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Symbiotic microbes induce profound genetic changes in their hosts

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Though bacteria are everywhere — from the air we breathe and the food we eat to our guts and skin — the vast majority are innocuous or even beneficial, and only a handful pose any threat to us. What distinguishes a welcome microbial guest from an unwanted intruder?

Research from the University of Wisconsin-Madison suggests the answer lies not with the bacteria, but with the host.

A study appearing online this week in the *Proceedings of the National Academy of Sciences* may help reveal what sets a platonic relationship apart from a pathogenic one. In the paper, researchers from the UW-Madison School of Medicine and Public Health and the University of Iowa identify a slew of microbe-induced genetic changes in a tiny squid, including a set of evolutionarily conserved genes that may hold the secrets to developing a mutually beneficial relationship.

"Interactions of animals with their microbiota have a profound impact on their gene expression, and to create a stable association with a microorganism requires a lot of conversation between the microbe and the host," says UW-Madison medical microbiologist Margaret McFall-Ngai, senior author of the new study.

Many studies have focused on the bacterial side of that conversation. But aside from a few "professional pathogens," like the bubonic plague-causing Yersinia pestis, most bacteria are not inherently good or bad, McFall-Ngai says. Instead, bacterial effects are highly contextdependent: She reported in 2004 that a common bacterial "toxin" — which causes tissue damage under some circumstances — also plays a critical role in host tissue development.

She now suggests that the outcome may rely on how the host itself responds to the bacterium. Problems most often arise when a normal balance is disrupted, she says. "A lot of these pathogens are just at the wrong place at the wrong time."

To listen into the animal-microbe conversation, McFall-Ngai takes advantage of a relatively simple host-bacterium relationship: the Hawaiian bobtail squid, a colorful critter less than two inches long that nurtures a single type of light-producing bacteria, called Vibrio fischeri. The bacteria take up residence in a specialized pouch on the squid's belly and produce light that the squid uses as anti-predator camouflage. In return, the bacteria receive easy access to nutrients from the squid.

In the new study, a team led by former UW-Madison graduate student Carlene Chun dissected the genetics of the squid host response, including a comparison with mutant bacteria unable to successfully colonize their host. They identified hundreds of genes affected by the establishment of a stable bacterial partnership, including some known to play a role in human responses to bacteria.

The involvement of several genes typically associated with responses to bacterial infection, such as members of common immune signaling pathways, suggests we may need to rethink our understanding of the main purpose of the immune system, McFall-Ngai says.

"We have thousands of bacteria that live with us, and yet there are only around 100 bacterial pathogens," she says. Given the numbers, "it seems like these pathways and these molecules are likely to be 'symbiosis' pathways more than 'anti-pathogen.'"

Her team also highlighted several genes corresponding to those previously implicated in establishing symbiotic relationships with gut bacteria in fish and mice, suggesting that the animal-bacteria conversation may be basically the same across evolution.

"All animals and plants evolved in the background of the presence of huge numbers of environmental bacteria… These genes might be considered the core conserved responses of animals to interactions with bacteria" along tissue surfaces like intestine walls and skin, McFall-Ngai says. "The language is ancient and highly conserved."

Source: University of Wisconsin-Madison

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