



## RETROSPECTIVE

# John Sulston (1942–2018)

A visionary biologist with a deep social conscience

By Judith Kimble<sup>1,2</sup>

**S**ir John Sulston, a pivotal figure in the Human Genome Project, died on 6 March 2018. He was 75. His extraordinary ability to tackle and solve biological problems of immense scale and vision, coupled with his lifelong commitment to ethics, shaped the *Caenorhabditis elegans* nematode and human genome communities. Sulston shared the 2002 Nobel Prize in Physiology or Medicine for discoveries in organ development and programmed cell death. In addition to his earlier work, Sulston will be remembered for leading the British effort to sequence the human genome and defending free access to the data.

Born in Buckinghamshire in 1942, Sulston described his young self as a mechanically minded artisan who preferred science to sport. As an adult, he combined those artisan's gifts of design and creation with vision and hard work. He received his B.A. in natural sciences in 1963 from Pembroke College, Cambridge, UK, and his Ph.D. in Chemistry in 1966 from the University of Cambridge. After a brief postdoctoral fellowship at the Salk Institute in California, he returned to Cambridge and took a position at the Medical Research Council Laboratory of Molecular Biology (MRC LMB). In 1992, Sulston became director of the Sanger Centre. After stepping down in 2000, he continued to devote himself to pressing societal issues.

John Sulston first touched my life through a 1975 letter to my graduate adviser detailing his unpublished method to glean cell-lineage

data from living nematodes. John had discovered that, by looking through a microscope, he could see not only each cell division but also the fate of each daughter cell, including its movement and differentiation. We were working on an organ peripheral to John's interests, and he suggested we use his method to determine its cell lineage. That generosity decided my Ph.D. project. I met John in 1977 at a *C. elegans* workshop. Already a major player because of his pioneering lineage work, John opted to present a poster. Astonishingly, the "poster" was just a 35-mm slide of the postembryonic lineage taped to a window! He wanted viewers to discuss concepts rather than data details, a decision some considered quirky but others like me found refreshingly focused on the larger picture.

John's intense commitment to pushing the limits of scientific frontiers, along with his approachability and easy-going nature, convinced me to do postdoctoral research with him at the MRC LMB. His 1976 lineage publication had reported reproducible cell deaths, paving the way for *C. elegans* studies to dissect the regulation of programmed cell death. Soon after I arrived at LMB in 1978, John sequestered himself to decipher the embryonic lineage. He sat in a darkened room each day for about 12 hours, time for the cells of an early embryo to transform themselves into a wriggling worm. Normally charismatic and social, John tackled each day of solitude with renewed drive to track each division and daughter cell as it assumed its role in the developing embryo. After more than a year, John finished his work, connecting the embryonic and postembryonic lineages to generate the first complete developmental map of a metazoan. This feat laid the foundation for the now-burgeoning *C. elegans* field,

which has revealed secrets applicable to all animals, including human health and cancer.

With his first megaproject complete, John settled on his next visionary idea: generating a physical map of the *C. elegans* genome. The scope of this effort was immense, but John understood the genome's significance as a path to molecular understanding. His first step, in 1982, established methods to break the genome into bits and assemble a map from its pieces. Ever generous, he made map fragments publicly available soon after assembly and long before publication, catapulting a host of molecular studies.

With the advent of DNA sequencing, John's vision broadened to the Human Genome Project. As director of the Sanger Centre, he led a large and talented team to improve methods, produce enormous quantities of data, and computationally analyze sequences of the worm and then the human genome. Throughout this time, John worked at the bench, devising new methods to sequence seemingly impossible parts of the *C. elegans* genome, which was published in 1998 as the first complete metazoan genome sequence.

John's greatest challenge came when Celera Genomics set out to sequence the human genome and patent its contents. The idea that a private company might sequence the human genome for profit and prevent free access to the scientific community was anathema to John. Given the enormous implications of the human genome for human health, he considered free access nonnegotiable. For the first time in his life, John became the center of controversy, but his heroic efforts kept the human, mouse, and now many other genomes in the public domain, as described in his book, *The Common Thread*.

In 2001, after stepping down as Sanger director, John reluctantly accepted an invitation to be knighted after being convinced that the recognition benefited science. He next was awarded a Nobel Prize in 2002. He then threw himself into his work as chair of the Institute for Science, Ethics, and Innovation at the University of Manchester and chair of a Royal Society task force to assess the effects of increasing human population on human health and the environment.

John and his wife, Daphne—inseparable for more than 50 years—raised two children, Ingrid and Adrian. As his first postdoc, I was included in family cycling outings and visits to his home, which was cluttered yet comfortable in classical English style. Each November, John invited the lab to celebrate Guy Fawkes Night, with glowing lanterns hung around their garden and a roaring bonfire. John Sulston and his wonderfully generous and humble spirit will be sorely missed. ■

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# Science

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