Move over, mice: Caterpillars could replace some mammals in the study of human disease

January 12 2023

Tobacco hornworm caterpillars (Manduca sexta). Credit: Dr. Anton Windfelder, Fraunhofer Institute for Molecular Biology and Applied Ecology

Rats and mice have been the backbone of biomedical research for decades—including research to understand cancer and pioneer new

treatments.

New drug compounds are tested for safety and effectiveness in animal models before being approved for clinical trials in humans.

But scientists at research institutions like Memorial Sloan Kettering Cancer Center's Sloan Kettering Institute are working to develop nonmammalian alternatives that could reduce the number of rodents used in biomedical research—a positive result in its own right, and one that could also lower costs and accelerate results.

Radiologist and nuclear medicine physician Jan Grimm, MD, Ph.D., recently co-authored a *Nature Communications* paper with collaborators from several universities in Germany and Switzerland that demonstrated caterpillars could be used as an alternative to rodent models to study gut inflammation—a risk factor for developing colorectal cancer.

Here, Dr. Grimm discusses the research and its significance.

Why caterpillars?

Our research used the larvae of the tobacco hornworm (Manduca sexta) because they have a high degree of similarity to the human gut structure and physiology—what scientists call a high degree of evolutionary conservation.

Tobacco hornworm caterpillars are large enough to be imaged with the same instruments used for human patients.

Caterpillars are basically just one long bowel, so they made a great model for studying inflammatory bowel disease.

Tobacco hornworm caterpillars (Manduca sexta) in an MRI scanner. Credit: Anton Windfelder, Fraunhofer Institute for Molecular Biology and Applied Ecology

And since some 75% of the known human disease-causing genes have counterparts in insects, these models could be helpful in future

preclinical research in other diseases including cancer, diabetes, neurodegeneration, and infection.

Unlike nematodes, which are roundworms used in research that are about the length of a staple, tobacco hornworms—which are actually caterpillars—are about the size of an adult's finger. So they're large enough to use with medical imaging scans, like computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scans. You can easily see the inflammation in the bowel.

What other advantages do caterpillars have over traditional mammalian models?

Everyone wants to reduce the number of animals—especially mammals—used in research, replace them with alternatives, and refine their use to limit the amount of distress they experience. Scientists call this the Three Rs.

As such, there are a lot of standards and policies that have been developed around the use of animals in research and their care. Starting a new experiment in a mouse model, just even trying another drug combination, can take several months to add it to a protocol and get it approved.

Since caterpillars are invertebrates, one faces less administrative burden. One can just design the experiment and then do it, significantly speeding up the research. The caterpillars are happy in a plexiglass container with some fresh leaves and wet paper towels. This allows us to test out new hypotheses quite rapidly.

Plus, mammals are very slow-growing and expensive to house compared

with invertebrates. So these experiments can be done at a lot less cost.

How did this collaboration start?

I saw the paper's lead author, biologist Anton Windfelder, Ph.D., from the Fraunhofer Institute for Molecular Biology and Applied Ecology in Giessen, Germany, give a talk on the topic at a Radiological Society of North America meeting. I asked him a couple of questions after his presentation, and then met with him afterward. I thought it was a really exciting idea and opportunity to collaborate.

Then, just before COVID-19 hit, Dr. Windfelder came to New York for a visit and we started working together. He taught us how to handle the caterpillars, how to feed them, how to induce inflammation with a bacterial mixture. We provided use of our imaging resources and analysis. And the rest is history and now a nice publication.

More information: Anton G. Windfelder et al, High-throughput screening of caterpillars as a platform to study host–microbe interactions and enteric immunity, *Nature Communications* (2022). DOI: 10.1038/s41467-022-34865-7

Provided by Memorial Sloan Kettering Cancer Center