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Researchers Uncover New Pathways in Bacterial Intercellular Competition

There's an epic battle taking place that's not on the national radar: intercellular competition. While it's not an Olympic event, new research demonstrates that this microscopic rivalry can be just as fierce as humans going for the gold.

Christopher Hayes, UC Santa Barbara associate professor of molecular, cellular and developmental biology, along with postdoctoral fellow Sanna Koskiniemi, graduate student James Lamoureux, and others, examined the role certain proteins, called rearrangement hotspots (Rhs), play in intercellular competition in bacteria. The findings appear today in the Proceedings of the National Academy of Sciences.

Rhs proteins and related YD-peptide repeat proteins are present in a wide range of bacterial species and other organisms, including human beings, where they help establish communications between neurons in the brain when the visual system is developing. Hayes and his team found that Rhs proteins enable Dickeya dadantii 3937, a phytopathogenic bacterium causing soft rot diseases on many crops, to compete with members of its own kind through touch-dependent killing.

While Rhs have been recognized for more 30 years, their function has been enigmatic. This new research sheds light on the mystery. Rhs proteins possess a central repeat region, characteristically the YD-repeat proteins also found in humans, as well as variable C-terminal sequences, which have toxin activity. C-terminal regions are highly variable between bacterial strains even in the same

species, indicating that a wide variety of weapons are deployed.

"Bacteria almost always have a different Rhs toxins," explained Hayes. "No one really knows why, but perhaps the toxins are rapidly evolving, driven by intercellular competition. In essence, these cells are fighting it out with each other. It's like an arms race to see who has the best toxins."

Cellular competition is analogous to that between humans and reflects a scarcity of resources. Like people, bacteria need a place to live and food to eat. "We think these systems are important for bacterial cells to establish a home and defend it against competitors," said Hayes. "In fact, bacteria have many systems for competition. And as we uncover more mechanisms for intercellular competition, we realize this is a fundamental aspect of bacterial biology."

These findings demonstrate that Rhs systems in diverse bacterial species are toxin delivery machines. "We have been able to show that gram-negative (Dickeya dadantii) as well as gram-positive (Bacillus subtilis) bacteria use Rhs proteins to inhibit the growth of neighboring bacteria in a manner that requires cell-to-cell contact," said Koskiniemi, the paper's lead author.

The toxic part of Rhs at the tip (the C-terminal region) is delivered into target cells after cell-to-cell contact. Some toxic tips destroy DNA and others destroy transfer RNA, which is essential for protein synthesis. These toxin activities help the bacteria expressing them to outcompete other members of the same species not carrying an antidote.

This work may help scientists design Rhs-based bacterial probiotics that kill specific pathogens but leave most normal flora unharmed. The research was supported by grants from the National Science Foundation and National Institutes of Health and by fellowships from the Carl Tryggers and Wenner-Gren Foundations.

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