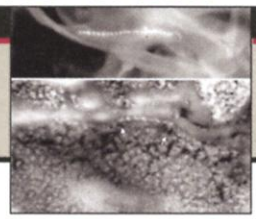

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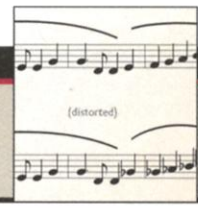
New claims, old doubts on Mars life



1879
Musical inheritance

GENOMES

Rat Genome Spurs an Unusual Partnership

Even as sequencing groups are struggling to finish the human genome—two-thirds of it remains in rough form—they're taking on a big new assignment. Last week, the U.S. government plunked down about $60 million in new money to have three labs—one academic center and two private companies—race ahead on the rat genome. A public-private effort to sequence the mouse genome is already under way, promising a rough draft this year and a finished, or gap-free, sequence by 2005. The rat is needed, researchers say, because it has been used more than the mouse for studies of physiology, and it offers an independent view of how genes work in a rodent. Nailing down this new genome will be almost as daunting as sequencing the human genome in draft form, however, because rodents also have 3 billion base pairs of DNA.

The plan calls for fast work, with delivery of a draft sequence of the Norway brown rat containing 90% or more of the functional genetic information by 2003. Francis Collins, director of the National Human Genome Research Institute (NHGRI)—which is funding this initiative jointly with the National Heart, Lung, and Blood Institute—says that having the genomes of three of the most important mammals in biomedical research in hand "will greatly speed the unraveling of the genetics and physiology" of human disease.

The rat project is remarkable for the new public-private coalition it creates and the efficiencies it aims to achieve. It brings together scientists who until a few weeks ago were competitors, melding their techniques. Richard Gibbs and colleagues at the genome center at Baylor College of Medicine in Houston, Texas, will lead the effort, and a group at Celera Genomics in Rockville, Maryland, will add brute-force sequencing power. Gibbs's team was one of 16 in the nonprofit consortium that raced Celera to the finish line on the draft human genome (*Science*, 16 February, p. 1177). Celera's principal investigator is sequencing expert Robert Holt, a pharmacologist who joined the company at its founding in 1998.

Genome Therapeutics Corp. in Waltham, Massachusetts, will provide more sequencing muscle, using funds reprogrammed from the mouse project after several companies pitched in with private support (*Science*, 13 October 2000, p. 242). Smaller grants for clone preparation are also going to Pieter de Jong of Children's Hospital Oakland in California, Marco Marra of the University of British Columbia in Vancouver, and Shaying Zhao of The Institute for Genomic Research in Rockville, Maryland.

RAT GENOME FUNDING, 2000–02 ($ MILLIONS)

	Reprogrammed 2000–02	New 2001	New 2002
Baylor College of Medicine	33.1	18.25	19.25
Celera Genomics	–	14.0	7.0
Genome Therapeutics Corp.	21.3	–	–
Clone preparation	–	5.1	–

Baylor will take on the difficult task of assembling the raw data into a coherent genome. Celera's assignment is more limited, says president J. Craig Venter: It will generate raw sequence data and offer advice. Gibbs says his group will rely less than Celera did on high-powered computer analysis to assemble the genome and more on a strategy that uses mapping and tight management of data. "It's fair to say the human genome was sort of kludged together heroically" with disparate techniques, Gibbs says. He hopes this project will set a new standard for efficiency, sequencing the rat genome just 4.5 times over, about half the level of redundancy used for the human genome. This will leave significant gaps, but human and mouse data should make genome assembly manageable.

Celera is "happy to be collaborating with Baylor" on this project, says Venter, although he thinks there was "some resistance" within the academic community to including his company in the effort. But he notes that he has always worked well with the Baylor group and that Celera was included for a simple reason: NHGRI reviewers concluded that its sequencing proposal was one of the best. Venter is doubtful, however, that the rat sequence can be assembled into the correct order with so little redundancy in the raw data.

Gibbs is confident. "We're going to break the $100 million barrier for a mammalian genome," he predicts. That may not sound cheap to a traditional small-lab biologist, but it's a fraction of the human genome's price.

Both teams will abide by a new set of mandatory data-release rules established last December. These require grantees to make public on a weekly basis raw information taken directly from sequencing machines—more detailed data than were required from human genome sequencers. The groups have agreed not to patent or use the data for research before making them public through the National Center for Biotechnology Information (www.nhgri.nih.gov:80/Grant_info/Funding/Statements/RFA/data_release.htm).

And then came the rat. The Norway brown rat will be the third mammal to have its genome sequenced.

Researchers are delighted by the pace of the project, not only because of the insights it promises to shed on human disease but also because rat DNA will provide a critical third point (with mouse and human data) for triangulating in on the function of human genes. "I have been a banner waver for the rat genome" for nearly a decade, says Howard Jacob, a molecular biologist at the Medical College of Wisconsin in Milwaukee. "I'm ecstatic about the speed with which the public sector is investing in this project."

–ELIOT MARSHALL

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