

Microbiology

Fighting back antibiotic resistance: a new hope from the soil

by Dan Kramer¹ | PhD student

¹:Department of Molecular and Cellular Biology, University of Berkley, California, USA.

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Bacteria live in a hectic world. They need to find food and a happy place to live all while dividing every 20 or so minutes. To complicate things further, they must also outcompete the other bacteria they share a space with. In the human gut, for example, there may be up to 1,000 different species of bacteria⁵. That's a lot of competition! In order to outcompete each other for nutrients, some bacteria produce molecules that seek out and destroy other species of bacteria. This is one of the ways that antibiotics are created. Most of the antibiotics that humans use are derived from different bacterial strains, or other small organisms like fungi.

Because bacteria grow and divide very fast, they can quickly adapt to new surroundings. When we use an antibiotic to get rid of disease-causing bacteria, we eliminate all the bacteria in that colony that are susceptible to the antibiotic. However, there will be a small portion immune to the antibiotic that will survive and continue to grow. This leaves us with a new colony of the same disease-carrying bacteria that are now resistant to the antibiotic. Antibiotic resistance is a major issue^{2,3} and doesn't appear to be going away any time soon. This means we are in a constant need of new antibiotics.

To combat antibiotic resistance, scientists search for new bacteria that naturally produce antibiotics, as synthesizing new antibiotics from scratch is a costly and extremely difficult task. In order to find new antibiotics, researchers need to keep the bacteria growing in a lab, in a controlled environment, to test each for their ability to produce antibiotics. There is a problem with this, however - the majority (nearly 99%) of bacteria scientists find won't grow successfully in the lab using the usual, artificial techniques¹. This leaves us with a small percentage of bacteria that we can successfully grow. But, we have been drawing from this well for so long that the pool of untested bacteria is rapidly shrinking.

To combat this, about 5 years ago, scientists developed a new technique that allows us to grow strains of bacteria that we were unable to culture before - expanding our pool of testable bacteria. The technique involves a tool named iChip that has thousands of tiny wells which allow researchers to cultivate individual colonies of rare bacteria directly in the soil they call home. In this way, they can grow up to 10,000 unique strains of bacteria in their natural environment. This was a breakthrough in our ability to grow bacteria in the lab. It increased the amount of bacteria that we could cultivate by about 50 fold.

Recently, a team of researchers used this technique to search for new antibiotics⁴. In a new strain of bacteria that couldn't be grown before the iChip, they discovered a new antibiotic they named teixobactin. This drug has a unique mechanism, as it attacks a molecule that is vital for bacteria to build its membrane. The process that teixobactin disrupts is so basic and essential, it makes it nearly impossible for susceptible bacteria to mutate and develop a resistance. Their research showed that, compared to other popular antibiotics, bacteria aren't developing a resistance. In an experiment where they measure the amount of antibiotic it takes to kill a colony of bacteria in successive generations (usually each successive generation will be more resistant), the same amount of antibiotic was as effective in the first generation as it was to the 25th. This is amazing especially compared to other antibiotics that required 256





times the normal dose to kill the same amount of bacteria at the 25th generation. They then tested teixobactin in several different disease models in mice, including <u>pneumonia</u>, to find it was more efficient in eradicating the diseasecausing bacteria than other effective antibiotics. So, not only is this antibiotic difficult to build a resistance to, but it is also more efficient at eradicating bacteria. A real win win!

This discovery represents a major breakthrough in the field, and our lives in general. It shows that the iChip method is successful in growing difficult-to-culture strains of bacteria. It has vastly increased the pool of bacteria we can search through to find new antibiotics. This research also shows that some of the antibiotics we find could be extremely useful, with potentially new targets that make building a resistance nearly impossible. It may be too soon to tell, but hopefully these findings are just the prologue to many more future discoveries.