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SCAN ME

Research Paper

THE USE OF *Caenorhabditis elegans* AS A MAJOR MODEL ORGANISM IN BIOLOGY

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Abstract

The disease models played crucial in advancement of biomedical research. The *Caenorhabditis elegans* (*C. elegans*) used as unique models to study human disease, genetic analysis, and high-throughput drug screening. *C. elegans* is versatile model due to their easy to grow in laboratory with few weeks life cycle need fewer nutritional requirements and has completely sequenced genetic profile. In addition, animal models such as mice have extensively used as models in biomedical research, however use of animal models need extensive research budget, alternatively *C. elegans* provides a cost-effective alternative for initial research. In this review article, we highlight the use of nematode models as model in biomedical research.

Key words: *Caenorhabditis elegans*, Alzheimer's disease, Disease models, and biomedical research.

INTRODUCTION

Caenorhabditis elegans are unsegmented, harmless nematodes that can be found in soil. They have transparent, cylindrical bodies, and grow up to 1mm long (Edgley, 1999, as cited in Oswald, 2000). They have a lifespan of approximately 18-20 days (approx. 2 weeks). As of 2015, there are 27 species of *C. elegans* that are available in culture (Frézal *et al.*, 2015). These species thrive in microbe-rich environments such as rotting fruits, flowers, and stems (Schulenburg *et al.*, 2017). *C. elegans* feed on microorganisms, particularly bacteria that live in soil and rotting vegetables (Nicholas, *et al.*, 1975, Oswald, *et al.*, 2000). C.elegans, though they have simple anatomy, have some molecular structures similar to humans; hence it is chosen as a good organism for research (Nitin *et. al.*, 2019). *C. elegans* are specifically used in studies involving aging; the various phases the organism undergoes can be screened both physiologically and genetically (Mullan, *et. al.*, 2019). In addition, effects of novel drugs on complex processes involved in human diseases can be screened on *C. elegans* (Mullan, *et. al.*, 2019). C.Elegans may appear to be small, not useful creatures, but in contrast, they serve a great purpose in the research field.

The discovery of *C. elegans* occured during the 17th century with the invention of microscopy. Antoine van Leeuwenhoek, the inventor of the microscope, reported in

1676 about small eel-like creatures also known as "vinegar eels" (Nigon *et. al.*, 2017). During the beginning stages many authors at the time were focused on describing and classifying these animals. Many initial studies include the comparison between these species and other species (Nigon *et al.*, 2017). Gradually, *C. elegans* began to be used to study biological processes near the end of the 19th century. There were experiments that were also conducted using *C. elegans* that lasted for generations. An important figure during these times was Emile Maupas who was a French librarian, protozoologist, cytologist, and botanist. (DBpedia.org). He made several contributions to the study of *C. elegans* as he was the first to isolate and name them, now *C. elegans* , as Rhabditis elegans (Nigon *et al.*, 2017). In addition, he was the first to perform crosses to identify mechanisms of sex determination. Later in the 20th century, research teams began to use these *C. elegans* as model organisms. The heads of these teams were Victor M. Nigon and Ellsworth C. Dougherty. They were able to refine culture conditions and experimental methods. Studies on *C. elegans* developed through research conducted by Sydney Brenner and his team. He experimented with many nematode species until he decided on *C. elegans* to be a model organism around 1966 (Nigon *et al.*, 2017). Through the research and experiments conducted by various scientists *C. elegans* are now a major model organism in biology.

Research conducted with *C. elegans*

C. elegans use for Alzheimer's disease (AD)

Alzheimer's disease (AD) is a chronic, progressive neurodegenerative disease in old age (Roussos *et al.*, 2023). Alzheimer's disease symptoms include memory loss, personality changes, and cognitive dysfunction (Roussos *et al.*, 2023). The main cause for AD is yet to be known, however some causative factors include changes in neurotransmitters, oxidative stress, metabolic disturbances, inflammation, plaques β-amyloid peptides (Aβs) and Tau microtubule protein (Roussos *et al.*, 2023). *C. elegans* genome sequence in 1998 (*C. elegans* Sequencing Consortium, 1998) demonstrated that roughly 38% of worm genes have a human ortholog, such as *APP* and *tau* (Shave *et al.*, 2011). Hence, *C. elegans* have many excellent advantages as an *in vivo* model for the study of AD and other neurodegenerative diseases.

C. elegans use for Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder (Roussos *et al.*, 2023). ALS effects around 3.8 per 100,000 persons every year (Roussos *et al.*, 2023). ALS mainly effects the spinal cord, motor cortex, corticospinal tracts, and brainstem motor neurons which may lead to muscular paralysis (Roussos *et al.*, 2023). *C. elegans* have been used to investigate genes involved in both sporadic and familial forms of ALS (Roussos *et al.*, 2023).

C. elegans use for Aging Research

C. elegans have a very short lifespan, easy to culture, high genetic homology (60 - 80%) with humans and becoming very popular in aging research. Aging research include the study of biology of aging and Anti-Aging therapeutics. *C. elegans* can be used in initial screening of drug molecules (Zhang, *et al.*, 2020). The fullerenol a drug which effects on the growth, development, behavior, and anti-stress ability was tested using *C. elegans* .

The studies indicated fullerenol can delay the aging process of *C. elegans* (Cong *et al.*, 2014).

C. elegans use for Huntington's Disease

Huntington's disease (HD), associated with motor, cognitive, and psychiatric problems, is an autosomal dominant neurodegenerative disorder. Huntington's disease is caused due to mutation in in HTT protein that triggers neuronal death (Roussos *et al.*, 2023). Studies using *C. elegans* HD models have identified potential modulators of poly aggregation and toxicity (Roussos *et al.*, 2023).

C. elegans use for Parkinson's Disease

Parkinson's disease is a disorder that gradually affects the nervous system. The causes of Parkinson's disease are unknown and could be caused by various factors. Genetic components that may lead to Parkinson's disease includes PARK1/ a-synuclein (neuronal protein) which cause disruptions in cellular homeostasis and neuronal death (Stefanis, 2012). However, the extent to which a- synuclein is involved in all cases of Parkinson's disease to be studied (Stefanis, 2012). C *C. elegans* have be used as model to understand how a-synuclein mutations can result in Parkinson's disease.

C. elegans use for Cockayne syndrome (CK)

Cockayne syndrome (CS) is a recessive neurodegenerative disorder and is characterized by premature ageing, dwarfism, mental disability, microencephaly, and severe photosensitivity (Roussos, *et. al.*, 2023). CS is caused by mutations in the ERCC6 and ERCC8 genes which code for Cockayne Syndrome group B protein and Cockayne Syndrome group A protein, respectively (Roussos *et al.*, 2023). *C. elegans* have been used to study the effects of the lack of CSA and CSB proteins lead to disability in development growth and lifespan shortening (Roussos *et al.*, 2023). *C. elegans* studies reveled lack of these proteins lead to altered energy metabolism due to the accumulation of dysfunctional mitochondria (Roussos *et al.*, 2023). *C. elegans* have similar pathological manifestations as humans allowing them to use as model (Roussos *et. al.*, 2023).

C. elegans use for Autosomal Dominant Optic Atrophy (ADOA)

Autosomal Dominant Optic Atrophy (ADOA) is a hereditary neurodegenerative disorder resulting in the progressive loss of vision and caused by mutations in OPA1, an inner mitochondrial membrane protein (Roussos *et al.*, 2023). *C. elegans* have been used to understand the pathophysiological mechanisms of ADOA (Roussos *et al.*, 2023). Research on ADOA using *C. elegans* has revealed key information about decreasing of mitochondrial content, neuronal degeneration, and impaired defecation cycle (Roussos *et al.*, 2023). Furthermore, it has been discovered that modulation of AMPK activity could aid in the development of novel therapeutic for ADOA disease (Roussos *et al.*, 2023).

C. elegans use for Immunology

The Immune system is responsible for defending against harmful foreign bodies and invaders. Immune systems key parts are white blood cells, antibodies, complement system, lymphatic system, spleen, bone marrow, and thymus. The immune system is divided into two sections the innate and adaptive immunity. *C. elegans* have been used

as model to study how innate immune system responds to pathogens which helps to understand how immune response works similarly in the human body (Yokoyama, 2020).

C. elegans use for Mitochondrial Diseases

Mitochondria is a component of the cell, and it is responsible for converting glucose into ATP (energy) through cellular respiration. Mitochondrias have their own unique DNA referred to as mitochondrial DNA, and DNA mutations can cause mitochondrial diseases. There is no effective treatment or cure for Mitochondrial Disease and can only be managed. *C. elegans* has genetic homology with human mitochondria which allowed researchers to elucidate the underlying mechanism (Yokoyama, 2020).

CONCLUSION

The *C. elegans* model is a highly useful model for initial research, to reduce of discovery time comparatively with animal models. The large number of molecular techniques, assays available to contribute value to study complex biological mechanisms and human diseases using *C. elegans* as model. In addition, *C. elegans* is a useful initial model to recapitulate the human disease pathology before embarking into clinical studies.

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