

Stopping MRSA before it becomes dangerous is possible, researchers find

December 3 2009



Sandia National Laboratories researcher Jeff Brinker sits next to a cell-suspension wheel that contains bacteria suspended in media. Brinker is also a professor at the University of New Mexico. Credit: Photo by Randy Montoya

Most scientists believe that staph infections are caused by many bacterial cells that signal each other to emit toxins. The signaling process is called quorum sensing because many bacteria must be present to start the process.

But the Jeff Brinker research group has determined that the very first stage of staph infection, when [bacteria](#) switch from a harmless to a virulent form, occurs in a single cell and that this individual process can be stopped by the application of a simple protein.

The Brinker group's nonantibiotic approach may make it easier to treat

staphylococci strains that have become drug resistant like the [methicillin-resistant Staphylococcus aureus](#) MRSA. The control of such strains is a formidable problem in hospitals.

"The good news is that by inhibiting the single cell's signaling molecules with a small protein, we were able to suppress any genetic reprogramming into the bacterium's more virulent form," said Brinker. "Our work clearly showed the strategy worked."

Brinker, with appointments at Sandia National Laboratories and the University of New Mexico, wrote about his group's findings in the Nov. 22 issue of [Nature Chemical Biology](#).

In the course of its experiments, the Brinker team achieved three firsts:

- They isolated Staphylococcus aureus bacteria in individual, self-assembled nanoscale compartments. Isolation of an individual bacterium previously had been achieved only computationally, leaving open questions of how a physically and chemically isolated bacterium would actually behave.
- They demonstrated that it was the release of signaling peptides from a single cell — not a quorum — that acted as a trigger to reprogram that same cell so that it released toxins.
- By introducing an inexpensive, very low-density lipoprotein (VLDL) to bind to the messenger peptide, they stopped the single cell from reprogramming itself.

The term "quorum sensing" itself may prove a misnomer, the result of observations made in cell cultures rather than in the body, said Brinker. Because signaling molecules tend to diffuse away, a liquid culture of cells would naturally require many bacteria to produce enough signaling

bacteria to begin reprogramming. The situation is otherwise in nature, where even a single cell may be sufficiently isolated that its own manufactured peptides would remain in its vicinity.

"Also, it's hard to believe that one cell's evolution could be based on what a whole bunch of cells do," said Brinker. "When we instead consider that an individual cell will do what's best for it, we can more clearly understand the benefits of that cell's behavior."

A bacterium may live longer by reprogramming itself to produce toxins or enzymes that allow it to access external nutrients, the Brinker group showed.

One aspect of experimental rigor was the team's ability to organize living cells into a nanostructured matrix. "We've already done this with yeast," said Brinker. "We just extended the process to bacteria."

A key question was whether a cell could distinguish between peptides emitted by itself from those sent by other cells. If signaling peptides were chemically the same, what would it matter which [bacterium](#) emitted it?

As it turned out, said Brinker, "Peptides could bond to surface receptors on their own [generating] cell. So a single cell's peptide molecules could activate its own genes to express proteins that make staph virulent."

Indicating that the experiment had isolated the actual cause of the transformation, when the number of peptides produced by a cell ultimately came to exceed the number of lipoprotein molecules in solution, a stalled "quorum-sensing" procedure started up again.

When still more signaling molecules were added to the mix, the cell's transformation occurred more rapidly.

Researchers hope to find a mechanism to locate bacteria reprogramming in the body so that the antidote can be delivered in time. The problem could be solved, suggested Brinker, by the insertion of VLDL-bearing nanospheres (another Brinker-group creation) into the bloodstream, linked to a 'searcher' molecule designed to find and link to suspect peptides or [cells](#) that produce them.

"Inhibiting this specific signaling molecule from turning on virulence wouldn't inhibit other bacteria," Brinker said.

Targeting is important because the human gastro-intestinal system contains many useful bacteria. These are often decimated by conventional antibiotics but would be spared by the Brinker group's method.

Source: Sandia National Laboratories ([news](#) : [web](#))

Citation: Stopping MRSA before it becomes dangerous is possible, researchers find (2009, December 3) retrieved 2 May 2024 from <https://phys.org/news/2009-12-mrsa-dangerous.html>

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