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New antimicrobial strategy silences NDM-1 resistance gene in pathogens

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Researchers have synthesized a molecule that can silence the gene responsible for severe antibiotic resistance in some bacteria. The research, presented at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), an infectious disease meeting of the American Society for Microbiology (ASM) could be a viable new strategy for treating resistant infections.

The focus of this new molecule is NDM-1 (New Delhi metallo-beta-lactamase-1) a gene carried by some bacteria that allows them to produce an enzyme called carbapenemase.

"NDM-1 confers bacterial resistance to all classes of beta-lactam (penicillin type) antibiotics including carbapenems, powerful antibiotics used when others fail," says Bruce Geller of Oregon State University and author on the study. "NDM-1 has spread rapidly to many bacterial pathogens, including E. coli, Acinetobacter baumannii and Klebsiella pneumoniae. Many of these pathogens are resistant to multiple antibiotics, which limits treatment options."

Molecule known as a peptide-conjugated phosphorodiamidate morpholino oligomer (PPMO) are synthetic analogs of DNA or RNA that have the ability to silence the expression of specific genes. In this study Geller and his colleagues at Oregon State University and the University of Texas Southwestern have design, synthesized and tested a PPMO that is complimentary to the NDM-1 gene, allowing it to bind specifically to NDM-1 mRNA, essentially silencing the gene.

"When the NDM-1 PPMO was added to growing cultures of multidrug-resistant E. coli, A. baumannii or K. pneumoniae that express NDM-1, it restored susceptibility to carbapenems at therapeutically relevant concentrations," says Geller.

NDM-1 infection was first identified in 2009 in people who resided in or traveled to the India and Pakistan. The first cases in the United States were identified in 2010, and the number of cases is growing. The concern is that these highly resistant bacteria carrying NDM-1 could supplant more antibiotic-sensitive strains.

"There is a critical need to find new treatments for antibiotic-resistant pathogens and using a gene-silencing approach, such as with a PPMO, could be one viable strategy for new antimicrobial development," says Geller.

More information: This research was presented as part of the ASM's 54th ICAAC held September 5-9, 2014 in Washington, DC.

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