Available online at www.ijpab.com

ISSN: 2320 – 7051
Int. J. Pure App. Biosci. **2 (5):** 19-27 (2014)

Research Article

INTERNATIONAL JOURNAL OF PURE & APPLIED BIOSCIENCE

Arising Model Organism Nervous System in *C. elegans* Biology: A Survey

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ABSTRACT

Although it's apparent simplicity, the nematode worm C.elegans has been a priceless tool for biological research, principally in the functional characterization of unique targets that have been identified the using genomics technologies. C. elegans and advanced organisms, along with the simplicity and cost-effectiveness of the agriculture, make for an effective in vivo model which is amenable to whole-organism high productivity compound screens and extensive target validation. This review shows how can be used C. elegans models to advance understanding of the molecular mechanisms of development and nervous system function.

Key words:*C. elegans,life cycle,Genome, nervous system.*

INTRODUCTION

Caenorhabditis elegans is a free-living (non- parasitic), transparent nematode (roundworm), unregimented, cylindrical body that tapers at both ends, 1 mm in length, that lives in temperate soil environments. The name is a mixture of Greek (caeno- - recent, rhabditis - rod-like) and Latin (elegans - elegant).First described by Emil Maupas in 1900[1].While C. elegans has been known and studied in laboratories nematologists for several years, it was not even Sydney Brenner in Cambridge, United Kingdom, chose this type of a new program in genetic research it has become a global phenomenon[2,3]. Wanted species that was easy to keep it .That was tractable genetics (so you can isolate mutants and crosses made), and that it was easy to observe. Brenner has attracted a team of geneticists remarkable to join him, and beat C. Elegans researchers three Nobel Prizes for discoveries made through the new object model. Caenorhabditis elegans (*Caenorhabditis elegans*, hereinafter referred to as *C. elegans*) was first developed in 1963 by Sydney Brenner as a model organism for developmental biology and neurobiology research[4].

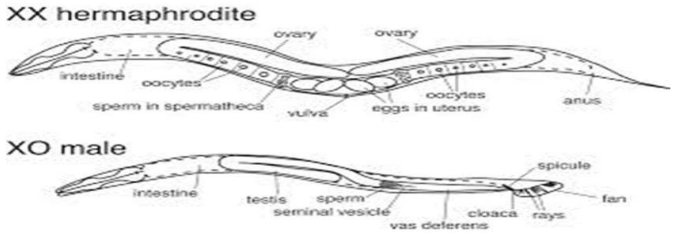
From the nematodes in the promotion of biotechnology in terms of: *C. elegans* cell lines identified widely used genetic techniques allow researchers to its produce great interest[5]. Researchers have used *C. elegans* as a research object in our knowledge of biological processes has made many important advances, such as development, apoptosis, and neurobiology gene regulation and aging and other fields[6]. But also as a very simple organisms, nematodes for the application of new technologies provides an ideal platform as the first to be sequenced[7] multi-cellular organisms, the researchers first will be applied to chip technology[8,9] and for the medical field of biomedical research provides broad prospects. For example, although the size of the genome of *C.elegans* genome of a human one-thirtieth, but it contains the majority of human gene homologues.

1-The reason for the study of nematodes *C. elegans*

From the structural characteristics of the nematode it is: Nematode sare small (length of about 1 mm), body transparent conducive experimental operation and observation, bacteria such as E. coli class for food, culture and inexpensive laboratory scale can be achieved culture. Nematodeshavefive pairs ofautosomes anda **single pair** ofsexchromosomes,two kindsofhermaphroditesandmales (as shown in figure 1).

Nematode sand fruit fliesto determine the gender of the same proportion of sex chromosomes and autosomes determine nematode sex. Hermaphrodite nematode scanre produce It self or with the male mating. In the laboratory, by the male or hermaphrodite self-hybridization with a specificmannerto produce progeny phenotype, there by to facilitate genetic analysis. Further more, by selfing *C. elegans* hermaphrodite can produce about 300 to 350 progeny, mating with the male progeny will produce more of these characteristics is very conducive to the needs of a large number of genetic studies in phenotype and genotype. Nematode reproduction cycle of fast and short, generally only three days, the same as the time .

Fig.1: The two sexes of C. *elegans*



Wormbook.org

Required for yeast genetic hybridization; under suitable conditions for survival, nematode life cycle of about 2 to 3 weeks.Compared with other model organism *C. elegans*, the biggest advantage is its wild-type individual contains 959 cells, the location and number of cells is one to one. By the Waterston, *et al*.[10] in the 1980s completed the full study investigated cell germ line genes influence cell fate mechanism provides a great convenience. We have nematodes by observing the in vivo cell division and cell migration in the process to determine the wild-type cell line[11]. From the point of view of optical imaging, nematodes are very suitable for analysis by an optical microscope. Embryos (about 55 μm) or adult (1 mm) in size just within the range observed in the microscope, whereby we can observe the maximum numerical aperture of the embryo or larvae to adults and even a specific part of the body. Therefore, we can observe in the context of the whole animal study subcellular localization and other related information.

Nematodes study of the nervous system is concerned, each nematode cells (adult hermaphrodites were 959, adult male with 1031) has been drawn the developmental outcome of the pattern[12], these cell strains of the type of the individual no great difference between. Nematodes also has the most simple biological nervous system, in hermaphrodites, there are 302 neurons constitute the connection has been completely drawn into a clear pattern, by researchers called the image of "small-world" networks[13]. Researchers have found many such as chemo taxis, vigorous resistance, hydraulic conductivity, and male mating behavior of neural mechanisms such as nematodes.

2-Life cycles of *C. elegans*

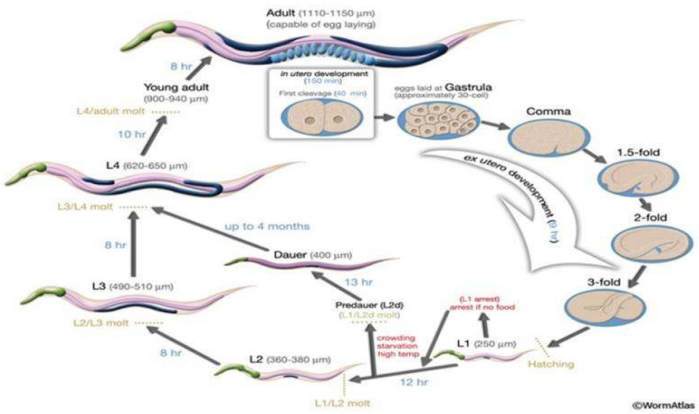
Have a short life cycle and production large numbers of progeny by sexual reproduction which occurs by self-fertilization in the hermaphrodite worms or mating with males? Self-fertilization allows worms homozygous for breeding and isolation of large real easy and maintenance of mutant strains. It is also a handy feature if paralyzed mutant animals because reproduction does not require movement in order to find and mate with males is necessary to move mutations between strains.

Hermaphrodite self-fertilized adult is capable of producing 300 progeny while male -fertilized hermaphrodites can produce more than 1,000 progeny .Each embryo to develop and hatch, and proceed through four larval stages (L1-L4) before becoming an adult[14].

Under laboratory conditions the optimal average life span of C. Elegans 2-3 weeks. Rapid life cycle. At 25°C embryogenesis (from fertilization until hatching) occurs in 14 hours. Evolution happens postembryonic in four larval stages (L1-L4) which lasts a total of about 35 hours.

Under the deprivation of food, which is called alternative development path Dauer larva can be launched. Dauer larvae can survive for several months at this stage and be structural, metabolic and behavioral adaptations that increase the life span of up to 10 times and assist in dispersing animals to new habitats. When food becomes available, Dauer larvae feed and continue development to the adult stage. (Figure 2) shows from zero min are fertilization; the blue numbers along the arrows refer to the length of time the animal spends at a some stage. First cleavage Occurs at about 40 min. post-fertilization. Eggs are laid outside in about 150 min. post-fertilization and during gastrula stage. The length of the animal at both stage are marked next to the stage name in micrometers (μm).

Fig.2: Life cycle of *C.elegans*



www.wormatlas.org

4-Laboratory Culture of *C. elegans*

Culture of *C. elegans* in the laboratory is simple and easily and relatively inexpensive[15]. Because it is typically grown in Petri dishes on agar seeded with a lawn of Escherichia coli as a food source also it can be grown in mass quantities using culture strategies and fermenteror-like these devices. Worm stocks are stored frozen in liquid nitrogen indefinitely with good viability. The ability to store *C. elegans* frozen dramatically simplifies culture strategies and reduces costs associated with handling and maintaining wild-type and mutant strains of the worm[16].

5-The online information resources for C. elegans

Widely use internet and World Wide Web (WWW) in the scientific community the corresponding rapid development of hypertext browser programs have made a bewildering array of online resources available for biological researcher[17].

In 1978 was created The Caenorhabditis Genetics Center (CGC) to support this rapidly evolving model system, and remains the only comprehensive resource that collects, maintains and distributes *C. elegans* breeds. Frozen stocks allow permanent storage of and consequent unlimited access to ancestral material, which makes *C. elegans* an attractive model for evolutionary biology. CGC works in closely collaboration with Worm Base, which imports all information on available strains and users can to locate these data through a specialized, and the search interface.

Other crucial task of CGC is the coordination of *C. elegans* labels. Historically, worm researchers have acceded to strict agreements that have ensured the uniformity of gene names, are derived from either the mutant phenotype or the molecular nature of the gene product.

This has virtually removed the confusions and clashes which are so common in other model organisms, and are proves that to be even more valuable today as automated phenotypic data extraction and literature analyses become the most common, the sites (as shown in table1 Box 1 and 2) listed constitute a basic set of the major electronic *C. elegans* resources on the Web .Each site, customized by its keepers, may contain links to many other more specific resources such as specialized programs written by *C.elegans* researcher, data search engines, electronic versions of standard print materials (e.g., the worm Breeders Gazette). Photographic images of worms, the information that is now verbatim at ones accessible requires only standard computer hardware, a graphical link to the internet, and a little of time[18].

Table 1: the online information resources for C. elegans fromAntoshechkin, & Sternberg, 2007[18]

Box 1 | ***Caenorhabditis elegans*** **online information resources**

C. elegans II	http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View..ShowSection&rid=ce2
WormBook	http://www.wormbook.org
WormClassroom	http://www.wormclassroom.org
WormAtlas	http://www.wormatlas.org
WormImage	http://www.wormimage.org
WormBase	http://www.wormbase.org
WormGenes	http://www.ncbi.nlm.nih.gov/IEB/Research/Acembly/index.html?worm
RNAiDB	http://www.rnai.org
PhenoBank	http://www.worm.mpi-cbg.de/phenobank2/cgi-bin/MenuPage.py
C. elegans RNAi Phenome Database	http://omicspace.riken.jp/Ce/rnai/jsp/index.jsp
InteractomeDB	http://vidal.dfci.harvard.edu/interactomedb
n-Browse	http://nematoda.bio.nyu.edu:8080/NBrowse/N-Browse.jsp
WormBase interaction browser	http://www.wormbase.org/db/seq/interaction_viewer
IntAct	http://www.ebi.ac.uk/intact/index.jsp
BioGrid	http://www.thebiogrid.org
EDGEdb	http://edgedb.umassmed.edu
NEXTDB	http://nematode.lab.nig.ac.jp/index.html
Hope Laboratory Expression Pattern Database	http://bgypc059.leeds.ac.uk/~web/databaseintro.htm
BC *C. elegans* Gene Expression Consortium	http://elegans.bcgsc.ca/perl/eprofile/index
Stanford Microarray Database	http://smd.stanford.edu/index.shtml
NCBI Gene Expression Omnibus	http://www.ncbi.nlm.nih.gov/projects/geo
EBI ArrayExpress	http://www.ebi.ac.uk/arrayexpress
C. elegans SAGE libraries	http://tock.bcgsc.bc.ca/cgi-bin/sage170
Structural Genomics of *C. elegans*	http://sgce.cbse.uab.edu/index.php
Protein Data Bank	http://www.pdb.org
NCBI PubMed	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed

Box 2 | ***Caenorhabditis elegans*** **online experimental resources**

Caenorhabditis Genetics Center (CGC)	http://biosci.umn.edu/CGC
CGC Strain Request	http://biosci.umn.edu/CGC/Strains/request.htm
CGC Nomenclature Guide	http://biosci.umn.edu/CGC/Nomenclature/nomenguid.htm
C. elegans Fosmids at Geneservice Ltd	http://www.geneservice.co.uk/products/clones/Celegans_Fos.jsp
BC GSC Fosmid Search	http://elegans.bcgsc.ca/perl/fosmid/CloneSearch
C. elegans Cosmids	http://www.its.caltech.edu/~wormbase/userguide/OtherResource/ObtainingReagents.html#elegans_genomic
C. elegans ESTs (NEXTDB)	http://nematode.lab.nig.ac.jp/index.html
C. elegans Gene Knockout Consortium	http://www.celeganskoconsortium.omrf.org
National BioResource Project of Japan	http://shigen.lab.nig.ac.jp/c.elegans/index.jsp
NemaGENETAG	http://elegans.imbb.forth.gr/nemagenetag
WorfDB	http://worfdb.dfci.harvard.edu
ORFeome at Geneservice	http://www.geneservice.co.uk/products/cdna/Celegans_ORF.jsp
ORFeome at OpenBiosystems	http://www.openbiosystems.com/GeneExpression/Non%2DMammalian/Worm/CelegansORFs/

6-Genome of *C. elegans*

C. elegans was the first multicellular organism to have a genome sequence perfectly. Sequence was published in 1998 although some small gaps existed, and was completed last gap by October 2002 .The C. elegans genome which is approximately 100 million base pairs long[19]. There are six chromosomes in C. Elegans five pairs of autosomes (chromosomes I, II, III, IV, and V) and sex chromosome X. Hermaphrodites have two chromosomes X (XX designated). Males have one X chromosome (designated XO); presence of only one chromosome instead of a pair called homozygous state. Can produce this case because of the loss of one X chromosome or by mating. Males cannot produce progeny of their own.

However, they can cross- fertilizing hermaphrodites. It is commonly used in C. Elegans genes for making combinations and a mitochondrial genome. Gene density is about 1 gene / 5kb, (5 kilo-base pairs). Introns, or non-expressed sequences, are 26% of the genome. Intragenic,some large regions contain repeated DNA sequences .Are arranged many of the genes in the operons, which are polycistronic series that are transcribed together. *C. elegans* and other nematodes are among a small number of eukaryotes currently known to be operons, and these include trypanosomes, flatworms notably the trematode *Schistosoma mansoni*, and tunicate a primitive chordate Oikopleura dioica. It is believed that will display many of the organisms have these operons[20].

The genome contains about 20,470 protein-coding genes. Number of known RNA genes in the genome has increased significantly due to the 2006 discovery of a new class of 21U-RNA genes[21] and is now believed that the genome contains more than 16,000 genes RNA, up from 1,300 a few, such as in 2005[22] .Scientific curators continue to evaluate a set of known genes: new gene predictions continue to be added, including incorrect modified or removed. In 2003, was determined the sequence of the genome of the nematode C.Related briggsae also, allowing researchers to study the comparative genomics of these organisms two[23]. The sequence of the genome of the nematode more of the same sex, for example. Remanei, *C. Japonica* and *C. brenneri* are under study[24] across the whole genome shotgun technique, which is less complete and accurate than the “hierarchical" or clone-by-clone approach that was used in *C. elegans*.physical map of the *C. elegans* genome, which consisting of overlapping cosmid and YAC clones covering most of the six chromosomes, has been constructed in order to facilitate cloning of genes that have been placed on the genetic map . In addition, ongoing efforts to obtain expressed sequence tags (ESTs) and open reading frame sequence by (OSTs) provided for all *C. elegans* genes a wide range of cDNAs nematodes. All ~ 20,000 had been predicted open reading frames (ORFS) in expression profiling under many conditions using sophisticated technology[25].

In addition, the analysis of genetics, such as "mapping genes,, epistasis , mutations and pleiotropy" and analysis of the genome, such as "chromosome organization, the repeated sequence and analysis of the promoter," intertwined.

In the genetic analysis, which is an attractive feature in the base of *C. Elegans* is the ease of generating mutations. Several chemical mutagens, particularly EMS (ethyl methane sulfonate) operate efficiently on a worm.

C. elegans is diploid, so very deleterious mutations can be induced and propagated without killing the animal. Because of the situation the main reproduction is hermaphrodite self-fertilization, so the effect of making any mutation homozygous can examined automatically, as a result of Mendelian segregation.

Moreover, the availability of multiple mutations is important in providing not only a knockout mutations that completely remove the activity of the gene, but also partial or conditional mutations that allow for dissection of complex gene function. The vast majority of these mutations are recessive, associated with partial or complete loss of gene function, but also has been the establishment of many of the rare gain function of mutations, which often provided the basic tools for further investigation[26].

7-Nematodes nervous system

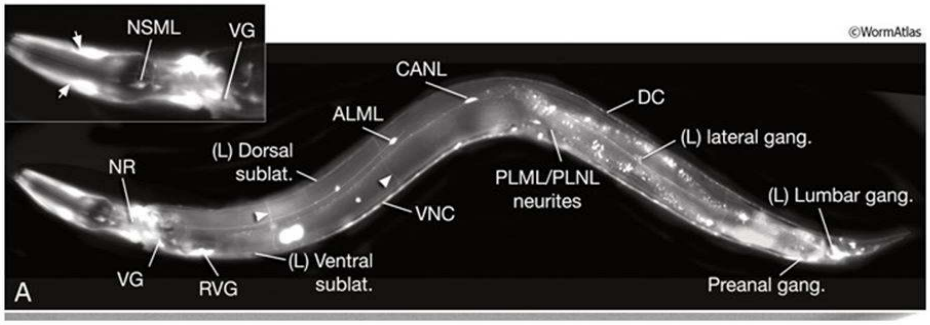
C. elegans nervous system is very simple, intersex adults’ only 302 neurons, adult males because mating needs, more than the number of neurons in the adult sexes, reaching 381. Including a nerve ring, an abdominal nerve cord, and a back and a head nerve cord complex nervous system[27]. Nerve ring nematode's brain can be considered, which is located in the head, including almost all of the neurons in the middle and most of the sensory neuron axons. Dorsal and ventral nerve cord from the nerve ring has been extended to the end, including a variety of motor neurons, abdominal nerve cord also contains information from many sensory neurons and intermediate neurons issued processes. In addition to the more important of these neurons, there are some small neurons located in other parts of the body. Males and females only 302 neurons, according to their morphological structure and characteristics are divided into 118 categories, these neurons through 5000 chemical synapses, 2000 neuromuscular junctions and 600 gap junctions interconnecting.

A typical neuron nematodes include a cell body, the cell body are called dendrites and two axons processes, branching dendrites generally do not responsible for smaller quantities from other neurons receiving synaptic input electron microscope postsynaptic structure is difficult to see, which increases the complexity of the synaptic connections. Axons are usually no bifurcation, responsible for synaptic output signals to a number of other neuronal and muscle. Typical of presynaptic structures can often be observed by an electron microscope, these features include the synaptic vesicle structure, dark matter in the presynaptic plasma membrane (darkening), and axon dark matter, and these materials must be provided for the storage vesicles space. Almost all of the synapses is in progress (en passant), and this indicates that the presynaptic axon becomes thicker and structures specialized storage spaces, and then narrowing distally extending[28,29]. Similarly, dendritic synapses along its structure to accept the input signal is not terminated or the formation of specialized branches and other structures. Based on these structural and functional information, about half of the neurons neurons in the middle one-third of sensory neurons, one quarter of motor neurons (in addition there are some neurons may have more than one function).

Hermaphrodite nematodes has 302 neurons that belonging to two separate neurons of the nervous system: A large body of the nervous system (somatic nervous system), including the 282 neurons; are located in various ganglia in the head and tail and also along the ventral cord, the main longitudinal axon tract, 20 of these neurons are located inside the pharynx. Both nervous systems only through a pair of interconnected neurons in the middle RIP. Nematodes two nervous system topologies are quite different. Body nervous system neurons and their processesare generally located between the epidermis and body wall muscles through the basement membrane and muscle apart[30]. Instead, throat neurons are located directly in the muscle of the pharynx; no base film of this structure exists. *C. elegans* nervous system classification is based on specific anatomical features, White *et al.*[31]. Based on electron microscopy observations of their topological structure and type of the synaptic connections of neurons into 118 categories, each category has a similar location, connection type axon synapses and dendrites[32]. Most of neuronal cell bodies concentrated in the head and tail ganglia[33].

C. elegans has 56, neuronal support cells (including the GLR cells, which supports only somatic nervous system connection. These neurons through about 6400 chemical synapses, 900 gap junctions (gap junction) and 1500 neuromuscular node (NMJs)[34,35]. 75% of individual nematode chemical synapses can be regenerated. Name of each nematode neuron is composed of two or three capital letters, uppercase letters indicate which category belongs to neurons, and some names contain numbers, in order todistinguishthe same categoriesofother neurons. If some neurons into radioactive symmetry (radially symmetrical), then these neurons will be named after the three capital letters plus L (on the left), R (on the right), D (back), V (ventral). Million to complete the list of nematode nerve, and their detailed description can be in the Individual Neuron Section Worm atlas[31,36]. (As shown in figure 3)

Fig.3: The *C. elegans* nervous system



C. elegans nervous system is almost dispensable for its fertility, only CAN and M4 two very important neurons. So, for the multiple mutations in *C. elegans* nervous system can be separated out as fertile mutations. Since nematode body transparent, easy to operate observed under an optical microscope, and its cell structure is almost no change, any one or a group of neurons also are available through the laser burning[37] *C. elegans* neurons are divided into four types according to the functions: 1- Motor nerves (motor neurons), has a synapse with muscle cells connected .2- Sensory nerve (sensory neurons), with a clear perception of specialized functions.

3- Intermediate neurons (interneurons), receive incoming synaptic signals, the output signal reaches the synapse to spread to other neurons. 4- Multi-mode neurons (polymodal neurons), can perform the above functions. NSML / R are a multi-mode neuron is one pair of pharyngeal neurons, with improved secretion end, is classified as secretory nerve (also has motor function). In addition to the above categories, there are some neurons so far its function is still unknown. Some of which may guide the process and maintain a more important aspects of its role in the neural circuits rather than inside[38,39]. for the nematode behavioral studies provide great convenience. In the larval stage of a few neurons can only lead to the loss of neurons in the nervous system function, without affect other functions of neurons can produce immeasurable damage, which allows us to examine a body or some neuron behavioral functions become possible. In addition, the application of technical records electrophysiological experiments nematode neurons and muscle activity of the technical problems have basically been solved, will greatly promote the *C. elegans* nervous system research fields and pace.

CONCLUSION

Small nematodes, *Caenorhabditis elegans*, and shares many of the structures and biological processes with more complex objects (such as humans). This, along with a short time to reproductive maturity (2-3 days), the period of life for two weeks, and detailed knowledge of our genetics have the function of each of the cells 959, Simple neuronal morphology makes it very easy to detect even minor developmental defects and make *C. elegans* organism's homepage scientists studying topics of the work of the nervous system. "This has helped" us to understand many aspects of human development, behavior, aging and diseases of the nervous system.

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