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NEWS

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE FOR THE YEAR 2002

The Nobel Prize in Physiology or Medicine for the year 2002 has been jointly awarded to Sydney Brenner, H. Robert Horvitz and John E. Suslton for their discoveries concerning ***"genetic regulation of organ development and programmed cell death".***

Multicelluar organisms develop from a single fertilized ovum. The zygote undergoes divisions and differentiation to generate the number and variety of cells characteristic of each species. This process of multiplication and division is accompanied by death of cells in precise and regulated manner. It is now well documented that programmed cell death is an essential part of the development process and also for maintaining the adult population of cells.

The unicellular organisms like Yeast, *E. Coli* which have served the geneticists and molecular biologists for decades are not suited for the study of the development processes. The mammals are far too complex and contain for too many cells to be appropriate to study these fundamental processes. Lack of a model organism was recognized by Sydney Brenner in 1963 and his search ended with *Caenorhabditis elegan. C. elegans* is a simple, multicelullar nematode (round worm) approximately 1 mm in length, has a short generation time of about 3 days. It is transparent enabling a direct observation of cell division and cell fate under microscope. By 1974, Sydney Brenner showed that specific mutations could be induced in the genome of *C. elegan.* He also recognized that different mutations could be linked to specific genes and to specific effects on the organ development.

The work of Sydney Brenner was extended by his disciples and later colleagues John E. Sulston and H. Robert Horvitz. John Sulston developed the technique to study all cell divisions in the worm beginning from single fertilized egg to a total of 959 cells in the adult worm. In 1976, he described the cell lineage for a part of the developing nervous system. He made an interesting and compelling discovery that the lineage is invariant meaning that the same program of cell division occurs in each and every worm. He also observed that same specific

cells in the cell lineage always die as a part of the development. An exact number of 131 cells always die in the process. He then described the mutations that resulted in defective cell death program and development of the organism.

Robert Horvitz extended this work delving further into the genetics and cell lineage of *C. elegans.* In 1986, he identified two 'death genes' namely *ced3* (human counterpart is *caspase*) and *ced4* (human counterpart is *Apdf1*) that were prerequisite for death program to be executed.

These critical and significant discoveries have lead to our present understanding of the delicate balance between cell division and programmed cell death that operates during the development and in adult life. The establishment of *C. elegans* model and the operative information gained thereafter has proven valuable for many research disciplines. The understanding of pathways controlling cell death is of prime importance in medicine. Cellular death occurs in AIDS, neurodegenerative diseases, stroke, myocardial infarction while cancers and some autoimmune conditions are associated with an escape of cells from the process of death. Understanding of molecular mechanism and pathways of these processes will equip diseases. One of the strategies of treatment of cancer is based on the stimulation of the 'suicide program' inbuilt in the cells.

Prof. Sydney Brenner is presently at Salk Institute and is now studying vertebrate gene and genome evolution. Dr. Horvitz is at Massachusetts Institute of Technology and continues his quest for defining a molecular genetic pathway for programmed cell death, links between genes and behaviour, morphogenesis, cell fate, signal transduction and neurological diseases. Sir John Sulston received knighthood for services to genome research in 2001 and continues to work on *C. elegans* at Wellcome Trust Sanger Institute.

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