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Book reviews

The Nematode Caenorhabditis elegans. Edited by WILLIAM B. WOOD and the Community of *C. elegans* Researchers. New York: Cold Spring Harbor Laboratory, 1988. 667 pages. US $97.00. ISBN 0 87969 307 X.

When, nearly 25 years ago, Sydney Brenner decided to move over from phage, phasmids, phagemids, *Escherichia coli* and the like, in order to start genetic studies on a small and little-known worm, eyebrows were raised that a senior molecular geneticist should set out on such a rash adventure. However, the worm has proved a fast runner, and it is now under study in over 60 laboratories, supports a biennial international conference and a twice-yearly newsletter – and is even on show in recent textbooks of Developmental Biology. Brenner started his work with *Caenorhabditis briggsae*, but soon changed to *C. elegans*, perhaps beguiled by its appealing name. The two species are described as morphologically identical and only distinguishable by mating tests; but they do show marked DNA sequence divergence in the non-coding or spacer regions which separate their genes.

The book under review is the first concerted attempt to bring the reader up-to-date on research on this organism. For those not acquainted with *C elegans*, it is a small (1 mm long) transparent nematode roundworm related to *Ascaris*. Free-living in the soil, with a life-cycle of just 3 days in culture, it grows very well on bacteria. Both sexes have five pairs of autosomes; males have one *X* and no *Y*, hermaphrodites two *X* chromosomes. Hermaphrodites can self-fertilize or mate with a male, which provides an ideal system for identifying and keeping recessive lethal or sterile mutations. Selfing gives almost entirely *XX* hermaphrodites, but rare males arise from loss of an *X* chromosome. An interesting point is that hermaphrodites outgrow males in mixed populations, while sperm from cross matings of male with hermaphrodite outcompete the hermaphrodite's sperm and preferentially fertilize the oocytes – with the result that only outcross progeny will be produced after mating. Most related nematodes have *XX* females rather than hermaphrodites, and also show 'chromosomal diminution', unlike *C. elegans*.

The *C. elegans* genome contains 8×10^7 base pairs of DNA, about 20 times that of *E. coli and* half that of *Drosophila*. There are some 4000 genes, interspersed with an average of 20 kb of spacer sequences. The genes have introns which are often unusually short (48 or 52 bp); and transposons (Tc elements) resembling P elements in having short inverted repeats have also been found. Of these, Tc1 is present in all wild strains examined, and is in low copy number (*c.* 30 copies) and in high copy number (about 300 copies) in different strains. Tc transposition can cause germ-line mutations, and provides a useful genetic tool. The adult worm has only 959 somatic nuclei in hermaphrodites and 1031 in males. This organism will be seen to provide an excellent basis for studies on the genetics, microanatomy, cell lineage and development of a simple multicellular eukaryote.

The book is divided into a number of substantial and well-written chapters which discuss Genetics, The Genome, The Anatomy, Cell Lineage, Genetics of Cell Lineage, Germ-line Development and Fertilisation, Embryology, Sexual Dimorphism and Sex Determination, Muscle, The Nervous System, and The Dauer Larva; while appendices give compilations of the Parts List, Neuroanatomy, Cell Lineage, and Genetics. Finally, there is a useful section on methods, a Bibliography of about 1000 references and a detailed Index.

The invariance of cell number and of cell fate within the somatic tissues of *C. elegans* has enabled every cell in the animal to be identified and assigned a unique label. By relating this picture to the cell lineages, a comprehensive description has been obtained for the first time of the ontogeny and ultimate differentiated state of all the variety of cells that comprise a metazoon. Programmed cell death is a prominent feature of the cell lineage, and accounts for one in eight of the somatic cells produced, but its basis is not yet fully understood. Two particular cases of cell death have rather fancifully been described as murders, since ablation (elimination by laser strike) of another cell in each case enables the cell in question to survive and in one case causes the growing worm to be sterile.

The very detailed anatomical picture of the worm

throughout its development, based on a combination of cell lineage studies and reconstructions of electron micrographs of serial sections, has made possible a genetic analysis of the control of cell lineage by studies of a large number of mutants which distort particular cell lineages. Many types of such mutants remain to be identified by new types of selection procedure, but this work is at the stage where molecular analysis of lineage mutants is possible – obviously a very important area for experimental embryology.

Muscle anatomy, assembly and function have been studied mainly on the body-wall musculature responsible for movement of the animal forwards and backwards. The major muscle components are similar to those of other animals: muscle extracts contain myosin with both heavy- and light-chain subunits, actin, paramyosin, tropomyosin and troponin-like proteins. The myosin heavy chain coded for by the *unc-54* gene, paramyosin coded by *unc-15* and actins coded by *act-1* and *act-3* are all body-wall muscle constituents, and their positions have been further defined using monoclonal antibodies, together with a number of other muscle-associated proteins. More than 25 genes whose mutations cause uncoordinated or slow movement have now been identified as muscle genes. The *unc*-22 gene, identified by its distinctive 'twitcher' mutant phenotype, codes for a polypeptide of more than 500 kD located in the myofilament lattice in the A band, but in spite of extensive molecular analysis its function remains mysterious, and it is not known whether it has an analogue in vertebrate muscle.

The nervous system is one of the main targets of genetic research in *C. elegans*, and is the most complex organ in the animal, containing 37% of the somatic nuclei in hermaphrodites and 46% in males. The complete nervous system of the hermaphrodite has been reconstructed, and a partial reconstruction of the nervous system in the male tail, where most of the sexual differences occur, has been described. Experimental studies include the development of the nerve cell lineage and the effects of both laser ablation of particular cells and of mutations on cell lineage and on behaviour, and pharmacological observations on effects of putative neurotransmitters, their agonists, etc. Behaviours that have been studied by mutational analysis include coordinated movement, chemotaxis, thermotaxis, osmotic avoidance, male mating, egg laying and mechanosensation. This system has been analysed to a resolution and completeness that has not been possible for any other animal, but we are still far from being able to design a computer or robot model of *C. elegans* which would mimic the behaviour of the real animal. Those who think they are well on the way to building a model of the human brain with a 4th or 5th generation computer should perhaps try to cut their teeth on *C. elegans*.

Let us finish with the chapter on sexual dimorphism and sexual selection, which also reports many interesting discoveries. The primary sex-determining signal is the *X/A* ratio, which appears to set the states of a small number of sex-determining genes, which then direct development along a particular sexual pathway. Of the seven major genes so far identified, the three *tra* genes appear to be required in the hermaphrodite but not in the male, the *her-1* gene is required in the male only, and the three *fem* genes are required for male somatic development and also for spermatogenesis in both males and hermaphrodites. Dosage compensation is thought to be achieved by increasing transcription from the single *X* chromosome of the *XO* male or decreasing transcription from the two *X* chromosomes of the *XX* hermaphrodite. Thus there are similarities between the sex determination and dosage compensation systems of *C. elegans* and *Drosophila*.

To summarize, *C. elegans* has fully borne out Sydney Brenner's hopes for its future: its has obviously become of unique value for analysing the genetic control of metazoan differentiation, and of the relation of behaviour to the nerve cell system in all its aspects.

The book under review, which covers in detail the whole field of *C. elegans* research, makes absorbing reading, and should be studied by all those with an interest not just in worms but in the wider problems of understanding gene action in multicellular organisms. This book should be of value to a wide readership for many years, and my only cavil it at its high price. A paperback edition at a much reduced price would certainly find its way to the private bookshelves of numerous geneticists, embryologists, cell biologists, etc., and I hope the publishers will take heed.

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Practical Isozyme Genetics By N. PASTEUR, G. PASTEUR, F. BONHOMME, J. CATALAN and J. BRITTON-DAVIDIAN. Chichester: John Wiley. 1988. 215 pages. £29.95. ISBN 0 745 8 0501 9.

This is an English translation of a French text published in 1987. It consists of three major parts. Part I comprises an outline of the principles involved in protein electrophoresis and discusses the genetic interpretation of gels, part II describes the laboratory techniques involved and includes staining protocols for about 50 enzymes, and part III outlines some (elementary) methods of data analysis. In line with the authors' experiences, the book concentrates on animal examples.

Unfortunately, for what is essentially a practical manual, coming from a major group of biochemical