New study hints at potential antibiotic breakthrough

September 27 2018

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The rapid emergence and global spread of antibiotic resistance demands a new approach for developing novel ones. A study published in *The FASEB Journal* uncovers a novel approach to combatting the fast spread

of multidrug-resistant bacteria.

Most antibiotics kill bacteria by targeting regions of their essential proteins that lie on the surfaces of these folded molecules. When mutations modify these surface sites, resistance to antibiotics develops. Rather than targeting the surfaces of proteins, researchers in this study targeted the tightly packed structural core buried behind the protein surfaces, an approach that makes it less likely for bacteria to develop resistance.

"These findings present an exciting new paradigm in antibiotic discovery," said Yaoqi Zhou, Ph.D., a professor at Griffith University's Institute for Glycomics in Queensland, Australia. "The results of this study could lead to a new set of tools in the ongoing battle against antibiotic-resistant infections that affect millions of people worldwide each year."

To target this structural core, Zhou and colleagues used structure-disrupting, self-derived peptides. They first studied KFF-EcH3, a peptide derived from an essential protein of *E. coli* and linked with a cell-permeating peptide. Researchers proved that KFF-EcH3 was indeed able to inhibit the growth and survival of *E. coli*—in both laboratory and clinical, multidrug-resistant strains. Significantly, the study did not detect any resistance developed against KFF-EcH3 over a 30-day period.

The research team used the same approach to introduce another structure-disrupting, self-derived peptide, KFF-NgH1, to target an *N. gonorrhoeae* essential protein. In the experiment, the peptide inhibited bacterial growth and also treated a gonococcal infection in a human cervical epithelial cell model in vitro.

"This study was based on a rational idea and the results are encouraging. We must always conceptualize biology in 3-D," said Thoru Pederson,

Ph.D., Editor-in-Chief of *The FASEB Journal*.

Provided by Federation of American Societies for Experimental Biology