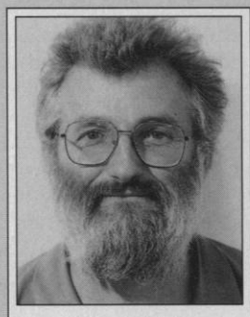
Britain Plans Large-Scale Sequencing Center

LONDON—While U.S. researchers debate the future of the genome project without James Watson, the Wellcome Trust—Britain's largest medical research charity—is laying plans for a bold step into large-scale gene sequencing. Last week, the trust announced that it has asked geneticist John Sulston, a senior researcher at the Laboratory of Molecular Biology (LMB) in Cambridge, to submit a proposal for a new multimillion-dollar center for human gene sequencing. Why Sulston? He's been using the latest automated gene sequencing technology to tackle the genome of the nematode *Caenorhabditis elegans*. And now that the nematode project has shown the potential of this production-line approach, the Wellcome Trust sees the chance to turn Britain into a major player in human genome sequencing.



MRC

John Sulston

Sulston declines to discuss the details of the plan until he has completed his proposal, saying only that the center would be built around a team of about 30 people working on a scaled-up version of the *C. elegans* project. They would churn out about five megabases of completed nematode sequence a year—about five times the present output of Sulston's group at LMB. The center's human gene sequencing effort could start off at about the same level, says LMB director Aaron Klug, who has been involved in discussions with Wellcome Trust officials. Over time, this could be ramped up substantially, he adds, prognosticating that "this technology could be and should be applied to the human genome on a massive scale."

To broaden the center's outlook, Sulston hopes that he will pull in gene mapping groups, and he intends to expand his group's existing work on genome databases, making his proposed center one of "the largest [genome] facilities in the world." If all goes well, the center could open—initially in rented accommodations in Cambridge—by the end of the year.

Sulston's decision to concentrate on launching a genome center in Cambridge kills speculation that he and his collaborator on the nematode project—Robert Waterston, from Washington University in St. Louis—will join a commercial sequencing company in Seattle. Before resigning, Watson had gotten into a bitter tussle with entrepreneur Frederick Bourke, who planned to set up the company with advice from gene sequencing pioneer Leroy Hood, who moves to the University of Washington in Seattle later this year (*Science*, 7 February, p. 677). Watson violently opposed the idea of moving the nematode project—one of the few truly international collaborations in genome research—into the private sector. Now Waterston says that discussions with Bourke had broken down in any case: Bourke's interest was in commercial contract sequencing and applying the technology to medical diagnostics, rather than the "pure genomic sequencing" that he and Sulston want to pursue.

This should be welcome news to the wider genome community, which seems to agree that there is a demand for the type of center that Sulston is planning. Doug Higgs, from the Institute of Molecular Medicine in Oxford, for instance, wants to sequence the end of chromosome 16, which contains the alpha-globin gene cluster. "I'm not really interested in the technology and the handle turning," he says, so if Sulston's planned center could do the job, that would be ideal.

The proposal also comes just as Sulston's employer, the UK Medical Research Council (MRC), is due to launch a far-reaching review of the British genome project, which will be 3 years old this summer. The MRC hasn't yet funded large-scale human gene sequencing but views the *C. elegans* work as a pilot project to reduce costs and refine the technology. If the Wellcome Trust does decide to back Sulston with a multimillion-dollar budget for human gene sequencing, however, this is bound to color the MRC's plans. The MRC is already bidding for government funds to expand Sulston's *C. elegans* work and is now setting up a joint working party with the Wellcome Trust to discuss Sulston's proposal.

Whether Sulston's center will be among the leaders in the race toward production-scale human gene sequencing now lies in the hands of referees and the Wellcome Trustees, who will reach a decision later this summer. But, given that the trust has taken the unusual step of making a public announcement about the project even before receiving a formal proposal, the betting is that Sulston can trust he's about to get a warm welcome.

–Peter Aldhous

nome project? In addition to coping with the varying interests within the U.S. scientific community, the new director will have to be willing to play the role of diplomat. He or she will not only have to keep enthusiasm—and funding—for the project high, in this country and abroad, but will have to try to prevent any country, including the United States, from becoming excessively proprietary about the work its scientists are doing. "That's part of the reason why somebody like Watson is so essential, says Alberts. The new director should be "somebody with credibility who knows what's going on and can give people confidence that this is quality stuff."

Last week, three of the major players in the project flew to Washington for a private talk with NIH Director Healy—who will choose Watson's replacement—to discuss where the project is headed and who might lead it there. Healy doesn't want to second-guess her search committee, but, according to one of the scientists, everyone, including Healy, seemed to agree that rather than a senior statesman, the new head should be a practicing genome researcher who can command the respect of the scientific community. Moreover, the scientists said they wanted someone firmly grounded in medicine who can understand—and, more important, convey—just what this vast project means for human health. Some of the names being discussed at a meeting of genome researchers held last week at the Cold Spring Harbor Laboratory included UCSF's David Cox, Nancy Wexler of Columbia University, and, most frequently, Francis Collins of the University of Michigan.

Whether one of these three—or anyone else—would take the job, should NIH come calling, is another matter. But already, discussions are under way about setting up an intramural genome program that would allow the new director to continue his or her research, at least part time, at NIH.

NIH announced last week that Ruth Kirschstein, director, National Institute of General Medical Sciences, and George Vande Woude, director, Advanced Biosciences Laboratories Basic Research Program, will co-chair a search committee to find Watson's replacement. Acting director Michael Gottesman says Healy told him to be prepared to stay in that capacity for at least 6 months. The program's momentum should carry it along for that duration without difficulty, but if by the new year the interregnum has not ended, the babble of differing opinions about how to proceed may reach a deafening roar, and make leading the genome chorus a nearly impossible task.

–Joseph Palca

With reporting from Leslie Roberts at Cold Spring Harbor.