Medical Xpress

'Conversation stoppers' fight deadly bacterial infections

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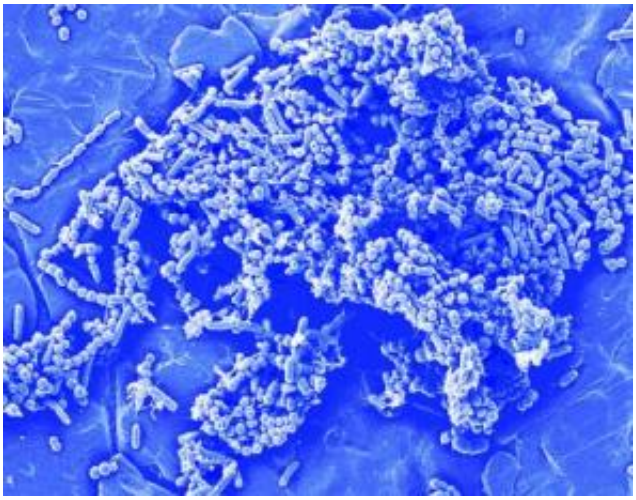

Bacteria can aggregate and produce dangerous biofilms that make them physically resistant to antibiotics. Researchers at the University of Wisconsin-Madison have designed a group of compounds that show promise for blocking biofilm formation, a strategy that could one day result in new drugs to fight infections. Credit: (Photo courtesy of USDA Agricultural Research Service)

Bacterial infections are becoming more deadly worldwide due to increased resistance to antibiotics. Now, chemists at the University of Wisconsin-Madison have developed a powerful strategy to fight these deadly infections: Instead of killing the bacteria directly, the scientists designed a group of compounds that can block the chemical signals that the bacteria use to communicate in an effort to stop their spread.

These compounds, small organic molecules that they call 'conversation stoppers,' could help deliver a powerful one-two punch to knock out deadly infections when combined with the killing power of antibiotics, the scientists say. In addition, these 'conversation stoppers' do not target bacterial growth, so the potential for the development of bacterial resistance is minimized. This research, which is funded by the National Institutes of Health, could lead to new drugs to fight infections, was described yesterday at the 232nd national meeting of the American Chemical Society.

"There is an urgent, global need for new antibacterial therapies," says study leader Helen Blackwell, Ph.D., an assistant professor of chemistry at the University. "The ability to interfere with bacterial virulence by intercepting bacterial communication networks represents a new therapeutic approach and is clinically timely."

Bacteria use chemical signals to initiate the majority of human infections. When these signals reach a certain threshold (in a process known as quorum sensing), pathogenic bacteria will change their mode of growth and produce virulence factors that lead to infection. These chemical signals also trigger the bacteria to produce slimy biofilms that cloak the bacteria and make the colony physically resistant to antibiotics.

Attempts to block bacterial quorum sensing are being conducted by a growing number of research groups. Many of these studies have focused on a group of small molecules called N-acylated L-homoserine lactones (AHLs), which are key signaling molecules used by Gram-negative bacteria.

But discovery of these molecules has been a relatively slow process until now. Blackwell and her associates have found that the use of 'microwave-assisted chemistry,' a novel laboratory technique for heating chemical reactions using microwaves, can dramatically accelerate the synthesis of

AHL analogs that can either block or stimulate bacterial communication.

"Using microwave heating and combinatorial techniques to generate libraries of molecules, we can now produce and test in one day a group of compounds that previously would have taken a month to study using conventional techniques," Blackwell says.

So far, the researchers have identified at least two compounds that show particular promise at blocking biofilm formation in Pseudomonas aeruginosa, a bacterium that is a common cause of death in people with cystic fibrosis, AIDS and severe burns. In collaborative research with Fred Ausubel, Ph.D., a molecular biologist at Massachusetts General Hospital in Boston, Blackwell and her colleagues demonstrated that several of these compounds can extend the lives of worms infected with P. aeruginosa.

Recently, Blackwell designed 'conversation stoppers' that are specific to one bacterial strain and not others, allowing more efficient, selective attack on specific bacterial strains. This selectivity can help avoid disrupting beneficial bacteria, such as those in the gut that aid digestion, she says.

Some 'conversation stoppers' also hold promise for fighting crop diseases, biofilm formation on medical implants and catheters, and even bioterror agents. More studies are needed, says Blackwell, adding that her compounds haven't been tested in humans or plants but says that those tests are anticipated.

Source: American Chemical Society