Researchers Discover Dual-Use Sexual Attraction and Population-Control Chemicals in Nematodes

August 1 2008

(PhysOrg.com) -- Organisms ranging from humans to plants to the lowliest bacterium use molecules to communicate. Some chemicals trigger the various stages of an organism's development, and still others are used to attract members of the opposite sex. Researchers at the California Institute of Technology have now found a rare kind of signaling molecule in the nematode worm Caenorhabditis elegans that serves a dual purpose, working as both a population-control mechanism and a sexual attractant.

The discovery, published online July 23 in the journal *Nature*, could lead to new ways to control parasitic nematodes, which affect the health of more than a billion people and each year cause billions of dollars in crop damage.

Caenorhabditis elegans worms have long been a favorite model organism among developmental biologists, in part because of their small size (1 mm long), simple nervous system, and ease of care. The normally soil-dwelling worms are almost always hermaphrodites--females that are capable of making sperm, with which they can fertilize their own eggs. About one in every 1000 worms is a true male.

Researchers studying C. elegans had long noted that hermaphroditic worms, left to wander about in a culture plate, will secrete a chemical that strongly attracts males. When males are exposed to the chemical,

dubbed "worm sweat" by C. elegans researchers, "males will act as if their desired mate is near, and start blindly feeling around to locate it," says molecular geneticist Paul W. Sternberg, the Thomas Hunt Morgan Professor of Biology at Caltech and an investigator with the Howard Hughes Medical Institute.

Jagan Srinivasan, a postdoctoral research scholar at Caltech, Sternberg, and his colleagues at the University of Florida, the United States Department of Agriculture, and Cornell University, assayed and analyzed worm sweat and found that it consisted of a blend of three related chemicals, called ascarosides. The chemicals looked suspiciously like another compound previously known to be involved in triggering an alternative developmental state in the nematodes, a spore-like condition called the "dauer stage"--from the German word for "enduring"--that represents a form of worm population control.

"When worm larvae are stressed out and hungry and crowded," Sternberg says, "they enter the dauer stage." In this alternate state, the worm larvae can withstand harsh environmental conditions. "The dauer stage is important because it is the infective stage in a lot of parasitic nematodes," he says.

The scientists found that purified samples of the chemicals, dubbed ascr#2, ascr#3, and ascr#4, induced sexual excitement among males, but only when the chemicals were combined, and only when presented to the worms in very dilute form. At higher concentrations, 100 to 1000 times stronger, males were repelled, sexual reproduction ceased, and existing worm larvae entered their hibernating stage.

"This is the first glimpse into the chemical code that nematodes are using to communicate," says Sternberg. Adds Srinivasan, "It is the first time that two distinct and different life history traits--reproduction and developmental arrest--have been found to be regulated by the same

family of molecules, suggesting a link, which we had not suspected, between the corresponding pathways."

The discovery offers hope for a solution to a global nematode scourge. Hundreds of thousands of nematode species occupy the earth, and many are pests or parasites whose activities cause disease or economic hardship, with damage amounting to billions of dollars per year. For example, hookworm, a parasitic nematode that lives in the small intestine of humans, is believed to infect one billion people worldwide and in developing countries is the leading cause of illnesses in babies, children, pregnant women, and malnourished individuals; the soybean cyst nematode, which attacks the roots of soybean plants, causes half a billion dollars worth of crop loss each year in the United States alone.

By decoding some of the signals that nematodes use to communicate, scientists may be able to offer new strategies to control the pests. One option could be to create chemical attractants derived from pheromones, similar to the pheromone-based substances that now are used to lure fruit flies and other bugs into traps. Alternatively, Sternberg says, compounds could be developed "that interfere with the chemical signaling involved in the reproductive process," thereby preventing the organism from multiplying.

The paper, "A blend of small molecules regulates both mating and development in Caenorhabditis elegans," was published July 23 in the early online edition of Nature and will appear in the August 28 print edition. The work was supported by the Human Frontiers Science Program, the National Institutes of Health, and the Howard Hughes Medical Institute.

Provided by Caltech