Finding fresh approaches for tried-and-true antibiotics

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There was a time when Catherine Wakeman thought she might become a physician, but then she had an opportunity to participate in laboratory research during her days as an undergraduate student.

An associate professor in Texas Tech University's Department of Biological Sciences, Wakeman has been hooked on research ever since.

The quest to uncover new knowledge and share those findings with the broader medical community is part of what's driving her current research. Wakeman is testing the effectiveness of unique combinations of already approved antibiotics against various strains of drug-resistant microorganisms.

"There is a big push for new antibiotic drug discovery with the emergence of antibiotic resistance and a possible next pandemic," she said "That is a great avenue and very important, but once you discover a new drug, it takes a long time to put it through clinical trials before it can be used. We want to restore the effectiveness of currently available antibiotics."

Two other Texas Tech faculty members are also part of the project.

Amanda Brown, an associate professor in Biological Sciences who specializes in metagenomics, the study of specific communities of microorganisms, and Allie Smith, an associate professor in the Honors College with a specialization in clinical microbiology, are using their expertise on the research in addition to Kendra Rumbaugh at the Texas Tech University Health Sciences Center.

The group's work looks to eliminate that new-drug timeline by taking currently available and approved antibiotics and testing them in unique combinations to target microbes that have developed resistance to drugs. Where one drug might no longer be effective, another drug (or combination thereof) might.

"There is some evidence showing that as resistance emerges toward certain classes of antibiotics, susceptibilities can also emerge," Wakeman

said. "We want to see if we can identify this phenomenon in a broader sense and then be able to make suggestions to clinical microbiologists that as you see resistance emerging to antibiotic X, consider trying antibiotic Y."

This characteristic of resistance also creating vulnerabilities is known as a fitness trade-off.

"Rather than discovering new antibiotics that might require many years to bring through clinical trials and FDA approvals, we can use currently available classes," she said. "We believe that fitness trade-offs can occur in ways that make certain antibiotics useful against unexpected types of microbes."

The other, equally important, thrust of the research will look at how microbes interact with each other to cause infections. In many chronic infections, more than one type of microbe is responsible.

"Chronic infections usually contain multiple species of microbes," she said. "However, the first step in clinical microbiology typically involves the isolation of what is believed to be the more pathogenic microbe, removing the community context during antibiotic susceptibility testing."

However, Wakeman said microbes behave differently in what she called a mixed-species condition. Consequently, certain antibiotics might not be effective because of how the microbes work together.

"One microbe might be able to protect another because it's protecting itself against the antibiotic," she said. "The way they change their behavior can make them less susceptible to some classes of antibiotics we use. Treatment of a chronic infection may be targeting a microbe based on data from a pure culture, but in an infectious context like this, there is often a much more complex community of microbes involved."

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