

## **GENOME SCIENCE OF INVERTEBRATES: THE NEMATODE *C.ELEGANS***

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### **Summary**

The nematode *C.elegans* was first chosen in the early 60s as a model for the study of development and the nervous system through genetics. Although very small it has the basic body plan of all animals. Several unique features make it suitable for genetic analysis. By the mid 80s, two fundamental works had been achieved; a description of the entire cell lineage from egg to adult, and the drawing of a wiring diagram of the nervous system. By the end of 1998, the entire genome sequence was determined, and *C.elegans* is now the front runner in the post genomics era, being supported by well-organized genetic and genomic resources.

### **1. What is a nematode?**

There are many species of roundworms, or nematodes (Malakhov, 1994). One major group is parasitic nematodes. They have been studied extensively as medical targets, with observations of structure and development first made in the late 19th century. The work on chromosome diminution in somatic cells is a classic. However, since experiments using transplantation and regeneration was impossible with nematodes and genetics was difficult with the parasitic varieties, amphibians and flies superseded the nematode in developmental biology and genetics, respectively.

There are numerous non-parasitic nematodes including various soil and marine nematodes. The population of nematodes is the largest in the animal kingdom and accounts for about 15% of the biomass of the earth, suggesting a great contribution to the ecological homeostasis of the planet. The number of species of nematodes is thought to be between 100,000 and 1,000,000, out of which only 20,000 have been described; 2,000 plant parasites, 5,000 animal parasites and 13,000 free-living. Despite such a large

number of species, body plan and developmental processes, particularly during embryogenesis, are similar.

## 2. What is *C.elegans* ?

*C.elegans* is a superstar of experimental biology. *Caenorhabditis elegans* is a non-parasitic nematode about 1 mm long, which lives in soil and feeds on bacteria (Wood, 1988; Riddle et al., 1997). *C.elegans* was originally found in Algeria in 1900. The same species was again found at Bristol, UK in 1946 and named Bristol sp. N2. This is the standard strain, abbreviated as N2, of today's *C.elegans*. *C.elegans* can be cultivated at between 10 and 25°C.

*C.elegans* is a tiny creature, but it has the basic body plan of an animal, namely, muscle, digestive organs, a nervous system, an epidermis and so on (Figure.1). Its body is transparent, therefore, one can observe every process of development in live animals. The somatic cells number is only 959, of which 302 are nerve cells (Sulston et al., 1983). Even with such a small number of cells, its nervous system is capable of complex behavior including forward and backward movements, chemotaxis, egg-laying, defecation, sexual intercourse, mechanosensation and so on.

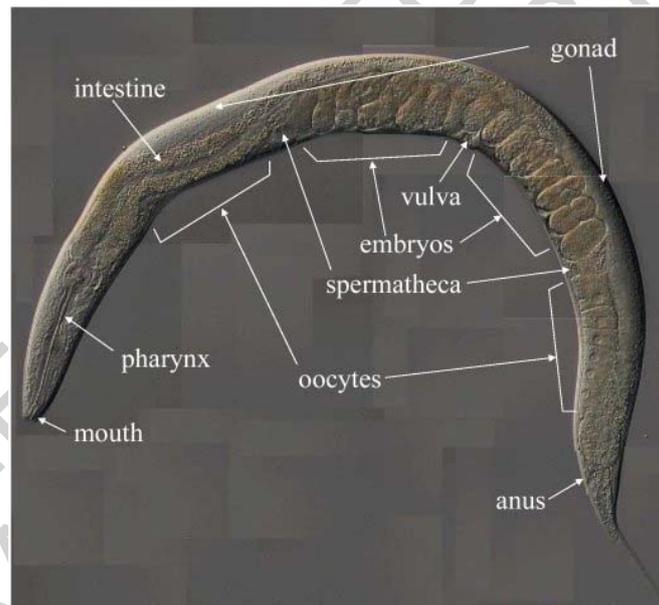


Figure. 1 Adult hermaphrodite of *C.elegans*.

Most *C.elegans* worms are hermaphrodites; as a gonad proliferates, sperms are made first, and then oocytes are produced. Fertilization occurs when a mature oocyte passes through spermatheca (sperm holding apparatus). Fertilized eggs are covered by a tough shell and develop in the uterus until mid embryogenesis. They are laid through the vulva and continue development outside of the parent body. Hatching occurs about 14 hr after fertilization. Larvae molt 4 times and become adult worms 3.5 days after fertilization. Oocytes continue to be produced as long as the hermaphrodite is well fed, but once the sperm runs out, no more offspring is produced. However, the percentage of males is about 0.1%. Males mate with hermaphrodites and inject their sperms through the vulva.

The injected sperm move to spermatheca and fertilize the egg. Surprisingly, even when hermaphrodite's sperm is still in the spermatheca, the male sperm supersedes the hermaphrodite sperm in fertilization.

It was Sydney Brenner, a British molecular biologist, who introduced *C.elegans* to the field of molecular genetics of multicellular organisms, in the early 1960s. His strategy was, first to describe everything about this organism including its pattern of development from egg to adult, the wiring of the nervous system and, perhaps genetic information of the whole genome, and then to analyze the molecular mechanisms that make up worms through a genetic approach.

A description of cell lineage from egg to adult (Sulston et al., 1983) and a wiring diagram of the nervous system (White et al., 1986) had been achieved by the mid 1980s, and the entire genome sequence was published at the end of 1998 (The *C.elegans* Sequencing Consortium, 1998). By combining all information and resources, scientists are now approaching an understanding of the entire genetic mechanism that makes up this tiny organism. Thus, *C.elegans* has become the front runner among model organisms in the post-genomic era.

### 3. Genetic resources of *C.elegans*: CGC

Among the superstars of model organisms, *C.elegans* has several unique features. First, *C.elegans* can be stored frozen by a simple procedure whereby L1 or L2 larvae are cooled gradually in the presence of glycerol (Brenner, 1974). This causes minimal genetic change during storage because no reproduction is necessary. Thanks to this feature, although a tremendous number of mutants have been isolated, all can be traced back to the original N2 worms that Sydney Brenner used and stored. This means that one can use many strains whose genetic background is clearly known. This is a great advantage to genetic analysis.

Second, the *C.elegans* research community has been eager to share resources and information. For this, CGC (Caenorhabditis Genetic Center) was established. The mission of the CGC is to store and distribute strains, to collect data on genetic crosses to update the genetic map, and to publish WBG (Worm Breeders' Gazette). The community has a rule that, when a researcher isolates a mutant, he/she has to deposit it (at least one allele) at the CGC. Currently over 4000 strains are stored at the CGC. Any of the strains can be obtained by mail upon written request.

The conditions for usage of the strains are only (1) to send back the results obtained using the strains to the CGC, and (2) to indicate the source in the paper when it is published. Over 8000 strains were distributed in the year 2000. These tasks are currently performed by one curator and one part-time worker under the direction of Bob Herman at the University of Minnesota, USA with the support of the NIH/NCRR (National Center for Research Resources).

A sub center is also operated by Jonathan Hodgkin at Oxford University, UK. Current strain lists and relevant information are available at the CGC homepage, <<http://biosci.cbs.umn.edu/CGC>>.

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### **Biographical Sketch**

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