Caenorhabditis elegans
Opens the Gates to the Nematode Pheromone World

by Fatma Kaplan

Nematodes are the most abundant animals on earth and parasitize nearly every plant, insect and animal. When they infect pests, they can be used as biological controls. However, when they infect plants and animals, they either threaten our food security by reducing plant yield or cause diseases in animals.

For example, nematodes cause many diseases in humans such as hookworm, pin worm and intestinal roundworm infection (acariasis). Approximately 1/6 of all humans are infected by nematodes worldwide. Even though nematode infections are effectively treated with drugs, nematodes are developing resistance to current nematicides, much like antibiotic-resistant bacteria. To treat nematode infections in the future, we need to develop novel drugs. Pheromones, small signaling compounds, are well known control agents for insect pests by interfering with mating or development.

In 2005, the nematode pheromone floodgates were opened with the discovery of dauer pheromone in *Caenorhabditis elegans*. Dauer pheromone regulates entry into a long-lived stress-resistant stage, dauer. Soon after, more dauer pheromones were discovered. Entry into dauer stage is controlled by individual pheromones, whereas social behavior is controlled by blends of the dauer pheromones. The first pheromone-regulated nematode behavior discovered was mating behavior. This was followed by many other behaviors including aggregation, attraction, dispersal and repulsion. Very recently, the same class of pheromones was found inside *C. elegans* and other nematodes. In insect parasitic and free living nematodes, pheromones regulate behavior and development of life stages analogous to dauer in *C. elegans*. Now the question: Can nematode pheromones be used to control plant and animal parasitic nematodes? Of course, the answer to this question will come with understanding the biology of nematode pheromones.

The application of concepts from *C. elegans* to plant and insect parasitic nematodes will drive major advances.

In the next five years, the pheromone field is heading toward three major basic research areas: 1) molecular biology of nematode pheromones; 2) application of concepts from *C. elegans* to parasitic nematodes; and 3) nematode chemical ecology. Molecular biology of pheromones is now a flourishing field including topics like function, regulation and signaling of pheromones. Nematode pheromones, called ascarosides, belong to a large class of compounds (> 150 identified). We currently know the function of a handful of ascarosides in C. elegans. There are many more with unknown functions. Questions that still need to be answered include: How many ascarosides are actually biologically active? Do the biologically active ascarosides function by themselves or in a mixture? Regulation is another important field of inquiry. How are the expression of biosynthetic genes regulated; transcriptionally and/or translationally? How is the pheromone activity regulated? Are the pheromones unstable or conjugated; sequestered in a subcellular compartment? What are the genes that pheromones regulate? Of course, signaling is a subject of current and future study. For example, the first step in signaling is the recognition of the signal, so researchers can begin to understand signaling by isolating the receptors in *C. elegans* and other nematodes.

The application of concepts from *C. elegans* to plant and insect parasitic nematodes will drive major advances. Many ascaroside pheromones were identified in *C. elegans*, making it easier to identify and study the function of ascaroside pheromones in other nematodes. Since plant and insect nematodes are parasitic nematodes, there is a potential to explore whether pheromones are involved in host parasite interaction. For example, nematodes use pheromones to determine their density like bacterial quorum sensing (QS). Furthermore, bacterial QS signals regulate bacterial virulence and reprogram animal and plant gene expression and immune systems. We do not know whether nematode pheromone/QS signals are involved in host parasite interaction or how they affect host gene expression and immune systems. Understanding how nematode quorum sensing signals affect host parasite interaction in plants and insects provides us a platform to apply concepts to nematodes that cause disease in humans and develop drugs that combat human parasitic nematodes.

"Do nematodes use pheromones to influence each other's population size?"

There will be major advances in the role of pheromones in nematode chemical ecology. Some potential questions are: Do nematodes use pheromones to influence each other's population size? If yes, how is this achieved? For example, do they jam competitor's signals by producing structural analogs or degrading each other's pheromones for development or social behavior? Are pheromones involved in interacting with other species? The nematode pheromone field will have major advances in understanding the biology of nematode pheromones, application of concepts to other nematodes and nematode chemical ecology.

Dr. Kaplan was the winner of an essay contest asking GSA members to write about the future of their field.

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