Developmental Biology of Caenorhabditis elegans: **Symposium Introduction**[1]

DONALD L. RIDDLE[2]

Journal of Nematology 14(2):238-240. 1982.

Many nematologists do not seem to be interested in nematodes for the nematodes' sake, but instead are concerned primarily with the plants or animals they may parasitize and the economic importance of nematode control. Perhaps as a consequence of this and other factors, nematology has developed along paths which were, in a sense, long ago predetermined by the historical divisions between plant and animal scientists. Obviously, a crucial role for the Society in the development of nematology as a scientific discipline is to bridge the natural gap that has been laid down by historical precedent.

The entry of geneticists and molecular biologists into the field has made the situation a bit more complex. Perhaps unfortunately for the nematodes, these biologists also are not necessarily interested in the worms for their own sake, but are simply using them as convenient laboratory models for the study of genetics, development, neurobiology, and behavior. Generally speaking, these scientists embrace the reductionist viewpoint that what is learned about the basic biology of a nematode may in some significant part be applied to other species. In other words, the basic strategies of gene expression and cellular function underlying animal development and behavior are believed to be largely conserved in evolution, so that relatively simple metazoans can serve as useful models for analysis of a wide range of biological processes common to all animals. Furthermore, it is argued that commonalities at the cellular level make certain studies with nematodes (for example those on genetics and aging) relevant to the treatment or prevention of human genetic disorders or to the understanding of the biology of human aging.

As important as these considerations may be, it clearly would be a mistake to claim that nematologists are not at all interested in nematodes, but instead in plants, higher animals, or in human medicine. Among the diversity of interests in nematology there is a great deal of common ground for all of us to share and appreciate. That common ground is the physiology of the nematode. As we learn more about how nematodes work, I predict we will grow to appreciate more and more how fundamentally similar the various species may be to one another, in spite of the fact that they inhabit strikingly dissimilar environments and employ many different survival strategies. The same is true for us mammals after all. The differences in appearance and life style between mammalian species is frequently only a thin veneer over fundamental physiological similarities.

Ultimately, it is up to each of us as individuals to make use of opportunities such as afforded by the following papers to gain the insights necessary to build on what already has been learned about nematode development and physiology. Geneticists and cell biologists certainly need this kind of input. Our needs arise partly from the fact that most of us are newcomers to the field. Many of us are molecular biologists who seek to apply some of the techniques and experimental strategies of that field to the study of multicellular eukaryotes. While we bring fresh talent to the study of nematodes, we have been slow to appreciate what insights may be gained from comparative nematology, or at least from an appreciation of the natural history of our laboratory organism.

The soil nematode, *Caenorhabditis elegans*, was chosen by Sydney Brenner in

Received for publication 19 January 1982.

[1]Introduction to the symposium papers presented at the annual meeting of the Society of Nematologists, Seattle, Washington, August 16-19, 1981.

[2]Caenorhabditis Genetics Center, Division of Biological Sciences, University of Missouri, Columbia, MO 65211.

The author's work is supported by grant HD11239 and Research Career Development Award HD00367 from the National Institute of Child Health and Human Development. The Caenorhabditis Genetics Center is supported by contract NO1 AG 9 2113 with the National Institute on Aging.

the mid-1960s initially as a model organism to study the genetic specification of behavior. From Brenner's point of view, the fundamental questions in behavioral genetics were those which addressed the problem of how genes specify the development and function of the nervous system. In practical terms, an experimental system was required which permitted the study of individual genes one at a time, along with the precise effects each gene has on neural structure and function. The decision to study *C. elegans* culminated an extensive, systematic search for an organism which was amenable to genetic study and which had a nervous system that could be completely described at the electron-microscopic level. The use of ultrastructure to identify literally every cell and every synapse was considered by Brenner to be an essential component of an approach to the question of how the nervous system works. This in itself was a monumental task, even with a 300-cell nervous system. A major effort in the early phase of the work involved developing the capability for computer-assisted reconstruction of neural morphology. After a decade of work, primarily by Dr. John White and others at Cambridge, the ultrastructural description of the *C. elegans* nervous system is largely complete. As Brenner's original plan developed, the genetic and ultrastructural data from *C. elegans* were to be correlated with electrophysiological studies on *Ascaris*. The *Ascaris* work has been carried on by Dr. Anthony Stretton at the University of Wisconsin.

Brenner's own labors in the laboratory centered on developing the fundamental basis for *C. elegans* genetics. This involved the generation of many mutant strains, developing numerous methods for their genetic analysis, and generating a genetic map. When Brenner published his 1974 paper on *C. elegans* genetics, more than 100 genetic loci already had been defined. Since then, other geneticists also have refined and added to the map, which now includes more than 350 genes and numerous chromosome rearrangements. In my judgment, it is one of the most sophisticated genetic maps available for any organism, based on classical methods of recombination analysis.

Meanwhile, back in Cambridge, a new project arose from the basic genetics. A series of paralyzed mutants were found which were affected in the structure and function of body wall muscle. These mutants were viable for two primary reasons. First, pharyngeal musculature was unaffected in these mutants, so feeding was not seriously hampered and growth was possible. Second, reproduction by self-fertilization made active copulation unnecessary. The ability to grow large populations of genetically homozygous mutants made biochemical analysis of muscle proteins possible, and nematode molecular genetics was born. Muscle genetics continues to be an active area of research in Cambridge as well as in this country.

It was primarily the development of *C. elegans* genetics that stimulated a broadening of the early focus on neurobiology to include not only the muscle problem but many other aspects of *C. elegans* development. In 1974, David Hirsh of the University of Colorado was the first American investigator to establish an independent laboratory aimed at the analysis of *C. elegans* development, emphasizing embryogenesis and gonadal development rather than neurobiology. A different sort of milestone was reached by John Sulston at Cambridge when he determined the cell lineages leading to maturation of the ventral nerve cord. This was done by observing the course of cell divisions and migrations in living animals with the aid of Nomarski optics. Eventually, the description of all post-embryonic cell lineages was completed. The lineage history of *C. elegans* from single cell to adult is now known. Studies of mutants with altered lineages, and the use of laser microsurgery, reveal how specific cell fates depend upon lineage history and upon cell-cell interactions.

The lineage studies represent a global approach to the analysis of *C. elegans* development. Many investigators, however, have chosen to focus on particular metabolic functions or on particular tissues and organs, such as muscle, cuticle, sperm, or somatic gonad, as models for gene regulation or cell differentiation. Others have focused on specific developmental branch points, such as sex differentiation or dauer larva formation, or well-defined portions of the

developmental cycle such as early embryogenesis. The papers presented here provide examples of these various approaches.