HIV-derived antibacterial shows promise against drug-resistant bacteria

June 19 2013

A team of researchers at the University of Pittsburgh has developed antibacterial compounds, derived from the outer coating of HIV, that could be potential treatments for drug-resistant bacterial infections and appear to avoid generating resistance. These new agents are quite small, making them inexpensive and easy to manufacture. The research was published in the June 2013 issue of the journal *Antimicrobial Agents and Chemotherapy*.

The first of many probable applications will likely be the chronic bacterial infections in the lungs of cystic fibrosis patients "that frequently develop resistance to all standard antibiotics, and are the leading cause of death in these patients," says senior author Ronald Montelaro.

The lead compound shows powerful antibacterial activity against clinical isolates of diverse pathogenic bacteria that are resistant to most antibiotics. These agents, called engineered cationic antimicrobial peptides (eCAPs) "may be applicable to treatment of other respiratory infections, topical infections, and systemic infections," says Montelaro.

The genesis of the new agent was basic research on HIV envelope protein structure and function, says Montelaro. As part of this research, "we identified highly conserved unique protein sequences that were predicted by computer modeling to assume structures characteristic of natural antibacterial peptides. Since antibacterial peptides specifically target and disrupt the integrity and function of bacterial membranes, we

thought that these similar peptide sequences in the HIV envelope protein might contribute to toxicity and death in infected cells by altering cell membranes."

The team engineered the original HIV peptides for greater effectiveness and smaller size, the latter to reduce manufacturing expenses. The engineering involved modifying amino acid content (they contain just two different amino acids), peptide length, charge, and hydrophobicity. The current paper describes the third generation peptides. The lead agent contains just 12 amino acid residues.

"Another potential application is biodefense, where eCAPs may be used as a rapid postexposure aerosol treatment in individuals after exposure to aerosolized pathogens, where the goal of immediate treatment would be to rapidly reduce bacterial dose from a lethal to a nonlethal or subclinical level," says Montelaro.

Provided by American Society for Microbiology