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In a move that many will regard as long overdue, the Nobel committee honoured Sydney Brenner with the Nobel Prize for Physiology or Medicine. John Sulston and Robert Horvitz will share the prize, which has been awarded in recognition of the triumvirate's seminal studies on the nematode worm *Caenorhabditis elegans*.

Their discoveries concerning genetic regulation of organ development and programmed cell death have given insights into these processes in many other organisms.

In the early 1960s, Sydney Brenner - then at the MRC-LMB in Cambridge and currently a Distinguished Professor at The Salk Institute, California, USA - realized that it would be impossible to use a mammalian system as a tool for studies on cell differentiation and organ development. He identified the nematode Caenorhabditis elegans as an ideal experimental organism because of its short generation time, small cell number (959 cells in the adult) and amenability to examination by both light and electron microscopy.

In 1974 he further extended understanding of the worm by showing that ethyl methane sulfonate (EMS) could be used to induce genetic mutations and that these had specific effects on organ development. The worm's amenability to fixation and thin sectioning enabled Brenner to undertake a detailed examination of its nervous system, leading to the publication in 1986 of a complete map of the *C. elegans* nervous system and ultimately to the identification and characterization of the *unc* genes involved in the animal's functional neurobiology.

John Sulston - working with Brenner in Cambridge - was key to much of the early work on the worm, by virtue of his development of techniques to study all the individual cell divisions in the worm, from fertilized egg to adult. He initially described a cell lineage for a part of the nervous system and in 1983 published a cell fate map detailing the lineage of every cell in the organism.

This work led to the discovery that certain cells always die at specific developmental stages via the programmed cell death (or apoptotic) pathway - in the case of *C. elegans*, precisely 131 of the initial 1090 cells are removed in this way. Sulston also identified the first mutations in the genes controlling this pathway, including *nuc-1*, the gene product of which is responsible for degrading the DNA of the dead cell.

Following his leadership (with Bob Waterston of the University of Washington, St Louis) of the project to sequence the entire genome of the worm, the unassuming Sulston served as the first director of The Sanger Centre, (now The Wellcome Trust Sanger Institute), Cambridge UK, and as an ardent advocate of the need to keep genomic information in the public domain. The aim of having both a developmental and genetic map of the organism is now all but complete.

"The worm worked so well because the community held an ethos of sharing - just as the public genome projects have - from the beginning. We gave all our results to others as soon as we had them. From sharing, discovery is accelerated in the community. Research is hastened when people share results freely," said Sulston.

Allan Bradley, who replaced Sulston as Director of the Wellcome Trust Sanger Institute said: "This is absolutely fantastic news! It's great for John and for British science. I am thrilled that John's work has been honoured by the highest award. John has been instrumental in laying out several of the foundations upon which almost all experimental work in the worm depends. This began with the lineage map and extends to the genome sequence. John's vision in developing and persevering to finish the job is an inspiration to us all."

Following on from Brenner and Sulston's discoveries, H. Robert Horvitz of the Massachusetts Institute of Technology, Cambridge, USA identified the first two genuine "death genes" - *ced-3* and *ced-4* - and showed that these are absolutely required for apoptosis to proceed. His lab subsequently identified a number of other genes in the pathway - including *ced-9*, which protects cells from death by modulating *ced-3* and *ced-4* activity - and also identified homologs of these genes in the human genome. It is now clear that these genes are evolutionarily highly conserved and central to the cell death pathway in all animals.

In addition, understanding of these fundamental biochemical pathways has yielded insight into numerous medical conditions. Understanding how cell death is regulated will be of great importance in conditions such as AIDS, stroke and myocardial infarction where excessive cell death is often fatal and cancer where reduced cell death has much the same effect. It may also be possible to manipulate these pathways such that undesirable cells can be removed from the body.

Paul Nurse, Chief Executive of Cancer Research UK and a Nobel laureate in 2001, sums up the feelings of many when he says, "This is a fantastic achievement and a great boost to British biomedical science. Sydney Brenner has long been a guru of British molecular biology and has been on the edge of winning several Nobel Prizes, so it's great that he's finally been rewarded. John Sulston is a great scientist and a sturdy defender of the principle that publicly funded science should be used for public benefit."

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