Can frisky flies save human lives?

Research into bacteria that makes fruit flies reproduce more has implications for disease, pest management

By Mikala Kass, ASU News
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When fruit flies are infected with Wolbachia bacteria, their sex lives — and ability to reproduce — change dramatically.

Arizona State University scientist Timothy Karr decided to find out why. What he discovered could help curb mosquito-borne diseases and manage crop pests. And that's just "the tip of the iceberg," he says.

Promiscuous flies

Wolbachia is a parasitic bacteria that lives inside insect cells. It infects at least two out of every five insect species. Since insects outnumber all other life on Earth, understanding how this bacteria affects them could have wide-ranging impacts.

“Insects rule this planet. Malaria, dengue, Zika viruses — they are all delivered by insects and kill millions of children and adults every year. The control of these insect pests is all dependent on our ability to understand their physiology and biochemistry and how that might be helpful,” says Karr, manager of ASU's Mass Spectrometry Facility and a research associate professor in the ASU-Banner Neurodegenerative Disease Research Center in the Biodesign Institute.

Like any good parasite, Wolbachia's goal is to spread to more hosts. But it can only pass from an infected mother to her offspring. To improve its chances, it influences its hosts so that infected females lay lots of infected eggs.

In fruit flies, Wolbachia makes infected males unable to fertilize uninfected females' eggs. An uninfected female is, after all, a dead end for Wolbachia. The same effect occurs in some other species, making the bacteria a potential tool for insect control.

In female fruit flies, Wolbachia has a different effect — it makes them friskier. Infected females are more likely to mate more often and lay more eggs, so much so that they will even accept other species to lay hybrid eggs.

While Wolbachia's effects on males are well studied, less was known about how it influences females. Karr and his colleagues from UC Santa Cruz — Brandt Warecki and William Sullivan — set out to study what is happening inside their cells to make them so promiscuous. A new paper with their findings published today in Cell Reports.

Protein shake-up

Female fruit flies rely on key brain functions like sensing and decision-making to pick their mates. When Karr and his colleagues studied infected female brains, they found Wolbachia in the regions responsible for those functions. It was perfectly positioned to influence mating behavior.

The team compared proteins in infected and uninfected female brains. This is the first time they used this technique to study Wolbachia's effect on female fruit flies.

"It took a protein approach to find things that genomic work alone couldn't find," Karr says.

Protein levels in infected brains were clearly different. Over 170 proteins changed, with some increasing and some decreasing in amount compared with amounts in the uninfected brains.

When researchers genetically changed the levels of three of those proteins in uninfected flies, those flies began acting like the infected ones.

The team also identified over 700 Wolbachia proteins in female brains. Using an AI program called AlphaFold, Karr and colleagues studied the most abundant of those proteins in the brain.

Two of them interacted with the host fly's proteins — the same ones tied to mating behavior.

"There are other hidden gems in that paper that could be more important than these proteins," Karr says. "Wolbachia produce other proteins that may have nothing to do with these behavioral proteins we identified directly, but everything to do with producing what we call essential amino acids."

Fruit flies (and humans) can't make the essential amino acids their bodies need. Instead, they get them from food or bacteria. Wolbachia appears to make these nutrients for its hosts, perhaps giving infected flies an advantage.

It's a pattern seen throughout evolution. Mitochondria, the famous "powerhouse of the cell," began as simple bacteria that infected cells. Over time, they made themselves so useful that cells depended on them. Karr believes a similar process might be happening in Wolbachia and is eager to study it more.

Learning who the players are

Other research has shown that Wolbachia can block viruses like Zika and dengue from growing in mosquitoes. Efforts to control these diseases and reduce mosquito populations have had mixed success.

“In my opinion, the most prominent reason is that we don't understand the molecular basis for any of these potential solutions. We're just beginning to make headway,” Karr says. “To cure any disease, to perfect any technique in biology, you need to know who the players are, and you need to know how they work.”

Understanding how Wolbachia proteins interact with host proteins could improve strategies to manage disease-carrying insects and protect crops with safer pesticides. Insights from this study might also help protect species like bees that face threats from viruses.

The team’s success with protein analysis may also inspire new studies using this method.

“Proteins are where the rubber meets the road,” Karr says.

And it’s a road that could lead to more lifesaving solutions.

About this story

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The ASU research in this article was possible only because of the longstanding agreement between the U.S. government and America’s research universities. That compact provides that universities would not only undertake the research but would also build the necessary infrastructure in exchange for grants from the government.

That agreement and all the economic and societal benefits that come from such research have recently been put at risk.

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Main image

A parasite that invades the brain cells of fruit flies enhances their ability to reproduce. Understanding how it works could help control mosquito-borne diseases. Illustration by Jason Drees