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HUMAN GENOME PROJECT

NEWS

NIH to Produce a 'Working Draft' Of the Genome by 2001

Many scientists were skeptical last May when DNA sequencer J. Craig Venter and his private backer—the Perkin-Elmer Corp. of Norwalk, Connecticut—said they were going to decode the entire human genome in just 3 years. At the time, the governmentfunded Human Genome Project wasn't due to deliver the goods until 2005. To some

academics and government genome sequencers, Venter's pace seemed too fast to be credible. Then, in August, Incyte Pharmaceuticals Inc. of Palo Alto, California, joined the race. It said it was going after the entire human genome too, aiming to get just the genes in 2 years. Now, faced with growing private competition, the skeptics of rapid sequencing have become believers. In a radical change of plan, the chiefs of the U.S. genome project announced this week that they intend to match the private sector's pace and deliver comparable results just as fast.

The U.S. National Human Genome Research Institute (NHGRI) unveiled a 5-year plan this week that promises to produce a "working draft" of the human genomeincluding highly accurate sequences of most of the protein-coding regions-by 2001. The plan also promises to yield a polished, gold-standard version of the entire genome by 2003, 2 years ahead of the old schedule. If successful, this scheme will not only speed up the pace at government-funded labs but also, according to some of NHGRI's advisers, release data so rapidly that companies such as Perkin-Elmer and Incyte may not be able to get exclusive rights to all the DNA they hoped to patent.

Francis Collins, director of NHGRI, and Ari Patrinos, head of the Department of Energy (DOE) genome program, presented this aggressive new strategy to a meeting of NHGRI's advisory council on 14 September. The council voted its approval, with minor revisions. The plan has already been reviewed and endorsed by DOE.

Collins claims the companies didn't prompt this new vigor but acknowledges that "all of this stir in the private sector has opened people's eyes to the possibilities" of rapid sequencing. "This is not a reaction," he insists: "It is action." NHGRI, he says, had been considering taking this step before Venter made his announcement in May.

In a friendly gesture, Collins called Venter last week to invite his newly formed sequencing firm, Celera Genomics Corp. of



Gaithersburg, Maryland, to collaborate on the new plan of action. Venter says he's already sharing data with DOE scientists and is "absolutely delighted" with the invitation. He is banking on a risky "whole-genome shotgun" approach to sequencing and says it would be "nice" to have help in identifying where certain DNA clones fit on the genome. The publicly funded groups will be using a more cautious approach that involves mapping DNA clones to the genome before sequencing. Venter says that he would be happy to include NHGRI-funded labs as coauthors on his papers.

With or without contributions from the private sector, Collins says, it will be "a stretch" to meet the targets in this "ambitious" new government plan. But the agenda is creating "a sense of excitement" among DNA sequencers, he adds. The strategy puts an emphasis on speed and "getting the good stuff," as Collins notes—a shift from the early approach of determining every DNA base to the greatest degree of accuracy. For example, Collins estimates that the current rate of sequence production at NHGRIfunded labs will double or triple, based on improving skill and technology. And, as an immediate goal, NHGRI-funded centers are being asked to focus on "gene-rich regions of the genome." The strategic plan calls for the creation of a peer-review panel to prioritize the hottest regions for sequencing and assign them to labs that bid for them.

By 2001, according to Collins, this process should yield final DNA sequence for about one-third of the entire human genome. And if the bidding system for hot areas works well, this batch of data should include complete versions of a majority of human genes. These completed segments, according to the plan, should be contiguous over an undefined "long range" and finished to a high degree of accuracy, with an error

rate of no more than 1 base per 10,000.

The genome will be sequenced less than completely in this initial push, producing a "working draft" that "could cover at least 90% of the genome" with an overall error rate of one per 100 bases. After 2001, the plan says, researchers will close the gaps and polish the data, producing a final draft in 2003 with a one in 10,000 error rate. But even this version, a footnote advises, may not include all the bases from areas that are hard to decipher or clone.

Some members of the genome community had been wary of the plan, fearful of compromising earlier and more demanding quality standards. Indeed, NHGRI council member Leroy Hood, molecular biologist at the University of Washington, Seattle, says he's been pushing for faster sequencing for "several years," but that cautious members of the community have resisted-until now. The new scheme represents the "strong consensus" of NHGRI center directors who met to discuss it on 3 September, Hood says, but it did not get unanimous support. Robert Waterston, director of the sequencing center at Washington University in St. Louis, says that between May and August, there was "considerable debate among the centers," but that now "the mood is strongly convergent." Richard Gibbs, director of the sequencing center at Baylor College of Medicine in Houston, says he thinks there are "almost no reservations" about the plan today-mainly because people have become more skilled in fixing flaws in the data and more adept in using sequencing technology.

What will it cost the government to double or triple the DNA sequence output of the Human Genome Project? Collins insists that

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Toward the universal library

the new plan is "not dependent" on any big increase in funding. It can be supported, he claims, within the typical budget increases NHGRI has received recentlyabout 10% a year. NHGRI's budget this year is \$220 million. But he adds with a twinkle: "Additional resources could be used very effectively." -ELIOT MARSHALL

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ARCHAEOLOGY

Traces of Ancient Mariners Found in Peru

Most immigrants to the Americas have arrived by sea, but the very first Americans simply walked in. Or so goes archaeologists' traditional view, which holds that the first inhabitants were the big game hunters called Clovis people, whose ancestors crossed the Bering land bridge and swept southward through the Americas perhaps 11,200 years ago. But dates as early as 12,500 years ago at a site in Chile have raised questions about this model, and many researchers have speculated about a shad-

owy alternative: that the first Americans set the pattern for later immigrants by arriving by boat, leaving few traces of their journey.

Now on page 1830 of this issue, two independent research teams report finding the first hard evidence, albeit indirect, for the maritime settlement theory. The discoveries, which reveal an ancient maritime culture in South America about 11,000 years ago, are "about the best kind of evidence that you're going to find that people familiar with the ocean were migrating down through the

Americas," says geologist David Keefer of the U.S. Geological Survey in Menlo Park, California, lead author of one study.

As long ago as the mid-1970s, archaeologist Knut Fladmark of Simon Fraser University in Vancouver proposed that coastal peoples from Asia settled the Americas by paddling southward down the Pacific Coast with simple watercraft and a hefty dose of maritime savvy. Fladmark also noted that the theory would be hard to verify, because most of the clues left along the coast by these putative coastal explorers would now be underwater, drowned some 10,000 years ago by sea levels rising after the last ice age.

Along the southern coast of Peru, however, the sea floor slopes steeply away from

the coast. As a result, "very little land horizontally was lost to rising sea level," says archaeologist Daniel Sandweiss of the University of Maine, Orono. "This is •Trujillo one of the reasons I was looking for sites in this PERU region." There, one U.S.-Peruvian team led by Sand-• Lima weiss and another led by Keefer found two ancient campsites of a Quebrada maritime culture. Radiocarbon tests on charcoal indicate that Quebrada Jaguay, Sandweiss's site, is 11,100 years old, while Keefer's, Quebrada Tacahuay, dates to 10,700 years, making these

cultures among the most ancient in South America. A few Andean sites are between 11,000 and 11,500 years old, and the famous Monte Verde site in central Chile has been put at 12,500 years old, although some researchers still have reservations about this date (Science, 28 February 1997, p. 1256).

Bones and other refuse found at the new



Seafarer's home? Ancient Americans may have traveled by water to the arid coastal site of Quebrada Jaguay.

sites show, says Keefer, that the inhabitants "were familiar with and were using the sea." At Quebrada Tacahuay, people concentrated on fishing for anchovies and hunting seabirds, particularly cormorants. "What we're seeing is really an economic specialization," says faunal analyst Susan deFrance of the University of Florida, Gainesville, a co-author of the paper on this site. "Clearly they focused on this small group of birds," she says, systematically butchering them to remove breast meat. So intently did Quebrada Tacahuay's inhabitants focus on the ocean that 99.8% of the bones at the site belong to marine creatures.

At Quebrada Jaguay, the inhabitants earned their living by gathering clams and Coastal finds. Campsites of an ancient maritime culture hug the Peruvian coast.

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Biodiversity

by computer

capturing small schooling fish, chiefly species in the drum family. Moreover, at both sites the teams found remains of small, calorierich fish, indicating an early net fishery-a very specialized maritime occupation, notes Keefer. But the coastal dwellers at Ouebrada Jaguay also had intimate Arequipa connections to the Andes. Quebrada Tacahuay Studies of trace elements in the obsidian they sometimes used for tools show

that the stone came from highland sources 130 kilometers to the east, indicating that these people either traveled to the highlands themselves or traded with people who did, says Sandweiss.

Cuzco

Jaguay

Both the early dates and the maritime lifestyle make it unlikely that these people were the descendants of land-lubbing Clovis people, says Anna Roosevelt, an archaeologist at the University of Illinois, Chicago. After they reached South America, the Clovis were thought to have headed first for the Andean highlands, where the temperate, open habitat supported big game. "They weren't supposed to reach the coast ... until later," says Roosevelt.

What's more, she and others have found equally old Paleoindian sites in South American rainforests, where they adopted a plant-collecting, foraging, and fishing lifestyle, again very different from that of the Clovis people (Science, 19 April 1996, pp. 346 and 373). Thus the ancient maritime sites "suggest that Clovis is just one of several regional early Paleoindian occupations. There's no apparent ancestral relationship between Clovis and these people in South America," says Roosevelt.

But if Clovis isn't the mother of these maritime cultures, who is-and how did the ancestral stock get there? The obvious answer is by sea, says Keefer, although such a claim is far from proven yet. In Keefer's view, the net fishery and reliance on ocean food sources indicate a sophisticated and ancient knowledge of the ocean. That means that "the most logical scenario would be for them to migrate down the coast," he says. The extreme aridity of the Peruvian coastone of the driest places on Earth, both then