MedicalXpress

Synthetic peptoids hold forth promise for new antibiotics

March 5 2008

Drug-resistant bacterial infections are a growing concern, and much research has been devoted to finding new classes of antibiotics to fight them.

Stanford researchers may have found some answers in peptoids, a class of manmade molecules very similar to natural proteins that play an important role in the human immune system.

"Peptoids could be an entirely new class of antibiotic drugs, which would be hugely important," said Annelise Barron, associate professor of bioengineering at Stanford.

Anti-microbial peptides are evolutionarily ancient infection fighters found in organisms from grasses to amphibians to humans. In the human body, the peptides show up in the mouth, lungs and intestines, and in body fluids like sweat and tears. Anti-microbial peptides target a variety of pathogens and generally kill by punching holes in the invaders' cell membranes.

"You can think of these types of antibiotics as the body's 'land mines' against invading pathogens," Barron said.

Because of this, bacterial resistance to the peptides is rarely observed. Bacteria can thwart other anti-microbial drugs by inactivating the drug, pumping it out of the cell, altering the drug's binding site so it is no longer recognized or working around the specific cell part attacked by

the drug.

But it is much tougher for bacteria to develop resistance to the damage caused by anti-microbial peptides. "The bacteria can't fundamentally alter their entire outer membrane," Barron said.

Such peptides seem like a natural choice for new antibiotics. One type showed promise in the treatment of diabetic foot ulcers. Unfortunately, their applicability has been limited so far to topical use; natural peptides are quickly degraded in the stomach. Thus, a peptide-based drug must be injected rather than swallowed. The peptides are quickly broken down in the bloodstream as well, and must therefore be injected in high concentrations.

Peptoids are synthetic molecules—oligomers—with structures that are similar to those of anti-microbial peptides, and offer the potential to overcome many of the problems associated with the natural molecules. Peptoids are much less susceptible to degradation in the stomach and bloodstream than peptides, so they will last longer in the body. They are also less expensive to produce than peptides, Barron said.

Barron and her colleagues had these peptoids tested against six strains of pathogenic bacteria. The peptoids showed anti-bacterial properties almost identical to those of the natural peptides.

"They did beautifully," Barron said. "They appear to be broad-spectrum antibiotics that interact and interfere with bacterial cell membranes analogously to the way these peptides do."

To see if the peptoids would be harmful to human cells, the researchers combined them with human red blood cells in the laboratory. They also mixed them with mammalian lung cells and skin cells. At their active concentrations, the peptoids left the mammalian cells unharmed.

Barron said that the next step is testing the peptoids in animal models of bacterial infection, and studies with mice are under way with collaborators.

"It's an exciting area," she said. "Society desperately needs new antibiotics, and I think this family of molecules has huge clinical promise."

PNAS paper: www.pnas.org/cgi/content/abstract/0708254105v1

Source: by Shelby Martin, Stanford University