Understanding Bacterial Crowd Control

Author: Ben-Ari, Elia

Source: BioScience, 58(1) : 88

Published By: American Institute of Biological Sciences

URL: https://doi.org/10.1641/B580117

Understanding Bacterial Crowd Control

STUDYING BIOFILM FORMATION

For more than two centuries, biologists thought that bacteria and other microbes lived a largely solitary existence. But in the past 20 years or so, scientists have learned that bacteria prefer banding together in organized, cooperative communities called biofilms. These microbial co-ops are responsible for many chronic infections and can also form in materials implanted or inserted in the body, such as catheters, contact lenses, and artificial joints. They are often resistant to antibiotics and difficult to eradicate.

Now, a team of researchers has devised a system that reproduces conditions in which biofilms form, and that could allow new treatments to be tested. Coupled with real-time microscopy, the novel silicone rubber device, containing a series of shallow, connected microscopic chambers that bacteria can colonize, lets researchers observe and capture on video the behavior of individual *Escherichia coli* cells in the initial stages of forming a biofilm.

"Understanding the initial stages may help battle the development of biofilms," says Andre Levchenko, of Johns Hopkins University. The microfluidic device used to study biofilm formation was designed and fabricated in collaboration with Alex Groisman's team at the University of California–San Diego. Hojung Cho, a graduate student in Levchenko's lab, is the lead author of the study, published in the November 2007 issue of *PLoS (Public Library of Science) Biology.*

Wherever water, a solid surface, and nutrients come together, bacteria and other microbes are likely to set up shop and form biofilms. These microbial metropolises, which provide refuge from stressful environmental conditions, consist of towers of cells with water channels running between them to deliver nutrients and remove waste. The entire community is embedded in a sticky molecular mesh that glues the film to a surface and holds it together.

"Recent studies have revealed that one of the important initial steps [in biofilm formation] might be for bacterial cells to actively seek out small cavities and populate them, reaching very high densities," Cho and colleagues write in *PLoS Biology.* But how do cells survive in such crowded conditions without starving? And how do some cells manage to escape and go on to multiply and form a mature biofilm?

"It seems that [bacterial cells] achieve both of those goals by self-organization," says Levchenko. As chambers in the microfluidic device filled with actively dividing *E. coli,* most of the rod-shaped cells oriented themselves so that their long axes faced the chamber exits. This self-organizing behavior kept the exits from being blocked by a bacterial stampede and allowed cells to move out in an orderly fashion. It also enhanced the flow of nutrients into the chambers. (Videos of the cells and the full text of the paper are available at *http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pbio.0050302.*)

Microchamber devices like those used in this study are likely to have many practical applications. "Not only can we observe the evolution of these highly organized colonies, but we can also try to screen various ways to disrupt this process," Levchenko says. Antibiotics now in use have not been tested against biofilms, in part because it has been difficult to grow biofilms under controlled conditions. Because bacteria are more vulnerable before they have hunkered down in a mature biofilm, an experimental system such as this could be used to screen for agents that target the initial stages of biofilm formation.

TARGETING CELLULAR COMMUNICATIONS

Finding a way to disrupt biofilms is one of the holy grails of medical research. A research team led by Bonnie Bassler of Princeton University has made a significant advance toward that goal by isolating a compound that cholera bacteria (*Vibrio cholerae*) use to talk among themselves in a biofilm. The compound, known as cholerae autoinducer-1 (CAI-1), is an example of what is known as a quorum-sensing signal. The team's findings, which suggest that CAI-1 could be used to prevent cholera infection, were published in the 6 December 2007 edition of *Nature.*

Bacterial communities use chemical signaling molecules to monitor changes in their population densities, a process known as quorum sensing. When enough of a bacterium's relations are assembled, secreted quorum-sensing signals reach a critical concentration that other bacteria sense, activating specific genes and triggering a coordinated change in behavior.

In most bacteria, quorum-sensing signals play a role in the formation of biofilms. But in the case of *V. cholerae,* the signals cause bacteria to stop forming biofilms and stop releasing the toxins, or virulence factors, that make people sick. The bacteria, which form a biofilm in people's intestines, are then shed from the body and go on to infect other people.

After isolating CAI-1, determining its structure, and synthesizing the compound in the lab, Bassler's team showed that the molecule inhibits expression of a key virulence factor. "If you supply CAI-1 to cholera, you can flip their switches to stop the attack," said Douglas Higgins, a graduate student in Bassler's lab and first author of the *Nature* paper. And, the authors conclude, "this work provides a demonstration that interference with quorum-sensing processes in general...has great promise in the clinical setting."

Elia Ben-Ari (e-mail: ebenari@nasw.org) is a freelance writer and editor based in Arlington, Virginia.

doi:10.1641/B580117
Include this information when citing this material.