TECHNOLOGY

Defensin-like molecules as novel antimicrobial agents

OVERVIEW

The ever increasing emergence of many pathogenic strains of bacteria resistant to commonly used antibiotics is a rapidly growing concern in public health and new classes of antimicrobial agents are desperately needed. One approach that has gained popularity recently is to study naturally-occurring antimicrobial peptides that have the advantage of both killing bacterial pathogens and modulating the immune response. One class of these peptides called defensins show broad antibacterial properties against many different bacterial strains despite being structurally conserved. Although the mechanism of action for these defensins is still being studied, recent reports show that human defensins can bind to and sequester the bacterial cell wall precursor Lipid II, preventing cell wall synthesis and killing the bacteria. Lipid II is a very popular target for antibacterial drugs because it is absolutely crucial for bacterial survival and is a bottleneck in bacterial cell wall synthesis. There are currently 4 classes of antimicrobials that target Lipid II, including the so-called last line of defense vancomycin, although bacterial resistance has developed to all of these compounds including vancomycin. Inventors at UMB are developing a new class of antimicrobial compounds by using molecular modeling to identify molecules that mimic naturally occurring defensins. Compounds were chosen based on their ability to bind Lipid II, preferentially kill a strain of Gram-positive bacteria (S. aureus) over eukaryotic cells, and exhibit limited cytotoxicity. Several identified compounds have proven effective in a murine model of sepsis.

APPLICATIONS

Treatment and/or prevention of infections caused by bacteria, in particular Gram-positive bacteria.

ADVANTAGES

-New class of antimicrobial to combat the rise of resistant bacterial infections. -Studies show that the development of bacterial resistance to naturally-occuring peptides is much lower than to foreign antimicrobial agents. -Lipid II is an excellent target for antimicrobials because it is necessary for bacterial survival, is highly conserved, is not found in humans or animals, and is a bottleneck in cell wall synthesis.

STAGE OF DEVELOPMENT

Second round of compound selection has been completed, in vitro bacterial killing and cytotoxicity studies have been completed, and preliminary in vivo studies in a murine model of sepsis are done.

LICENSING POTENTIAL

UMB seeks to develop and commercialize by an exclusive or non-exclusive license agreement and/or sponsored research with a company active in the area.

CONTACT INFO

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PATENT STATUS

U.S. Patent 8,796,323 issued 8/5/2014 (for ED-2010-066), CIP Applicatioon filed (for ED-2012-088)

CATEGORIES

- Diagnostics
- Therapeutics

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