Researchers study bacterial immunity to understand infectious disease

January 8 2019, by Emily Scott

Professor of Microbiology Rachel Whitaker, with graduate students Whitney England and Ted Kim, are using pseudomonas aeruginosa as a model system for health effects of viral/bacteria interactions. Credit: University of Illinois at Urbana-Champaign

Patients with cystic fibrosis are often infected by *pseudomonas*

aeruginosa, a bacterium that infects the lungs and prevents breathing, often causing death.

P. aeruginosa itself can also be infected by viruses, which can affect the clinical outcomes of cystic fibrosis patients.

"Just like humans get infected by bacteria, the bacteria get infected by viruses," said Rachel Whitaker, a professor of microbiology and leader of the Infection Genomics for One Health research theme at the Carl R. Woese Institute for Genomic Biology at the University of Illinois at Urbana-Champaign. "There's this nested, layered set of ecosystems and interactions of infection."

Whitaker and her graduate students, Whitney England and Ted Kim, had the idea to use *P. aeruginosa* as a kind of "model system" for understanding how bacteria's interactions with viruses may affect human health.

Their findings, published in *mSystems*, provide insight into this bacterium's diversity and immune system.

Scientists believe *P. aeruginosa* likely comes from the environment. Most serious infections of the bacterium happen in hospitals.

"There are lots of efforts to prevent children (with cystic fibrosis) from getting that infection, but that initial infection almost always happens," Whitaker said. "The strain that you get is the strain that you pretty much have for the rest of your life."

The specific strain that a patient is infected with affects their treatment. Some strains are resistant to antibiotics, while others contain genes that make the infection worse.

"One of the big differences between those strains is whether they, the bacteria, are infected by viruses," Whitaker said.

Bacteria's immune systems, called the CRISPR/Cas system, prevent them from being infected by viruses. The researchers analyzed this immune system within *P. aeruginosa* in a group of cystic fibrosis patients at a clinic in Copenhagen, Denmark and they found that the bacterial immune profiles were diverse.

"The bacterial population in Copenhagen looks like the global diversity," Whitaker said. "Within a person it's not diverse, but within this community, within this one hospital, it is."

From there, they wanted to see if they could determine which viruses had a chance of infecting that population of bacteria. They compared the bacterial population to known viruses of *P. aeruginosa*, and found that some viruses were highly targeted by the bacteria's immune system, while others were not.

"That's kind of a surprise, because you would think that maybe there'd be one virus or something that would be the focus of immunity," Whitaker said. "But really there's a diverse immune profile to a diversity of viruses."

Whitaker said this knowledge could be used to target—or at least be cautious of—certain viruses that could invade bacterial populations in specific hospitals.

"It kind of gets to community medicine ideas . . . can we predict how this epidemic is going to spread in this bacterial population?" she said. "These data can be used to do that."

For now, the research is at more of a predictive stage until scientists

figure out where these viruses come from.

"Until we know that, it would be hard to design a strategy to stop transmission," Whitaker said. "There are some other pieces of the puzzle that we need before we can really design strategies to prevent this transmission. This is sort of the first step."

However, scientists don't always want to protect *P. aeruginosa* from potential viruses. In this case, viruses are helping cystic fibrosis patients by killing off deadly bacteria.

Cystic fibrosis patients will often use phage therapy, which uses viruses to kill bacteria, to target *P. aeruginosa*, which has some strains that are resistant to antibiotics. Knowing the immune profiles of the bacteria's population may help improve this kind of therapy.

"The next step is to try to figure out where the viruses are coming from and how they spread, and whether we might be able to use them in phage therapy," Whitaker said.

On a larger scale, this research lays a foundation for other researchers who study bacterial infections, whether they're looking to stop antibiotic resistance or prevent epidemics.

"It's using the basic evolutionary principles of immunity to understand infectious disease," Whitaker said.

This is one of the goals of the IGOH theme, which applies evolutionary and ecological principles to the dynamics of infection—whether it's good or bad infection.

"We don't really want to prevent epidemics in this case—we want to promote epidemics of the viruses that kill the bacteria," Whitaker said.

"I think that this is a big step in that direction."

More information: Whitney E. England et al, Metapopulation Structure of CRISPR-Cas Immunity in Pseudomonas aeruginosa and Its Viruses, *mSystems* (2018). DOI: 10.1128/mSystems.00075-18

Provided by University of Illinois at Urbana-Champaign