



HUMAN GENOME PROJECT

Genome Institute Wrestles Mightily With Its Future

WARRENTON, VIRGINIA—The job is finally done. After more than a decade, the National Human Genome Research Institute (NHGRI) in Bethesda, Maryland, is about to finish determining the order of the 3.1 billion bases that make up the human genome. Now, NHGRI needs to figure out what to do next, and that's proving not to be an easy task.

Since 1990, NHGRI's budget has ballooned from \$60 million a year to \$429 million in 2002, the majority of that going to its flagship enterprise, the Human Genome Project. With the human genome practically finished, "it's more challenging to convince Congress and the public [that] this is not the end of the road but the beginning," says Elias Zerhouni, director of the National Institutes of Health (NIH), NHGRI's parent institution.

After a year of struggling to craft a new mission for itself, NHGRI unveiled a draft plan for its future last week at a meeting here. The initial response of the audience—some 100 biologists, bioinformaticists, social scientists, and policy-makers—was tepid at best. The plan "kind of read like an organizational identity crisis," says Elliott Sigal of Bristol-Myers Squibb in Princeton, New Jersey. Like many others, he said that the institute needed to be clearer in what it wanted to accomplish.

The revamped NHGRI would continue to apply genomics to biological research—collecting genome sequence, assessing gene function, for example, and developing technologies and databases to enable other researchers to do the same. On the social front, the institute would strengthen its efforts to prevent genetic discrimination, for instance, and

to work with companies to ensure academic access to genomic data. But in a major departure from the past, NHGRI would get more directly involved in medical research and education and even set up its own clinical studies.

One of the concerns about this ambitious plan is that it lacks the concrete goals that have been the hallmark of past proposals. Five-year plans issued in 1993 and 1998 contained specific milestones: a physical map with markers every 100,000 bases, a draft of the human genome by 2001, and so on. And that's the type of fixed timeline that many expected of the 2003 plan. Instead, this draft seems "squishy,"

or "fuzzy," with projects that seem to stretch indefinitely into the future, says Richard Gibbs, director of the Baylor College of Medicine's Human Genome Sequencing Center in Houston, Texas.

NHGRI did make some specific promises, such as finishing 45 to 60 gigabases of sequence by 2008. That's the equivalent of about 18 mammalian genomes and will likely include fungi, the chimpanzee, the cow, and other organisms recently designated as

high priorities (*Science*, 31 May, p. 1589).

But the goals became more vague—and the participants more uneasy—when NHGRI said it also wanted to define the function of all the parts, such as genes and regulatory elements, of the human and other genomes, a task that could take many years. The reviewers had trouble even agreeing on what constituted a "part" or how far NHGRI would be expected to go in determining function. "If NHGRI is not clear about this, then [it's] going to get accused of overreaching," says Thomas Pollard of Yale University

in New Haven, Connecticut.

NHGRI director Francis Collins explained that this was not just a 5-year plan but a vision of the future, one that would guide efforts into the early 21st century. "It [was] meant to inspire NHGRI and its constituencies, NIH and the public," says Richard Lifton of Yale, a member of the NHGRI advisory committee. But almost everyone agreed that, as written, it fell short of that goal.

The most controversial part of the draft plan is NHGRI's proposed foray into clinical medicine. Collins thinks his institute is well poised to pioneer new approaches to health, such as studying genes in people who don't get sick even though many of their relatives suffer from, say, heart disease. In addition, NHGRI would like to play a leading role in establishing a long-term study of the health of several hundred thousand people, in part to track links between genetic variation and disease. Without this large group of people, the HapMap, a major undertaking to map variation in stretches of human DNA called haplotypes, will be of limited use, says Lifton.

However, some were troubled by the logistics of NHGRI starting its own clinical studies. "I would hate to see this institute get bogged down" in recruiting participants, says Gerard Schellenberg of the Veterans Affairs Medical Center in Seattle, Washington. Others wondered how NHGRI would muster the epidemiological and clinical expertise needed for these efforts.

Less ambitious projects fared better. There was much support, for instance, for NHGRI investing more in helping to find genes in single-gene disorders. And all agreed that NHGRI needs to figure out ways to get physicians and medical schools to take advantage of what genomics could offer in terms of diagnosis, understanding disease mechanisms, and eventually, treatments. "This is an enormous problem," says Robert Tepper, chief scientific officer at Millennium Pharmaceuticals Inc. in Cambridge, Massachusetts.

After a harrowing 2 days, Collins conceded that "we have our work cut out for us" in revising the plan—again. The draft circulated last week had already undergone multiple revisions, he says; to get this far, he and his staff hosted an information-gathering meeting last year and, since then, about a dozen workshops on specific topics, such as proteomics and genetic variation.

Several of Collins's colleagues were worried that he might be discouraged by the "vigorous" feedback, asking Collins midway



Full speed ahead. NHGRI's Francis Collins is charting a new course for his institute.

Chipping
away at
potato blightLively speculation
about VenusProfile: The man
behind the skull

through, "Are you OK?" But for Collins, such debates are not new. His sense was that, overall, the group was enthusiastic about NHGRI's new directions. And as for the tough critique, he says, "This is how the genome community operates."

—ELIZABETH PENNISI

MARINE ECOLOGY

Scientists Brace for Bad Tidings After Spill

VIGO, SPAIN—From a distance, the rocky beaches of Galicia, Spain's northwestern province, look as if they're slathered with chocolate mousse. The illusion dissolves with the first whiff of petroleum, a reek stronger than that at any gas station. Fighting the stench, Peregrino Cambeiro, a technician with the Higher Research Council's Institute of Marine Research in Vigo, shovels sludge (a mixture of seawater and petroleum solids that resembles molasses to the touch) into plastic buckets, then loads them onto a flatbed truck. These are the first samples of the spill that will be brought back to the institute for analysis so that researchers can figure out what sort of oil they are dealing with and assess what impact it will have on marine and other life.

It has been a week since the hull of the tanker *Prestige* first tore open and began disgorging a cargo of fuel oil off the Spanish coast. Every day, more sludge washes ashore, driven by gusts of wind that top 100 kilometers an hour. On 19 November, fearsome, wind-whipped waves overwhelmed the stricken tanker, which ripped in half and sank. So far, 10,000 tons of oil are known to have leaked. The challenge for scientists is to predict what will happen to another 67,000 tons that went down with the ship and how it might harm life on the seabed. "There's still another shoe to drop here," says David Kennedy, director of the U.S. National Oceanic and Atmospheric Administration's oil-spill response program. "The size of that shoe is hard to determine, but history shows there's more to come."

Back in Vigo, Cambeiro unloads the sludge and wearily strips off his slime-covered overalls. Crown Resources, the oil trading firm based in Switzerland that chartered the *Prestige*, has stated that the ship was carrying

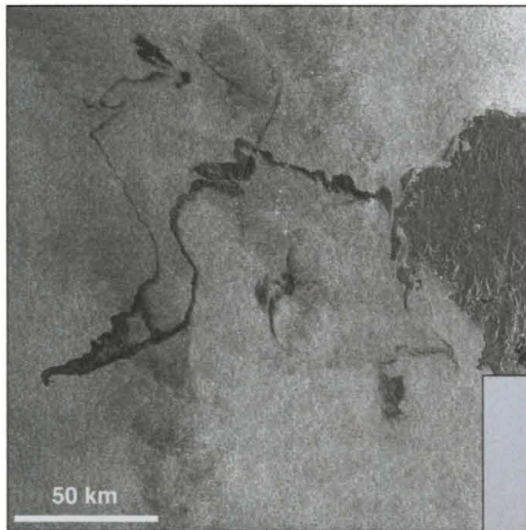
bunker oil, a viscous mix of different grades of petroleum used by ships and power plants. Ricardo Prego, an environmental chemist at the Vigo institute, will use Cambeiro's samples to determine the oil's precise composition. While Prego probes the sludge's chemistry, institute director Antonio Figueras will test its lethality in a range of life forms, including bacteria, fish, and human cells. "This is a crude measure," says Figueras, who will also look for sublethal effects, such as how the sludge affects the immune system and reproduction.

The Spanish government is waiting anxiously for the results of the analyses, which will come in over the next several weeks. On 18 November, it slapped a ban on fishing and

cluding the last 15 to 20 breeding pairs of the common murre in the region. "We can expect a substantial impact on birds," says Malcolm Spaulding, a marine environment modeler at the University of Rhode Island, Narragansett. "They're in for a sticky mess."

Spain's environment minister, Jaime Matas, predicts that 1.5 million square meters of beach will have to be cleaned by hand. The cleanup and direct economic losses will likely top \$145 million. (The European Union has pledged \$115 million in assistance.) Many scientists blame politicians for the disaster's scale. The French, Spanish, and Portuguese governments all refused to allow the leaking tanker into their ports, and Spain even considered bombing it with F-18 fighters to incinerate the fuel. "The Spanish government has shown an evident incapacity to manage the crisis," fumes Dominguez. "We think we can dump anything we want, and it will just go away," says Figueras. "But it will come back to haunt us."

Mariano Rajoy, Spain's vice president, has asserted that the tanker's disappearance beneath the waves averted a much larger disaster because the high pressure and low temperature (3°C) at 3600 meters, where the wreck is said to lie, will solidify any fuel oil left inside the



Disaster in the making. Satellite image of the slick on 17 November, before the *Prestige* sank; scooping out "chocolate mousse" for analysis in Vigo (right).

shellfish harvesting along 300 kilometers of spoiled coastline. Aquaculture of bivalves such as blue mussels is Galicia's largest industry and is second only to China in annual harvest. It's also the industry that's most vulnerable to the sludge, which smothers filter feeders. The bulk of the bunker oil spilled so far has swung north of the key estuaries where mussels are cultured. But until it can be proven that the seafood is safe to eat, more than 5000 Galician fishers and aquaculturists will be out of work.

Other forms of wildlife are, as expected, taking a huge hit. Jesús Dominguez, an ornithologist at the University of Santiago de Compostela, says the spill could have devastating effects on several species of endangered birds that winter along the Galician coast, in-



hull. But Richard Steiner, a marine conservation biologist at the University of Alaska, Fairbanks, who studied the 1989 *Exxon Valdez* oil spill, says that to believe the sunken oil will remain stable is "more wishful thinking than reasoned expectation." If the oil containers break, much of it could still reach the surface.

Even if the oil stays near the bottom, experts are split about its potential impact. "We really don't have much experience with this," says marine chemist John Farrington of the Woods Hole Oceanographic Institution in Massachusetts. Steiner warns that toxic com-