have formed a consortium to sequence the pig genome. The project, expected to take several years, is the first to tackle livestock; when completed, it would be the fourth to tackle a mammalian genome, after the human, mouse, and rat. The partners hope that information from the project will benefit pig-breeding industries in both countries as well as basic science and medicine.

The project links the Danish Institute of Animal Sciences, the Royal Veterinary and Agricultural University (KVL), and representatives from Denmark's pig industry with the Beijing Genomics Institute (BGI) of the Chinese Academy of Sciences (CAS). Leaders of the four groups struck a deal on 20 October during a visit here by a Danish delegation. The partnership is a "perfect match" between China's powerful sequencing capacity and Denmark's expertise in pig breeding and experience in comparative and functional genomics research, says BGI Director Yang Huanming. "We came here with the intention of signing an agreement, and we are satisfied with the result," notes KVL pro-rector Torben Greve, who is head of the Danish Pig Genome Consortium.

The two sides have agreed to split the $15 million cost of the first phase of the project, a 3-year effort to identify valuable genes, develop markers for physical and genetic mapping, and provide research tools for xenotransplantation. A second phase, taking several more years and costing up to $60 million, would aim for a working draft covering 90% of the sequence and 95% of the genes. The pig genome is estimated to contain 3 billion base pairs.

BGI will do the sequencing and sequence analysis using a supercomputer and more than 100 of the latest capillary sequencing machines. BGI plans to redirect its current roster of 45 machines from work on the international human genome project to the pig project, says BGI deputy director Yu Jun. Denmark will be responsible for developing genetic markers for valuable traits such as disease resistance, growth, and litter size. Its scientists will also build about 100 libraries of cDNA clones containing partial gene sequences that will help the teams identify the full-length genes.

Each side has agreed to put up $2 million for the initial phase. CAS has already provided the Beijing institute with money. The Danish ministries of research and of food, agriculture, and fisheries are expected to fund work in Denmark, while the National Committee for Pig Production and the Danish Bacon and Meat Council support the BGI sequencing team.

Researchers had hoped to make the sequencing data available to the scientific community immediately, as has been the case under the so-called Bermuda rules used in the human genome project. But industry contributors asked for release to be delayed several months. "Both sides have agreed to create a balance between the Bermuda rules, which require immediate release within 24 hours, and the present data-release policies by other private sectors to protect commercial applications," says Yang.

Even so, the partners say that they remain committed to the concept of sharing. "This project is just like any other international collaboration project, and there will be no new restrictions," says Orla Gron Pederson of Denmark's national committee. The final terms of data release are still being hashed out, Yang says, along with provisions for scientific procedures, intellectual property rights, and future partners. Yang says that institutes in Singapore and France have expressed an interest in the project but so far lack funding.

The project marks "an important step" for China toward sequencing the country's resource

CREDIT: (BOTTOM) CHINA FEATURES

Gene partners. Beijing's Wang Jian explains the genomics institute's capabilities to Danish delegation led by, at left, Torben Greve and Orla Gron Pedersen.

ScienceScope

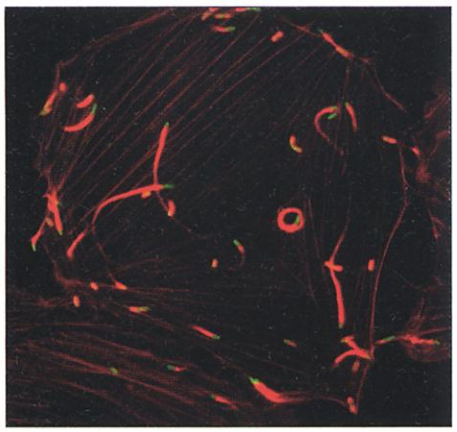
Moving On? Apparently disgusted by this year's uglier than usual budget fight, Senator Arlen Specter (R–PA) (below), head of the appropriations subcommittee that oversees the budget of the National Institutes of Health (NIH), says he may move on to other leadership responsibilities. The hint, dropped in several press interviews last week, has alarmed biomedical research advocates, who count Specter among the handful of key lawmakers who have successfully pushed to double NIH's budget by 2003.

According to the *Washington Fax* newsletter, Specter said that "I don't expect to be on this subcommittee next year because of the futility of what we've done here." The comment came amid highly partisan political wrangling that has stalled approval of this year's NIH bill, which reportedly includes a 15% increase for the $17.9 billion agency.

Specter's departure would leave NIH spending panels in both the House and Senate leaderless, because Representative John Porter (R–IL), a major NIH booster, is retiring this year. Few of the potential replacements share either man's zeal for the cause, lobbyists say. But some caution against reading too much into Specter's comments, saying they could be designed to motivate supporters to lobby him to stay. Says one: It may be his " 'Tell me you love me' dance."

Reform Light More than 3 years after Claude Allègre, France's former research minister, launched his ill-fated campaign to radically overhaul the basic research agency CNRS, the French government has approved a scaled-down version of his reform package (*Science*, 31 March, p. 2387). The Council of Ministers approved a decree on 25 October giving the 26,000-researcher organization greater scientific autonomy, especially by removing government appointees from its scientific advisory council. On the other hand, the minister strengthened the powers of the CNRS executive board, which answers to the government and decides broad-based research strategy. And for the first time, foreign scientists will be asked to join the CNRS's external scientific evaluation committee.

Physicist Edouard Brézin, president of the executive board—whom Allègre had charged with carrying out the reform effort—announced that he will step down now that his work is done.



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