Do ants hold key to drug resistance?

They carry bacteria to fight fungus — and it's worked for millions of years

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Some ants, it seems, are packing more than your picnic lunch.

According to researchers at the University of Wisconsin-Madison, a particular tribe of ants, known as attine ants, have pockets throughout their thick, outer armor crammed full of antibiotic-producing bacteria. They use these bacteria to kill off a parasitic fungus that could destroy their way of being.

And according to Cameron Currie, a UW bacteriologist, the ants, the bacteria they cultivate and the fungus they fear have been in a stalemate for millions of years. This prompts the question: How come the fungus has not evolved to resist this particular strain of bacteria? This question could trigger insights into the battle against antibiotic-resistant strains of disease.

The research is published today in the journal Science.

Attine ants, which include New World leaf cutters, appear to depend on a particular kind of fungus to live. They grow and cultivate farms of friendly fungi, which provide them with nourishment and shelter; the queen and larvae feed exclusively off the fungal garden.

The ants tend to the garden like good farmers: weeding, fertilizing and providing nourishment to their fungal fields. In return, the fungi benefits from the ants' meticulous care.

The relationship isn't unique. There are hundreds, if not thousands, of examples across the living universe in which two different organisms rely upon each other - something called *obligate symbiosis* in the zoological nomenclature.

But Currie discovered that the attine ant-fungus association was more complex than scientists thought.

The ants and their fungi live under constant siege from a parasitic fungus called *Escovopsis*. This fungus can damage their gardens and hamper, and sometimes destroy, their livelihood. But somehow the ants are generally able to keep the bad fungus at bay.

Currie found that the ants carry a particular strain of antibiotic-producing bacteria that is primed to kill the threatening fungus, leading him to document one of the natural world's few cases of "quadripartite symbiosis," or an evolved system that includes four interacting partners.

He said that even though these ants had been extensively studied for more than century - with more than 3,000 scholarly papers published on their behavior, ecology and biology - no one had realized what they were looking at.

But, "it's pretty obvious once you see it," said Currie, whose research was conducted with an international team of scientists from the University of Copenhagen, University of Texas and Catholic University of Leuven in Belgium.

The bacterium, which is white and fiberlike, is conspicuous. But like other observers of fungus-growing ants, Currie initially dismissed the white fuzz on their bodies as "some sort of dermatitis, you know, like a skin infection on humans."

As the years clicked by, he noticed a pattern to the fuzzy white blemishes and thought, "wait a second, this must be important."

Indeed, he was finding it in every species of attine ant he studied, but never on nonfungus-growing ants.

Then he noticed that those ants in the colony whose job it is to tend the fungus garden had more of the white fuzz on their bodies than others - so much so that he called these garden-tending workers "sheep."

"They're completely covered," he said.

When he first published his results, in 1999, it was erroneously reported that the bacterium was a kind of *Streptomyces,* a group of bacteria well-known for producing human antibiotics.

This result was received with some skepticism, said Ulrich Mueller, an ecologist at the University of Texas who was not involved in this study.

Some claimed that *Streptomyces* was common, Mueller said, and therefore not necessarily a unique product of this system. Currie later discovered the bacterium was not of the *Strep* variety, but instead one that isn't as widespread.

But, Currie said, whether the bacterium was *Streptomyces* or *Pseudonocardia* - as he later discovered - was hardly a huge deal. What is important in this work, he said, is showing that the ants rely on a particular type of bacteria to fight the fungus.

Bacteria live in exoskeleton

Currie demonstrated that these ants have evolved to house and cultivate bacteria by modifying their exoskeleton so that it is perfused with large crypts - caverns that hold the bacteria, which the ants presumably cultivate with specialized gland cells.

And, Currie said, each species of attine ant he has investigated has its own crypt-morphology, or uniquely shaped physical caverns, to house its specific strain of bacteria.

"This clinches the idea that these things must be absolutely essential for these ants to function," said Ted Schultz, chairman of the department of entomology at the Smithsonian Institution, who wasn't part of the study. "They can't get along without it."

He said Currie's research "opens a whole lot of questions we never thought to ask. And clinches the idea that these bacteria have been part of the system from the beginning."

And this brings researchers to wonder how, if the system has been in place for 50 million years, the antibiotic is still effective against the fungus.

"Why is it that humans, who've been using antibiotics for 70 years, are constantly having trouble with resistance evolution?" Schultz said. "There probably is something we can learn from it. What is it that changes in the bacteria, or the fungus, that we can zero in on?"

"If we understood this system better," he said, we might learn something that could benefit ourselves.

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