


A New Class of Antibiotics Could Stop Drug-Resistant Bacteria in their Tracks

Antibiotics, among the most commonly prescribed drugs in the world, are becoming increasingly ineffective against a growing number of multi drug-resistant strains of bacteria. Bacteria can become resistant to antibiotics in a few different ways. Commonly, patients prescribed with these life-saving drugs do not complete a prescription regiment. This allows the bacteria, which were **not** killed by the antibiotics initially, to gain tolerance to the drugs. These ‘tolerant’ bacteria then reproduce and, if treatments resume, will be resistant to the antibiotics. According to the Centers for Disease Control and Prevention, over 2 million people become infected with antibiotic-resistant bacteria and 23,000 people die as a direct result of these infections in the United States alone. To combat this issue, scientists around the world have been searching for new, creative approaches to combat bacterial resistance.

Bacteria, among earth’s first life forms, are microscopic organisms that have developed a powerful array of techniques to survive in some of the world’s harshest environments. Unbeknownst to most, these seemingly mundane little beings actually communicate with one another in much the same way that people talk over the telephone. If I wanted to contact a friend in Bangladesh, for example, I would dial his phone number, thus sending out a specific signal. My friend across the Pacific, recognizing my unique phone number, would (hopefully) answer the phone. Telephone communication thus requires that I understand both my friend’s phone number and, if I want my friend to answer when I call, that I possess an identifying phone number of my own. This simple logic aptly describes the manner in which many of our microscopic counterparts communicate.

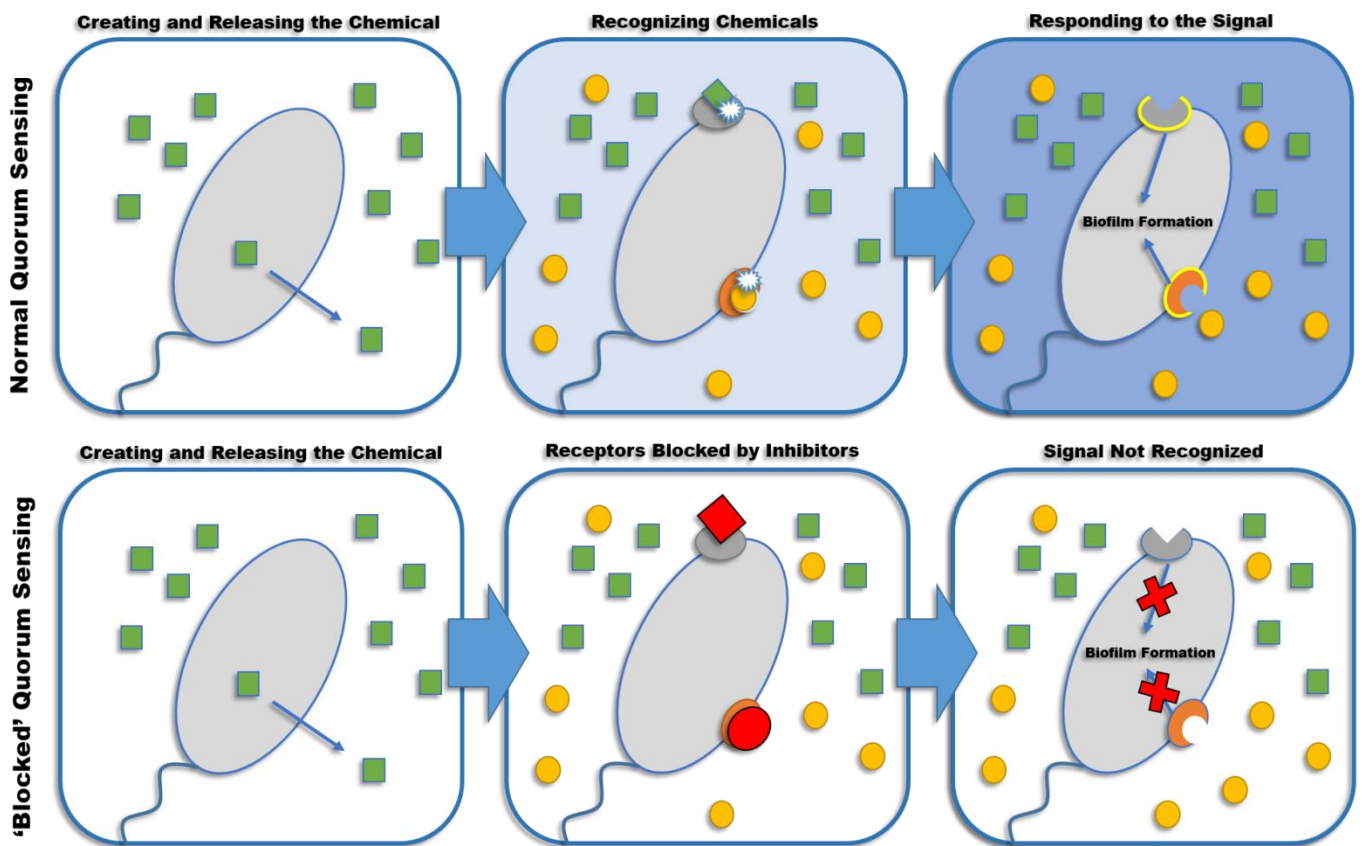
In 2009, Dr. Bonnie Bassler gained international renown with her TED talk entitled “How bacteria ‘talk.’” As a world-renowned American molecular biologist and 2002 MacArthur Fellow, Bassler has been instrumental in advancing our understanding of "quorum sensing," a fancy term for the way that bacteria communicate with one another.



“When antibiotics became industrially produced following World War II, our quality of life and our longevity improved enormously. No one thought bacteria were going to become resistant.”

-Bonnie Bassler

Bacteria synthesize and release chemicals at an astounding pace. These same bacteria also possess a receptor that recognizes, and binds to, the chemicals that they themselves have released. Every species of bacteria releases a different chemical and has a unique receptor which binds to their own identifying chemical. Essentially, bacteria of the same species have the same "area code," which allows them to recognize their "family" when placed among many different species. As the numbers of bacteria grow on a petri dish or within the human body, these receptors become more and more activated. When the number of chemicals surrounding the bacteria increase over a certain threshold, it indicates to the bacteria that there are members of the same species nearby. When these bacteria sense that there are enough of their species in the same area, they may attack the host or form a biofilm, both of which can result in dangerous infections or disease. This simple communication principle lies at the heart of quorum sensing and is depicted in the cartoon image below.



By analyzing the unique chemical signals, or "area codes," of different bacteria, the Bassler lab has created an exciting class of antibiotics aptly named "quorum sensing inhibitors." These are drugs that block the way bacteria communicate by cutting off their landline. To create these quorum sensing inhibitors, a few key steps are involved. The scientists begin by creating a drug that looks similar to the chemicals that the bacteria normally release on their own. The quorum sensing inhibitors must bind to the same receptors that the normal chemicals do. The main difference between the drugs made in the Bassler lab and the chemicals that the bacteria normally release, however, is that the artificial inhibitors attach to the bacterial receptors and never let go, thus blocking their communication system and putting the receptor out of business. If enough of these quorum sensing inhibitors are present, every bacterial communication receptor will be down for the count, and the bacteria will be unable to recognize and communicate with nearby members of their species. This lack of communication prevents the bacteria from gathering enough forces to attack the host or form a dangerous biofilm.

In a research study published in the journal *Proceedings of the National Academy of Sciences*, the Bassler laboratory successfully created a compound that blocks the communication of *Pseudomonas aeruginosa*, a largely antibiotic-resistant strain of bacteria that commonly causes hospital infections by forming dense biofilms in a host. Biofilms are essentially large colonies of bacterial growth that are difficult to get rid of and cost the healthcare industry billions of dollars each year. Biofilms of *P. aeruginosa* can be found on catheters and cardiac stents after surgery. Consequently, patients are at increased risk for infection and must pay to replace these devices every couple of years.

The compound that the Bassler Laboratory created to block *P. aeruginosa* communication is called meta-bromo-thiolactone (or mBTL for short). mBTL has a structure similar to the chemical that *P. aeruginosa* normally uses to communicate and proved effective in targeting two very important *P. aeruginosa* communication receptors. It was able to bind and deactivate both of these receptors and prevent signaling molecules from entering the receptor sites, thus cutting off *P. aeruginosa* signaling.

This scientific breakthrough may be the foundation upon which a new class of antibiotics are created. With alternative antibiotics available to combat these pesky microbes, doctors will have access to more options for patient treatment without jeopardizing community health.