Genome project faces commercialization test

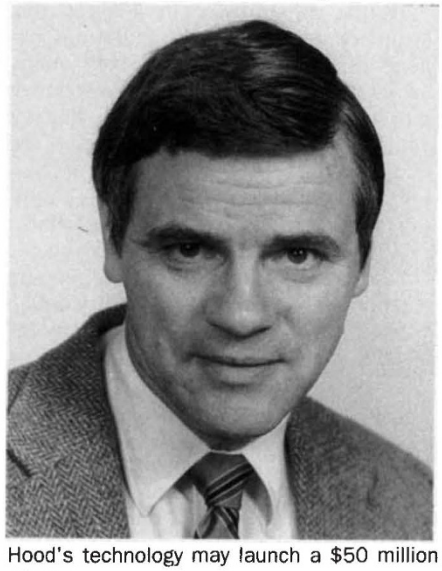
- US investor recruiting leading researchers
- Company aims to dominate gene sequencing

Washington & London

ARMED with tens of millions of dollars in capital, a private investor is making the first serious bid to commercialize the Human Genome Project. Frederick Bourke, a wealthy entrepreneur, is on a worldwide search for top genetic researchers to join a new company he plans to set up in Seattle, Washington. With state-of-the-art technology and the best talent money can buy, he aims to dominate the effort to sequence the estimated 3,000 million chemical bases of the human genome, as well as those of other species. The heads of the two teams now leading the effort to sequence the nematode, *Caenorhabditis elegans* are now in negotiations with Bourke and seriously considering leaving their academic posts to join the company, which has not yet been incorporated or named.

Robert Waterston, at the Washington University in St Louis and John Sulston of the UK Medical Research Council (MRC) Laboratory of Molecular Biology at Cambridge — the two principal collaborators in the $6 million worm genome project — say they are convinced that it is time to move to the next step in the effort, the development of advanced sequencing technology and eventual production-scale automation. As a highly repetitive task, large-scale gene sequencing is tailor-made for a company. Furthermore, moving this sort of 'production line' work out of academic laboratories frees university resources for basic research, they say.

The fact that Bourke might make a



Hood's technology may launch a $50 million company.

hefty profit by essentially monopolizing the high-efficiency gene sequencing market may bother some genome purists, but many others see it as a natural evolution of the project. "It was inevitable that the genome project would be commercialized soon," says Maynard Olson, another Washington University geneticist who is on the US Genome Project advisory panel. "It clear that the [sequencing side of the] project has to scale up in some way, and it's clear that it can't be done in an academic environment. I see no moral principal that one should turn one's back to efficient sequencing in industry."

Indeed, Olson is so taken by the concept that he has decided to leave St Louis to accept a position this summer in the new department of molecular biotechnology at the University of Washington, Seattle. Although plans have not been finalized, it appears certain that the new biotechnology department — created last year with a $12 million gift from Microsoft co-founder William Gates — will be closely affiliated with Bourke's new company. Olson will take with him several members of his laboratory, and says that he expects to eventually have some scientific collaboration with the company.

The magnet behind this migration of leading scientists to Seattle is Leroy Hood, a gene sequencing pioneer who started Applied Biosystems Inc. (ABI), one of the largest makers of automated gene sequencing equipment. Last October, the University of Washington announced that, armed with the Gates endowment, it had recruited Hood and several members of his laboratory from the California Institute of Technology, where he is a professor and director of the university's National Science Foundation (NSF) Science

A turn of the worm

WHAT galls researchers most about the threat of a corporate grab of the project to map and sequence the genome of the nematode *C. elegans* is not just the possibility of a derailed effort to understand a model species, but the implication for the entire Human Genome Project. *C. elegans* research is one of the only truly international collaborations in the 15-year, $3,000 million undertaking, and as such, has been something of a model itself.

Robert Waterston, at Washington University in St. Louis, and John Sulston at the UK Medical Research Council (MRC) Molecular Biology laboratory in Cambridge, are by all accounts one of the success stories of the genome project. They have been collaborating on the worm for five years, and in 1990 the US National Institutes of Health (NIH) and the MRC began an unprecedented three-year project to support jointly full-scale sequencing at the two laboratories. Total support is about $6 million, of which NIH provides two-thirds and MRC the rest. The money is spent equally at the two facilities.

The researchers are now about halfway through a pilot project to sequence three million of the 100 million bases in the worm genome. Given the success of the venture, and the conspicuous lack of similar collaboration elsewhere in the initiative, genome leaders would be sorry to see the worm researchers go.

"I like the idea of a big project that is shared by two countries," says James Watson, director of the NIH genome centre. "I hope that isn't lost." On the other side of the Atlantic, Dai Rees, MRC secretary, is facing the prospect of giving up a key part of one of relatively few research laboratories in which Britain is indisputably world-class. "We've put 20 years of investment into this project, and it's just reaching its culmination. It's just rather a pity if that's creamed off," he says. Rees is hoping to find enough additional money for the project to persuades Sulston to stay.

Waterston and Sulston both say that they have every intention of continuing their worm work, even if it is in a privately-held sequencing company in Seattle. "*C. elegans* would represent a beginning", both in learning how to sequence several hundred thousand bases a day and in interpreting those sequences, Waterston says. "That will help down the line, when you want to work on human DNA." The company will have to prove it can actually do real world sequencing, and *C. elegans* is as good a demonstration project as any, he points out.

But whether Waterston and Sulston will actually be able to finish the *C. elegans* genome in a corporate culture remains to be seen. There is, after all, little market for the nematode gene sequences themselves. Frederick Bourke, the entrepreneur who is recruiting the researchers, is hoping to turn a profit in five years. It is hard to imagine a worm standing in the way.

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and Technology Center for Molecular Biotechnology. Hood will chair the new University of Washington department, the university announced.

Although Hood's financial relationship with Bourke's company has not yet been decided, Bourke says he considers Hood a "co-founder". ABI will be a principal supplier of equipment for the operation. NSF has not decided if it will renew funding for his centre, which now gets about $3.5 million a year from the agency. (Nine of the 11 Science and Technology centres were renewed last year, but a decision on the Caltech facility was delayed, pending resolution of Hood's status.) Mary Clutter, director of the NSF biology division, says that she expects Hood to submit an application for renewal this month. A Caltech official says that the university will not challenge Hood's intention to take the centre with him.

Some researchers are concerned that Hood's involvement with both the NSF centre and the company (which will presumably be competing for government contracts) could represent a conflict of interest. Bourke says he is aware of the concern and intends to avoid such a conflict. Hood declined to be interviewed.

Initially, Bourke is aiming to take a large slice of a contract sequencing market expected to be worth over $100 million by the middle of the decade. But the eventual worth of a mapped and sequenced human genome is orders of magnitude beyond that. Isadore Edelman, who directs the human genome centre at Columbia University and is a principal collaborator with Bourke on the new company, says that the company's intention is ultimately to capitalize on the genetic information it obtains through sequencing, by producing gene-based diagnostic tools and therapeutics.

"I think that the ability to sequence DNA in the genome will become the next industrial revolution," says Bourke. "Being able to do something as basic as sequencing gives us a generic position in this revolution." He notes that Japan is well on its way to developing a gene sequencing effort as a collaboration between industry, government and academic institutions. That effort, now funded at about $14 million, is also aimed at developing automated sequencing technology (see *Nature* **351**, 593; 1991). "I'm concerned that we're being left behind," Bourke says.

Bourke expects start-up funding for his company to be around $50 million. The company will eventually consist of at least three divisions: a large-scale sequencing effort operating on contract for the government and the pharmaceutical industry; a group developing database and computer technology to deal with the vast amounts of information the sequencing operation will generate; and a division to carry out company-initiative genetic research. The last group, working with genetic mapping laboratories in academic institutions, will focus on finding genes and other genetic information that could be used in commercial products, such as diagnostics tests for genetic conditions and infectious disease such as AIDS.

Edelman hopes that within three to five years the company will be able to sequence as many as 200 million bases a year. Initial plans are for about 100 automated gene sequencing machines "about twice as good as the best now available," he says. Each would be able to sequence about 500,00 base a year, at a contract price of $.25 to $.50 each.

While most researchers agree that sequencing in academic institutions has generally not been working well, many are uneasy about Bourke's plans to move it to industry. Mostly, they worry that the company will sequence large parts of the human genome with the sole aim of finding genes and patenting them, thus claiming property rights to substantial portions.

Edelman says this will not be the case. "We're not trying to sequence the genome and dominate all of biology and medicine with a patent position." The company intends to publish its work, and only patent genes if their function has been determined and such patents are considered "acceptable practice", he says. Both Waterston and Sulston say they were adamant that the gene sequences the company finds remain in the public domain. "Rather to our surprise he [Bourke] was still interested," Sulston says.

Nevertheless, many researchers are taking a wait-and-see position. And it seems clear that, whatever the company does to change the commercial prospects of the genome, its impact on the genome project will be significant. If it can indeed sequence far more efficiently than an academic operation, the US genome project will be hard pressed to find an argument against giving it most of the sequencing work and retaining only genetic mapping and basic research for the universities. This is a blow for the project, which now must face the probability that the lion's share of its funding will probably soon go not to academic researchers, but to industrial operations like Bourke's.

UK officials take a more parochial view. Dai Rees, secretary of the UK Medical Research Council, says he would "be happy to contract out work to a British company," but not to Bourke's operation. "If the [worm] project goes to that company, then they can fund it," he says. Speaking in an unofficial capacity, Sir Walter Bodmer, president of the Human Genome Organisation, said he was personally concerned that if sequencing contracts start going to companies rather than academic institutions, then so will the spin-offs of technological development, which would presumably then be proprietary company information.

For the worm genome community, which is now the most focused on sequencing of all the model-species genome projects, "this is going to be a major change in the power structure," says Christopher Fields, a NIH researcher. "I can imagine the *C. elegans* community being very threatened by this." Sulston says that even if he joins the company, he intends to maintain collaborations with his Cambridge colleagues on the worm genome, and the MRC is hoping to find extra money to encourage project researchers to stay in Britain (see page 483).

While the debate continues, Bourke is still recruiting. Among the researchers he has had meetings with are NIH researcher Craig Venter, David Lipman, who is a database expert at the NIH Library of Medicine, and C. Thomas Caskey, a Baylor College of Medicine geneticist, as well as members of Caskey's laboratory. "There's hardly a lab that he hasn't approached," says one researcher. So far, no one has signed on the dotted line. But if Waterston and Sulston do indeed make the move, others are expected to follow.

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INDIRECT COSTS

Dingell probe expands

Washington

CONGRESS' continuing investigation into the overhead charges for federally-funded research has expanded to include contractors for Environmental Protection Agency (EPA) and the Department of Energy (DOE) weapons laboratories. Representative John Dingell (Democrat, Michigan) announced at a hearing last week that his investigations and oversight subcommittee was auditing some of the contractors and that "the initial results are starting to make the universities look like small potatoes." He has scheduled hearings on the new probe in March.

Officials from the two agencies — the Office of Naval Research and the Department of Health and Human Service — that monitor government research grants testified that they have now expanded their university investigations from a handful of high-profile institutions such as Stanford University and the Massachusetts Institute of Technology to virtually all of the 300 universities under their jurisdiction. They explained that even special agreements between certain universities and the government, that have been in effect for nearly a decade, are now under question. By law, the agreements (known as memoranda of understanding) must be "equitable". Many were not, said J. Dexter Peach of the congressional General Accounting Office, and cancelling them retroactively would not be a "changing of the rules", it would be a "shift in enforcement". **Christopher Anderson**