The Common Thread: A Story of Science, Politics, Ethics and the Human Genome

by John Sulston and Georgina Ferry
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Few scientific events have generated more furor and excitement than the sequence of the human genome—humanity's common thread. The complete sequence of the 3.2-billion base pairs of the human genome has been revealed. The journey from the first murmurings of the desirability of determining the sequence of the whole genome to actually achieving it entails a long and contentious debate among leading scientists of the usefulness of the whole endeavor. Though many feared that this mega-project would siphon away federal funds from important biological problems, the scientific community and the lay public alike have been both fascinated by the controversy and excited by the possibility of decoding the book of life. It is perhaps fair to say that the increased public awareness and US federal support in the last decade was fueled by the promise that the sequence of the human genome will help in finding cures for many diseases.

John Sulston—a key player in sequencing the human genome—has written an account of the politics, personalities, ambitions, ethics and commercial aspects of one of the largest international scientific operations. Though cowritten with Georgina Ferry, it is Sulston's story, written in his voice. Sulston was a chemistry undergraduate who by chance became a biologist and reluctantly grew into the leadership role of this mammoth undertaking. After a short post-doc at The Salk Institute working on the synthesis of prebiotic nucleic acids, he joined Sydney Brenner to work on *Caenorhabditis elegans*. Sulston writes about his shift from chemistry to biology, uncertain of his abilities to lead a group and be contented to look through a microscope for years. But for this painstaking work, Sulston was awarded the 2002 Nobel Prize in

Medicine and Physiology, along with Brenner and Robert Horvitz.

The book chronicles the events leading to the establishment of the international consortium for physical mapping and eventual sequencing of the human genome. The crucial role played by Jim Watson, then director of the Cold Spring Harbor Laboratories to encourage Sulston, Robert Waterston and colleagues to start sequencing the genome of *C. elegans* as proof of principle, the role of newly established National Human Genome Research Institute (NHGRI), Watson's advocacy, his influence on the scientific community and his political acumen with the legislature make wonderful reading. The chapter "In Business" gives a glimpse of how commercially naive scientists are treated by seasoned business entrepreneurs. There is a fascinating account of the meeting with Fredrick Bourke, a wealthy investor who wanted Sulston and Waterston to head the commercial sequencing organization and commented in frustration, "Dealing with scientists is like being a sheep dog rounding sheep."

Like in all good novels, there must be a villain and here it is Craig Venter, former CEO of Celera. Venter is an unabashed showman who revels in controversy and loves to rattle cages of the establishment. He has many firsts to his credit—expressed-sequence tagging for sequencing cDNA (though Sulston credits this to Paul Schimmel and colleagues), starting the Institute of Genome Research where the first full microbial genome sequence was done, and using the 'shotgun' DNA-sequence approach.

On 12 May 1998, Venter announced that he was forming Celera with Elmer Perkins and would sequence the entire human genome in 3 years, about 3–5 years before the publicly funded human genome project. The implications were that since Celera could do it cheaper and faster, why should public funds be expended on this venture? There were congressional hearings and public and scientific debates over letting the legacy of the human genome fall under a private company. The book provides a fascinating and fast-moving description of the events, the scientific polarization, the mudslinging, the stepping in of The Wellcome Trust

Fund to provide additional support to the Sanger Center and massive commitment of resources from NHGRI. After considerable haggling and breaking of established scientific practices for publication, in February 2001, Celera published the complete human genome sequence in the journal *Science*, and the publicly funded project appeared in *Nature*. Celera clearly benefited from the publicly available data in filling in the gaps in their sequencing strategy. Many scientists and bioinformaticists are still debating if Celera could have accomplished the task without the help of data available from the publicly funded project.

It is clear throughout the book that the prime motivation of Sulston and colleagues at the Sanger Center and publicly funded genome project in the US was to make all the data immediately available to the entire world. This aspiration clashed with the stated goals of Celera, which wanted to sell the data, mine it for their own drug-discovery programs and hence set limitations on the access to the data. This book is an account of contemporary events and therefore does not

have the benefit of historical perspective. For instance, Sulston is emphatic that with or without Celera, the sequencing project was in high gear to accomplish the task by 2001–2002, yet Maynard Olson, another pioneer, suggests that Celera indeed prodded the public project to accelerate its pace (*J. Mol. Biol.* 319, 931; 2002). The book is a bit parsimonious in ac-

knowledging the contributions of other scientists; for instance, a single sentence states that Eric Lander took the lead to write the final paper published in *Nature*. I suspect Lander made much greater contributions in pushing automation, bioinformatics and data collation. There is also some grandiosity in the book, such as the statement that the continued feud between Celera and the human genome project may reflect badly on Al Gore's chances for election is a bit far-fetched. No doubt there will be accounts of this marvelous achievement by other principle players, but for now Sulston has given a masterful personal account of the incredible tale of the effort that will shape the study of biology and our inheritance for decades to come.