Research reveals plant pathogens repurpose phage elements for bacterial warfare

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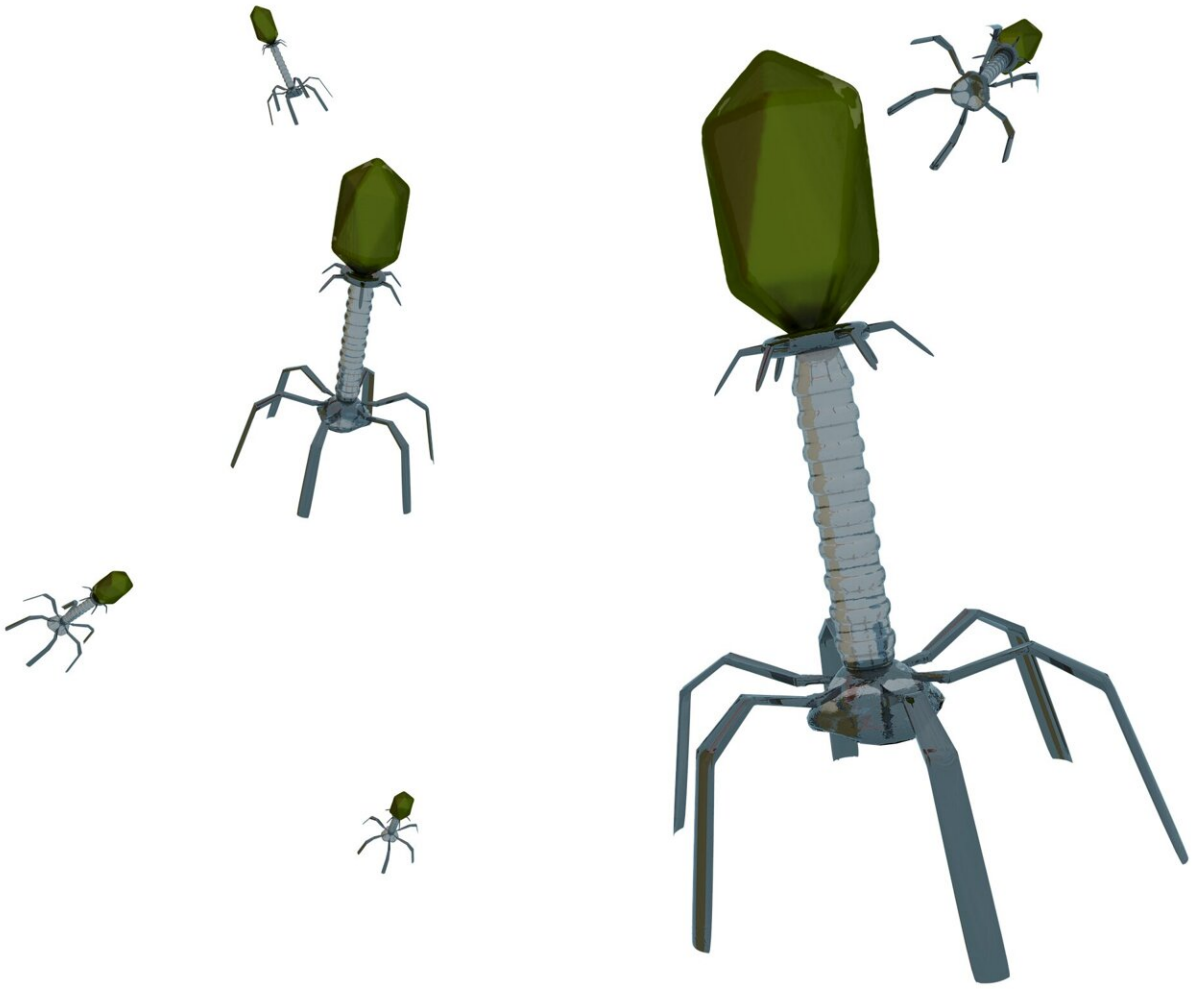

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Bacteriophages, viruses that attack and destroy bacteria, are everywhere in the natural world where they play a vital role in regulating microbe populations in ways that are not yet well understood.

New research led by the University of Utah and University College London (UCL) has found that plant bacterial pathogens are able to repurpose elements of their own bacteriophages, or phages, to wipe out competing microbes.

These surprise findings suggest such phage-derived elements could someday be harnessed as an alternative to antibiotics, according to Talia Karasov, an assistant professor in the U's School of Biological Sciences. Titled "A phage tail–like bacteriocin suppresses competitors in metapopulations of pathogenic bacteria," the study was published in *Science*.

This result was hardly what she expected to find when she embarked on this research with an international team of scientists.

Microbial pathogens are all around, but only a fraction of the time do they sicken humans, other animals or plants, according to Karasov, whose primary research interest is in interactions between plants and microbial pathogens. The Karasov lab is seeking to understand the factors that lead to sickness and epidemics versus keeping the pathogens in check.

For its prior research, the lab looked at how a particular bacterial pathogen, Pseudomonas viridiflava, manifests in agricultural and wild settings. On cultivated land, they found, one variant would spread broadly in a crop field and become the dominant microbe present. But that was not the case on uncultivated land, prompting Karasov to find out why.

"We see that no single lineage of bacteria can dominate. We wondered whether the phages, the pathogens of our bacterial pathogens, could prevent single lineages from spreading—maybe phages were killing some strains and not others. That's where our study started, but that's not where it ended up," Karasov said.

"We looked in the genomes of plant bacterial pathogens to see which phages were infecting them. But it wasn't the phage we found that was interesting. The bacteria had taken a phage and repurposed it for warfare with other bacteria, now using it to kill competing bacteria."

According to her study, the pathogen acquires elements of the phages in the form of non-self-replicating clusters of repurposed phage called tailocins, which penetrate the outer membranes of other pathogens and kill them.

After discovering this ongoing warfare in the bacterial pathogen populations, the Karasov lab and lab of Hernán Burbano at UCL mined the genomes of modern and historical pathogens to determine how the bacteria evolve to target one another.

"You can imagine an arms race between the bacteria where they're trying to kill each other and trying to evolve resistance to one another over time," Burbano said. "The herbarium samples from the past 200 years that we analyzed, provided a window into this arms race, providing insight into how bacteria evade being killed by their competitors."

Mining herbarium specimens for their microbial DNA

Burbano has pioneered the use of herbarium specimens to explore the evolution of plants and their microbial pathogens. His lab sequences the

genomes of both host plants and those of the microbes associated with the plant at the time of collection more than a century ago.

For the phage research, Burbano analyzed historical specimens of Arabidopsis thaliana, a plant from the mustard family commonly called thale cress, collected in southwestern Germany, comparing them and the microbes they harbored to plants growing today in the same part of Germany.

"We discovered that all the historical tailocins were present in our present-day dataset, suggesting that evolution has maintained the diversity of tailocin variants over the century-scale," he said. "This likely indicates a finite set of possible resistance/sensitivity mechanisms within our studied bacterial population.

Lead author Talia Backman wonders if tailocins could help solve the impending crisis in antibiotic resistance seen in harmful bacteria that infect humans.

"We as a society are in dire need of new antibiotics, and tailocins have potential as new antimicrobial treatments," said Backman, a graduate student in the Karasov lab.

"While tailocins have been found previously in other bacterial genomes, and have been studied in lab settings, their impact and evolution in wild bacterial populations was not known. The fact that we found that these wild plant pathogens all have tailocins and these tailocins are evolving to kill neighboring bacteria shows how significant they may be in nature."

Like most pesticides, many of our antibiotics were developed decades ago to kill a broad array of harmful organisms, ones that are both harmful and beneficial to human and plant health. Tailocins on the other hand, have greater specificity than most modern antibiotics, killing only

a select few strains of bacteria, suggesting they could be deployed without laying waste to entire biological communities.

"This is basic research at this point, not yet ready for application, but I think that there is good potential that this could be adapted for treating infection," Karasov said.

"We as a society have, in how we treat both pests in agriculture and bacterial pathogens in humans, used uniform and broad-spectrum treatments. The specificity of tailocin killing is a way that you could imagine doing more finely tailored treatments."

Participating in the research with the U School of Biological Sciences were University College London, the Max Planck Institute for Biology, the Complex Carbohydrate Research Center Analytical Services and Training Lab at the University of Georgia, New York University, the U's Department of Biochemistry and Lawrence Berkeley National Laboratory.

More information: Talia Backman et al, A phage tail–like bacteriocin suppresses competitors in metapopulations of pathogenic bacteria, *Science* (2024). DOI: 10.1126/science.ado0713. www.science.org/doi/10.1126/science.ado0713

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