HHMI
HOWARD HUGHES MEDICAL INSTITUTE

RESEARCH NEWS

AUGUST 08, 2008

Scientists Manipulate Group Behavior in Bacteria

Bacteria band together to plan their battles against the body. They organize the assaults using a series of cell-to-cell communication signals that determine when to launch an attack against the host.

Now Howard Hughes Medical Institute researchers have shown that bacterial communication can be intercepted and chemically manipulated to control group behavior, such as virulence or the production of a useful products.

"We're in desperate need of new antibiotic strategies. We can't simply keep killing bacteria, because they develop resistance."
— Bonnie L. Bassler

In work reported in the August 8, 2008, issue of the journal *Cell*, a team led by HHMI investigator Bonnie Bassler has uncovered new details of how bacteria detect one another's presence to initiate group behaviors. Their findings suggest unprecedented opportunities to control bacteria, ranging from new strategies to fight infection to enhancing industrial processes that rely on microorganisms.

Bassler is a pioneer in studies of quorum sensing, the communication process that bacteria use to coordinate gene expression among millions of cells to accomplish particular jobs in unison. You need a lot of bacteria working together to make some tasks successful," Bassler explained. Quorum sensing is how bacteria work together in groups. They communicate with chemical molecules, and they recognize when they are alone and when they are in groups.

Manipulating this chemical crosstalk has been a goal of researchers for a variety of reasons, Bassler said. Some species of virulent bacteria release toxins only when there are enough bacteria around to resist being overwhelmed by an immune response; shutting off their communication might reduce infection and virulence. We're in desperate need of new antibiotic strategies, she noted. We can't simply keep killing bacteria, because they develop resistance. In other cases, researchers might want to enhance quorum sensing for useful purposes, such as ramping up the production of industrial, medical, or agricultural products.

Using a bioluminescent marine bacterium known as *Vibrio harveyi*, which lights up when a threshold number of bacteria are present, Bassler's team explored the workings of a protein called LuxN. LuxN, which sits in the inner membrane that surrounds the bacterial cell's contents, is the receptor that detects signaling chemicals known as autoinducers released by nearby bacteria. Quorum-sensing bacteria typically use autoinducers to measure two things, Bassler said: "Am I alone or in a group? Am I with friend or foe?" So, when autoinducers signal that a sufficient number of neighbors are nearby, LuxN tells the cell to turn certain genes on or off.

Bassler and her colleagues wanted to understand how LuxN keeps the bioluminescence genes off until enough autoinducer has been released by a quorum of bacteria. They screened 30,000 genetic LuxN mutants of *Vibrio harveyi*, searching for those that failed to light up and those that lit up before the bacteria reached a quorum.

The team then screened about 35,000 chemicals in search of those that could inhibit the bacteria's bioluminescence. They found 15 chemicals that did—some with quite potent effects.

By combining data from these two experiments with quantitative analysis of the different LuxN variants, Bassler and her colleagues obtained clues into how the system is built to kick in only when a signaling threshold is reached. The LuxN receptor is positioned in the membrane in a way that allows it to detect autoinducer only when it arrives from the outside of the cell. Autoinducer that is produced inside the cell - that is, to be released into the environment — cannot trigger that cell's LuxN receptors. "The receptors are poised to ignore the signal until it builds up," Bassler said. "They wait. If they react instantly (to a signal), it can be catastrophic."

Because similar signaling systems occur throughout biology, Bassler says the approach her team used in this study can be employed to understand other types of transmembrane receptors, which are notoriously difficult to study. Anyone with a favorite receptor in any organism can use this type of analysis to deduce signaling parameters from living cells, she said.