Using venomous proteins to make insect milkshakes

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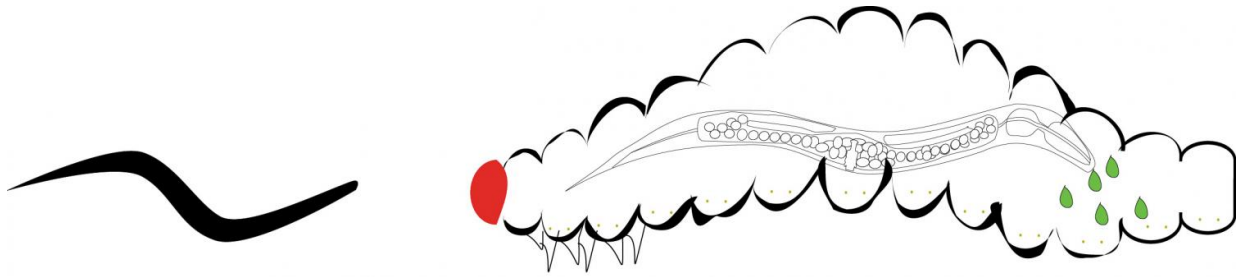

The squiggly black line represents the infective juvenile nematode, before it enters a host. Once inside the host, as depicted on the right, the nematode resumes development and releases venom proteins (represented by the green drops). Credit: Adler Dillman

Nematodes are microscopic worms that fall into an often ignored corner of the animal kingdom. While many of them are parasitic, meaning they live inside other organisms, they also help control diseases in humans and kill insects that damage agricultural crops.

It's those beneficial qualities of nematodes that draw the focus of Adler Dillman, an assistant professor at the University of California, Riverside.

In a just-published paper in the journal *PLOS Pathogens*, Dillman and several collaborators found that nematodes secrete a deadly cocktail of proteins to kill many insects that damage crops. The finding overturns a

long-held belief that it is exclusively bacteria, working in conjunction with nematodes, that kill the insects.

"It's all really science fiction-like," Dillman said. "These microscopic nematodes crawl into the host, poop out toxic bacteria and then spit out the venom and turn the host into an insect milkshake."

Nematodes have adapted to live in nearly every ecosystem, including oceans, lakes, soils, polar and tropic zones and at all elevations. They are round but don't have segments like earthworms. They are generally 0.1- to 2.5-millimeters long and are thought to represent 80 percent of animals on Earth.

The research by Dillman and his collaborators focused on *Steinernema carpocapsae*, a well-studied nematode that is known to kill more than 250 insect pests that attack plants such as peaches, tomatoes, corn, sweet potatoes, oranges, and pine trees. *S. carpocapsae* can be bought at online gardening stores and are marketed as an organic gardening solution. One web site sells 10 million of them for $37.98.

S. carpocapsae belongs to a group of insect-parasitic nematodes known as entomopathogenic nematodes. These differ from other insect parasites because they kill their hosts quickly, within a day or two, and associate with bacteria to facilitate their parasitic lifestyle.

These nematodes are born, stop development and only restart development once they infect a host insect. Little is known about the early stages of parasitism and how these parasites initiate the parasitic phase of their life cycle and reinitiate development. The research by Dillman and his collaborators helps to unravel that mystery.

The *PLOS Pathogens* paper outlines a new method the researchers developed to work with the nematodes when they are outside the insect

host they parasitize, a common challenge when researching parasites.

The researchers were able to collect the venomous proteins from the nematodes after exposure to insect tissue in flasks in the lab. They found the protein mixture was highly toxic to multiple species of insects including adult fruit flies (*Drosophila melanogaster*), which are commonly used in scientific experiments.

In addition, they used RNA sequencing technology to compare the expression of genes in nematodes from inside the insect host and those exposed to insect tissue in flasks. They found the gene expression profiles were similar, demonstrating the validity of the model they developed to work with nematodes outside an insect host.

Finally, they then identified 472 proteins presumably involved in parasitism. These proteins will serve as a foundation for future studies that have agricultural and medical applications.

On the agriculture side, researchers are hopeful that they will find new insecticidal compounds that can be used to control insect pests around the world.

On the human medicine side, nematodes have recently been shown to help control auto-immune diseases, such as Celiac disease, irritable bowel syndrome, and Crohn's disease. Future research by Dillman and his collaborators could lead to better methods involving nematode molecules to combat those diseases.

The findings are especially relevant for closely related human parasites such as threadworm (*Strongyloides stercoralis*), which infects an estimated 100 million people globally.

The *PLOS Pathogens* paper is called "Activated entomopathogenic

nematode infective juveniles release lethal venom proteins."

Provided by University of California - Riverside