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UCLA School of Dentistry Researchers Prepare to STAMP Out Pathogens With Smart Bomb Antimicrobial Technology

New technique offers promising alternative to traditional antibiotic therapy

Researchers from the UCLA School of Dentistry report they are the first to synthesize chemically a new antimicrobial composition that efficiently eradicates harmful bacteria while leaving helpful bacteria undisturbed. Their research is presented in the April issue of Antimicrobial Agents and Chemotherapy.

The human body is home to millions of different bacteria, some of which cause disease, but many of which are vital for optimal health. Meanwhile, the majority of antimicrobial compounds in clinical use are broad-spectrum antibiotics. While these antibiotics have the advantage that they can be effective against bacterial infections without precise diagnosis, a negative aspect of their use is that they also kill benign and beneficial bacteria. Overuse of broad-spectrum antibiotics can seriously disrupt the body's normal ecological balance, rendering humans more susceptible to bacterial, yeast and parasitic infections.

In addition, according to the Centers for Disease Control, half of the more than 100 million antibiotic prescriptions filled annually are unnecessary and, as a result, in many cases microbes have adapted and are resistant to antibiotics due to constant exposure and improper use of the drugs. It is estimated that the annual cost of treating drug-resistant infections in the United States is approximately $5 billion. The continued emergence of antimicrobial-resistant bacteria, fungi, yeast and parasites has encouraged efforts to develop other agents capable of killing pathogenic microbes.

The new composition developed at UCLA belongs to a new class of peptides known by the acronym STAMP, or Specifically Targeted Anti-Microbial Peptide. Representing a major step forward in antimicrobial treatment, a STAMP combines a targeting peptide with an antimicrobial peptide to first recognize a target microbial organism and then unleash an antimicrobial effect on that organism.

Recently, there have been a number of reports on the use of fusion proteins for treating disease. For example, malignant disease can be treated using a genetically engineered

protein construct including an immunological component that binds specifically to tumor cells and a cytokine capable of eliciting significant anti-tumor activity. However, until now there have been few reports of directing antimicrobial agents to infected regions of humans or animals using target-specific molecules.

UCLA researchers used a peptide synthesis machine to create a 36-amino-acid peptide that exhibited strong antimicrobial activity as well as selectivity against a single-target bacterium. Focusing their attention on *Pseudomonas*, an opportunistic human pathogen that targets immuno-compromised individuals and can cause urinary tract infections, sepsis, pneumonia, pharyngitis and increased mortality, scientists fused a *Pseudomonas*-specific targeting moiety (KH) to a general killing peptide (novispirin G10). The resulting peptide, G10KHc, selectively eliminated *Pseudomonas* from mixed cultures and showed enhanced antibacterial activity and faster and longer-lasting killing action against *Pseudomonas* compared to G10 alone.

“This work lays a foundation for generating additional target-specific ‘smart’ antimicrobials as an alternative to currently available conventional antibiotics,” said Dr. Wenyuan Shi, professor and chair of the section of oral biology at the UCLA School of Dentistry.

Where broad-spectrum killing or general mechanical removal disrupts the normal flora, possibly leading to post-treatment complications or recolonization by the pathogen, target-specific peptides like the one developed at UCLA produce no collateral damage and are expected to be especially suitable for infections of the mucous membranes including the mouth, vagina, gastrointestinal tract, esophageal tract and respiratory tract.

Shi suggests that in the future, based on this research, STAMPs could be generated against any undesired bacterium or group of bacteria, a particularly appealing concept as some chronic infections are caused by multiple microorganisms rather than a single species. Further, an exceptionally resilient species could be targeted with a combination of antimicrobial peptides present on one STAMP molecule.

“The work performed in Dr. Shi’s laboratory will help transform the concept of targeted antimicrobial therapy into a reality. We are proud that UCLA will become known as the birthplace of this significant treatment innovation,” said Dr. No-Hee Park, dean of the UCLA School of Dentistry.

Antimicrobial treatment using STAMP technology is expected to be available for clinical use in five to seven years.

“We are excited about the commercial potential of STAMP technology and are seeking worldwide patent coverage for this groundbreaking discovery,” said Emily Loughran, director of licensing for UCLA’s Office of Intellectual Property Administration.

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Other authors of the paper include Randal Eckert, Fengxia Qi, Daniel K. Yarbrough, Jian He and Maxwell H. Anderson.

The UCLA School of Dentistry is dedicated to improving the oral health of the people of California, the nation and the world, and has established an international reputation for its teaching, research, patient care and public service initiatives. The school provides education and training programs that develop leaders in dental education, research, the profession and the community; conducts research programs that generate new knowledge, promote oral health, and investigate the cause, prevention, diagnosis and treatment of oral disease; and delivers patient-centered oral health care to the community and state. For more information, visit http://uclasod.dent.ucla.edu.

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