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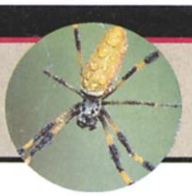
Spider silk genes

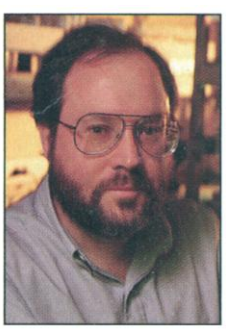


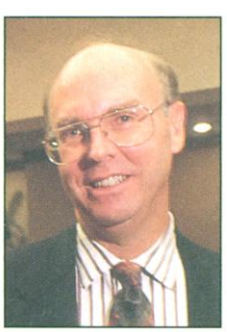
1378
Eros in close-up

GENOMICS

Fruit Fly Genome Yields Data and a Validation

WASHINGTON, D.C.—The humble fruit fly has just soared to the top of the genome charts. Using an approach dismissed as unworkable a mere 2 years ago, a team of publicly and privately funded scientists announced last week that they had decoded more than 97% of the genome of *Drosophila melanogaster*. As with all genome projects, parts are missing: The team sequenced only gene-containing regions, and about 1600 gaps remain. Even so, *Drosophila*, which has been long studied by geneticists, is the largest creature ever to be sequenced, genomewise, and only the second multicellular organism. What makes this milestone especially noteworthy, however, is that it validates the controversial "shotgun" approach. As such, it could pave the way for a public-private effort to complete the human genome, said J. Craig Venter, president of Celera Genomics in Rockville, Maryland, the private half of the team.





Fly catchers. Gerald Rubin *(left)* and J. Craig Venter *(below)* orchestrated a public-private venture to sequence the fruit fly genome.

The last two big successes of the genome project, the nematode (*Science,* 11 December 1998, pp. 1972, 2012) and human chromosome 22, recently published in *Nature* (*Science*, 24 September 1999, p. 2038), were both done using the "clone-by-clone" approach. This involves determining the order of the bases in a series of overlapping clones, whose locations on the chromosomes are known.

In May 1998, Venter stunned the genome community when he said he would tackle the human genome with the whole-genome shotgun approach that he had pioneered on microbial genomes (*Science*, 18 June 1999, p. 1906). To "shotgun" a genome researchers shred the entire genome into random pieces, sequence all the pieces, and then reassemble them in the correct order with the aid of a supercomputer. At the time, critics argued that Venter would be unable to put the millions of DNA fragments back together. As a test case, Venter teamed up with Gerald Rubin and the Berkeley Drosophila Genome Project to try the fruit fly.

The effort "worked better than anyone expected," Rubin reported at the annual meeting of the American Association for the Advancement of Science, which publishes *Science*. Geneticists and molecular biologists are ecstatic. "[Venter and Rubin] have really pushed the envelope of what's possible," raved Daphne Preuss, a geneticist at the University of Chicago. Added geneticist Lawrence Goldstein of the University of California, San Diego: "The quality of what I saw was really exceptional."

One key to their success was an assembly program designed by Celera's Eugene Myers. In short order, the program was able to assemble the 120 million bases into 26 long stretches, or "scaffolds." Myers relied on existing genome maps to order these stretches. Still, the program left 1800 gaps, which Myers reduced to 1600 by adding sequence data from his academic collaborators. What's more, the shotgunned data matched already finished fly sequence quite well. Myers is confident that this approach will work on the far larger human genome. But skeptics are waiting to see how difficult the remaining gaps are to close, a task Rubin's team is taking on, before giving the thumbs-up.

Meanwhile, analyses so far suggest the fruit fly could have as many as 13,000 genes, half of whose functions are unknown, said Celera's Mark Adams. With the sequence in hand, Goldstein expects research to "catapult ahead." For Rubin, this achievement is sweet because everyone worked together well: "It has been one of the most pleasurable scientific experiences that I've had in my academic career."

–ELIZABETH PENNISI

INTELLECTUAL PROPERTY

HHS Probes Genesis of Gene Sequencer

During the past 6 months, biologist Leroy Hood and members of his former lab at the California Institute of Technology (Caltech) in Pasadena have become ensnared in a tangled federal probe of the origins of the DNA sequencing machines that now play a central role in decoding the human genome. Responding to subpoenas, the researchers have been turning over files from more than 15 years ago to inspectors from the U.S. Department of Health and Human Services (HHS).

Hood's Caltech lab developed the key technology behind the sequencing machines and the reagents needed to run it that now are marketed by PE Corp. At issue in the HHS probe is whether Hood's lab used grant money from the National Science Foundation (NSF) as part of that research. If it did, then Caltech, which holds the patent on the technology, may improperly have received royalties from sales of the machine to government researchers.

Nobody is accusing the researchers of wrongdoing, and Hood and Caltech vigorously deny that NSF funds were involved in the key research. But the issue has developed into a cause célèbre since the *Los Angeles Times* broke the story last week. A member of Congress is concerned that the federal government may have been ripped off, and Caltech president David Baltimore has responded with a public statement.

Caltech officials, the researchers themselves, and lawyers from PE all say they

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