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The Nematode Caenorhabditis elegans: A Convenient Model for Studying Immunology and Microbiology

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The Nematode *Caenorhabditis elegans*: a Convenient Model for Studying Immunology and Microbiology

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ABSTRACT

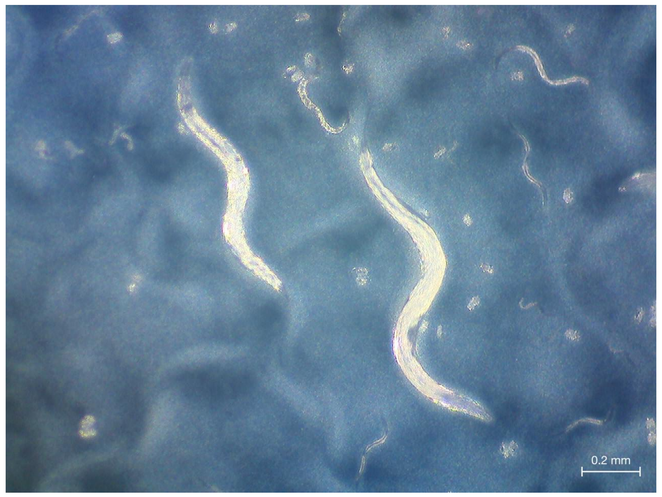
Caenorhabditis elegans is a nematode that survives naturally in a variety of environments throughout the world. This nematode has been used for decades as a model system for development, cancer and aging, since it shares with humans key genes and signaling pathways that are involved in disease. In addition, this nematode is easy to maintain in the laboratory and is genetically tractable. Major discoveries relevant for human cancer, innate immunity and longevity have been made with *C. elegans*, but this nematode has not been used yet for studying genes or microbiota relevant for oral health. Several laboratories in the world are starting to study the effect of the gut microbiota on the health of *C. elegans*. We propose to study the effect of the oral microbiota on *C. elegans*, by feeding the nematodes bacteria isolated from human saliva. From a dentistry perspective, being able to characterize the human oral microbiota with data analyzed from *C. elegans* can provide a convenient approach to screen rapidly effects of different oral bacteria and could provide a fresh outlook on several oral diseases.

Advantages of *C. elegans*

Symbiotic relationships are often found in the microbial environment both outside and within species. These interactions with the microbiome are important to understand because disruptions (dysbiosis) can lead to a wide range of consequences from development to metabolism. Mammalian microinteractions are commonly studied with murine models. Though commonplace, these models have drawbacks such as cost and complicated analysis with a variety of cofactors. *Caenorhabditis elegans* has many advantages over these commonly used murine models. *C. elegans* has had its entire genome sequenced, and because of the animal's simplicity it allows for easy genetic manipulation. The translucent appearance of *C. elegans* also provides for easy visualization of its anatomical structures and use of techniques such as fluorescent tagging. With all of these advantages working together, *C. elegans* serves as an organism that is both easy to work with and easy to maintain, allowing for research at a rapid rate and in situations with limited resources, and offering new perspectives on microorganisms relationships.

Microbiome of *C. elegans*

C. elegans in the wild displays constant interactions with its adjacent environment, which includes microbial species all the way to larger organisms such as mollusks. Typically *C. elegans* is found in temperate climates in rotting organic matter. This is in contrast to the laboratory setting where *C. elegans* is grown in homogenous agar plates. In addition to its outer microbiome, *C. elegans* shows great variation in its inner microbiome as *in vitro C. elegans* usually carries only one bacterial species which is very different from the many different bacterial species usually present in *C. elegans* in the wild. The two common relationships between *C. elegans* and its microbiome in the wild are mutualistic and antagonistic.



Contrast phase microscopy of *C. elegans* gliding on agar plates in our laboratory.

Methods of Study

In laboratory settings, researchers manipulate environmental conditions like temperature and food availability to create controlled environments for studying *C. elegans*. Culturing methods, such as axenic and monoxenic cultures, play a significant role in this research, enabling the study of specific microbial interactions with the nematode. For instance, axenic cultures, devoid of microbes, promote heat tolerance and lifespan extension in *C. elegans*. Meanwhile, monoxenic cultures, commonly utilizing *E. coli* as a food source, allow researchers to vary bacterial diets and observe resulting effects on gene expression and metabolic responses. Experimental approaches involve exposing *C. elegans* to different bacterial diets, including gut microbes from animal feces or the standard *E. coli* OP50 strain, to study growth and lifespan variations. Notably, *C. elegans* fed murine gut microbes exhibit reduced body size and fecundity but prolonged lifespan similar to dietary restriction effects in mammals. Additionally, *C. elegans* serves as a model for investigating human infections with pathogens and screening drug-microbe interactions. To expedite drug screening, automated platforms and high-throughput microfluidics are employed. These technologies enable researchers to test multiple drug concentrations while maintaining consistent nutrient levels, thereby facilitating the process of drug discovery and analysis in *C. elegans* models.

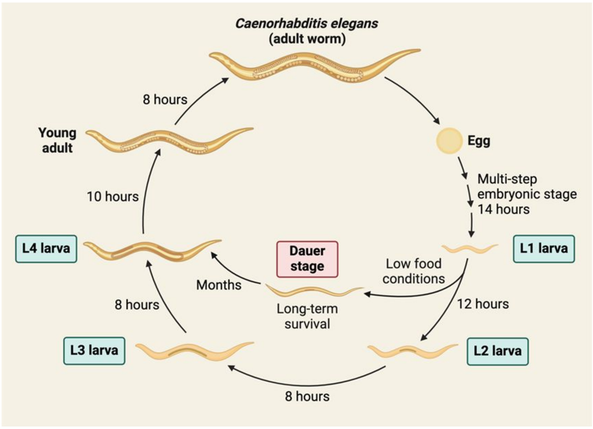


Figure 1. Life cycle of *C. elegans*. One full generation is completed every 3.5 days at 20°C. This chart shows both the main larval stages (L1 to L4), and the long-term survival stage (Dauer).

Future Directions

Researchers can uncover genes and processes influencing interactions with the microbiome by using *C. elegans*, which opens the door to a better comprehension of host-microbiome interactions using a simple, convenient model system. The functional characterization of microbiome components influencing host features, a mechanistic dissection of host-microbiome interactions, and investigation of the microbiome's role in host aging and stress responses are among the upcoming applications of *C. elegans* in microbiome investigations. Additionally, examining the effects of the human oral microbiota on *C. elegans* resistance to infection and longevity are examples of studies that will improve our knowledge of host-microbiome interactions and how they affect health and disease in nematodes, animals, and humans.

REFERENCE

Cheng-Yeu Wu, Scott Davis, Neekita Saudagar, Shrey Shah, William Zhao, Arnold Stern, Jan Martel, David Ojcius, Hung-Chi Yang. *Caenorhabditis elegans* as a convenient animal model for microbiome studies (2024) submitted.