The race between the public (International Human Genome Consortium) and private (Celera) efforts to sequence the human genome was relatively fierce by scientific standards. But as last month's publications in *Science* and *Nature* show, the two groups crossed the finishing line together. *Nature Medicine* talked to the man who, as part of the Consortium, lead the Sanger Centre in Cambridge, UK, through this historical time to sequence the second largest part of the genome outside the US.

Sir John Sulston

The opening few minutes of our interview define the type of man that Sir John Sulston is. He had read the first two profiles in this series—featuring Harold Varmus and Thomas Cech—and immediately offered his humbled apologies that he felt he didn't quite fit the line-up.

He reeled off the names of colleagues at the Sanger Centre and around the world who, he insists, deserve more recognition as it is they who have really done the sequencing work, and reminded me that he has stepped down from the position of director now that the job is done. Finally, he added that with respect to the head of the Howard Hughes and the National Institutes of Health, he's not an empire builder.

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Sir John Sulston

So how did such a modest, self-effacing man come to hold such an important, high profile, yet in his words, "uncharacteristic" position? He manages to make the answer sound equally unpretentious: "Because of the worm."

Back in the early 1980's, Sulston returned to the United Kingdom from his postdoc in California to work with Crick, Sanger and Perutz at the Cambridge Laboratory of Molecular Biology. He was recruited by Sidney Brenner to work on *Caenorhabditis elegans* and was joined on the project by Alan Coulson when Sanger retired in 1983. It was a Gordon Conference lecture around that time on "walking the *Drosophila* genome" that Sulston says gave him the idea that the worm could be sequenced more quickly if it was cloned and mapped first.

"That was the program and it worked within 3–4 years," he says. By the time the worm was mapped, discussion on sequencing the human genome was already at an advanced stage. "I was introduced to the Wellcome Trust by Aaron Klug, who was keen for there to be a large component of the Human Genome Project in this country," remembers Sulston. "The Trust looked kindly on this idea, and we were funded to start the Sanger Center. That's how I was suddenly catapulted from a small time effort to being director of something that was not only going to house the worm sequence, but was going to make a substantial contribution to the human genome."

If events had taken a different turn, Sulston says he would have been happy to continue charting the cell lineage of the worm, an admittedly solitary occupation—he "doesn't like crowds"—and one that he says he loves. Today he would have been a bench molecular geneticist, but believes that many of his post-docs are more skilled at this than he.

However, last month's publication in *Nature* is now an official record of the fact that Sulston has overseen the mapping and sequencing of the second largest section of the genome within the public consortium's effort.

The clone and map strategy used for the worm had become the basis for the consortium's work on the human genome. Things went well until 1998 when Celera announced that its new method of whole genome shotgun sequencing would be faster and better. Sulston recalls the pressure on the consortium to pull out of a race it surely couldn't win. "Congress was told that there was now an American company that knew a much better way of sequencing the genome and that the public labs should stop. But we asked a few clever people who are good at computational mathematics, like Phil Green and Maynard Olsen, and they said 'No, its not going to work.' That's why we didn't stop."

He says that the release of the Celera data last month in *Science* vindicates that decision. "Actually the human genome is too complex in terms of the repeats, and the product that they make with their method is pretty disconnected. They've taken our map and sequence data and layered theirs on top. That makes perfect sense to us and I think it should be acknowledged that this is what has happened." He believes that both groups will find the finishing process—closing the gaps—equally difficult.

In true socialist style, Sulston insists, "A consortium is not inefficient, it's the way things should be done. Everybody should pull their weight." He was of the view that if the genome was to be sequenced then as many groups as possible had to have a stake in it. "There's a real danger in having a monopoly in something which is as valuable and as emotive as the human genome. We have to share the financial burden and spread the ethical commitment among nations."

But the effort has changed him. "One direct result of the last two years is that I've become more political. I was horrified to see that people were not behaving in a very altruistic way with the genome. It was just like the Klondike gold rush, picking out the riches and ignoring the devastation to the landscape. Instead of accepting that this is one of the most important things that we can do, and everybody sharing it, it's become competitive.

"Part of the problem [with science] is the notion that every single discovery has to be exploited to the full as soon as possible. This is very dangerous, both for the progress of science and for society because the truth is that as a society we need to know a lot more than we choose to do. It's taught me that maybe I do have views about society."

So what next for Sir John? "Because of what happened with the genome, I do now have a wide-ranging political interest," he says, "I can't define a role at the moment but it's to do with the way our society operates. For now though, I intend to put the finishing touches to the worm genome, which has suffered because of what we've been doing lately."

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