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RESEARCH NEWS

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Say What? Bacterial Conversation-Stoppers

While a chattering crowd of various species of bacteria is essentially a microbial tower of Babel, certain snippets of their chemical conversation are almost universally understood. HHMI researchers have found that bacteria of different species can talk to each other using a common language - and also that some species can manipulate the conversation to confuse other bacteria.

The interspecies crosstalk and misdirection could have important consequences for human health, said Bonnie L. Bassler, an HHMI investigator at Princeton University whose study was published in the September 29, 2005, issue of *Nature*. "The ability of cells to communicate with one another and the ability to interfere with the communication process could have consequences in niches containing competing species of bacteria or in niches where bacteria associate with humans," Bassler said. "In the gut, you can imagine how the normal microflora might interfere with cell-cell communication to thwart bacterial invaders."

Using a chemical communication process called quorum sensing, bacteria converse among themselves to count their numbers and to get the population to act in unison. A synchronized group of bacteria can mimic the power of a multi-cellular organism, ready to face challenges too daunting for an individual microbe going it alone. Swelling populations trigger their quorum-sensing apparatuses, which have different effects in different types of bacteria. One species might respond by releasing a toxin, while another might cut loose from a biofilm and move on to another environment.

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- Bonnie L. Bassler

Each species of bacteria has a private language, but most also share a molecular vernacular that Bassler's lab discovered about 10 years ago. A chemical signal called autoinducer-2 (AI-2), originating from the same gene in all bacteria, is released outside the cell to announce the cell's presence. Nearby bacteria take a local census by monitoring AI-2 levels and conduct themselves as the circumstances warrant.

Researchers have speculated that AI-2 is a universal language, and the new study from Bassler's lab is the first to show those conversations taking place - and producing consequences -- between co-mingling species.

Postdoctoral fellow Karina Xavier mixed *E. coli*, beneficial bacteria that live in the human gut, with *Vibrio harveyi*, a marine species that naturally glows in the dark in the presence of a crowd. In the test tube, AI-2 production by either species turned up the marine bacteria's light and turned on the quorum-sensing genes in *E. coli*. That confirmed what the scientists already suspected: the linguistic versatility of AI-2.

But this common language does not guarantee the correct message gets through, the researchers discovered. In earlier work, Xavier had found that *E. coli* both produces and consumes AI-2. In this study, she set up an experiment where multitudes of *E. coli* first produced then devoured enough AI-2 to dim the lights of the marine bacteria, essentially fooling the thriving oceanic gang into thinking its members were few, thereby terminating its quorum-sensing behaviors.

In a more realistic encounter, Xavier mixed *E. coli* with *V. cholerae*, the cholera-causing bacteria that mixes with *E. coli* in human guts. When cholera bacteria sense a quorum, they turn off their toxins and excrete an enzyme to cut themselves loose from the intestine, so they can move out of the body where they can infect another person. Here, *E. coli* squelched much of the quorum-sensing response of the cholera bacteria, although the effect was not as dramatic as with the marine bacteria.

"The real take-home point is the interference," Bassler said. "Consumption of the signal could be a mechanism that allows one kind of bacteria to block another kind of bacteria from counting how many neighbors they have and, in turn, properly controlling its behavior."

"This study moves us closer to really understanding how these interactions happen in nature," Bassler said. "Bacteria can communicate between species, and they have evolved mechanisms to interfere with the communication. Probably this is but one of many cunning strategies they have for manipulating chemical communication. You can imagine that, in niche one, the bacteria we consider good guys might be using AI-2 and winning. And unfortunately, in niche two, the bad guys might be using AI-2 and winning."