'Nanofactories': Stopping Bacterial Infections Without Antibiotics

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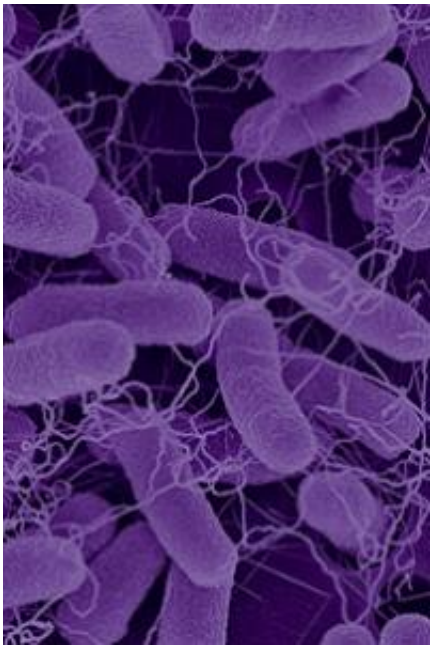

A scanning electron microscopy image of the bacterium Escherichia coli. Many bacteria, including E. coli, "talk" to each other by secreting and perceiving small molecules, a process called quorum sensing. Flagella and appendages that extend out of the cell walls can be produced in response to this signaling. Nearest neighbors control group behavior. Disrupting this intercellular communication could prove to be a new way to fight infection or disease.

(PhysOrg.com) -- New research at the A. James Clark School of Engineering could prevent bacterial infections using tiny biochemical machines - nanofactories - that can confuse bacteria and stop them from

spreading, without the use of antibiotics.

A paper about the research is featured in the current issue of *Nature Nanotechnology*. "Engineered biological nanofactories trigger quorum sensing response in targeted bacteria," was authored by Clark School alumnus Rohan Fernandes (Ph.D. '08, bioengineering), graduate student Varnika Roy (molecular and cell biology), graduate student Hsuan-Chen Wu (bioengineering), and their advisor, William Bentley (professor and chair, Fischell Department of Bioengineering).

The group's work is an update on their original nanofactories, first developed in 2007. Those nanofactories made use of tiny magnetic bits to guide them to the infection site.

"This is a completely new, all-biological version," he says. "The new nanofactories are self-guided and targeted. We've demonstrated for the first time that they're capable of finding a specific kind of bacterium and inducing it to communicate, a much finer level of automation and control."

The new nanofactories can tell the difference between bad (pathogenic) and good bacteria. For instance, our digestive tracts contain a certain level of good bacteria to help us digest food. The new nanofactories could target just the bad bacteria, without disrupting the levels of good bacteria in the digestive tract (a common side effect of many antibiotics). Nanofactories target the bacteria directly rather than traveling throughout the body, another advantage over traditional antibiotics.

Bacterial cells talk to each other in a form of cell-to-cell communication known as quorum sensing. When the cells sense that they have reached a certain quantity, an infection could be triggered. The biological nanofactories developed at the Clark School can interrupt this

communication, disrupting the actions of the cells and shutting down an infection.

Alternatively, the nanofactories could trick the bacteria into sensing a quorum too early. Doing so would trigger the bacteria to try to form an infection before there are enough bacterial cells to do harm. This would prompt a natural immune system response capable of stopping them without the use of drugs.

Because nanofactories are designed to affect communication instead of trying to kill the bacteria, they could help treat illness in cases where a strain of bacteria has become resistant to antibiotics.

"The work by Dr. Bentley is extremely exciting as he is using the ability of engineering to "build" using nature based components," says Philip Leduc, associate professor in the Departments of Mechanical and Biomedical Engineering and the Lane Center for Computational Biology and Biological Sciences at Carnegie Mellon University. "Understanding the science of cells is wonderful, but then using these components and constructing systems that leverage biological advantages is a huge step forward. His work in this paper uses his synthetic biology approach to build new nanofactories toward new areas of antimicrobials as well as opening new findings in quorum sensing."

The nanofactories' ability to alter cell-to-cell communication isn't limited to fighting infections.

"Quorum sensing and signaling molecules are actually used to accomplish a lot of things," Bentley explains. "Sometimes disease develops because communication is not taking place—a good example is digestive disorders that involve an imbalance of bacteria in the digestive tract. In that case, nanofactories could be used to start or increase communication instead of disrupting it."

More information: Paper -- www.nature.com/nnano/journal/v …/nnano.2009.457.html

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