Compounds shown to thwart stubborn pathogen's social propensity

August 21 2012, by Terry Devitt

Acinetobacter baumanni, a pathogenic bacterium that is a poster child of deadly hospital acquired infections, is one tough customer.

It resists most antibiotics, is seemingly immune to disinfectants, and can survive desiccation with ease. Indeed, the prevalence with which it infects soldiers wounded in Iraq earned it the nickname "Iraqibacter."

In the United States, it is the bane of hospitals, opportunistically infecting patients through open wounds, catheters and breathing tubes. Some estimates suggest it kills tens of thousands of people annually.

But like many species of bacteria, *A. baumanni* is a social creature. In order to unleash its pathogenic potential, current research suggests that it must accumulate into large colonies or aggregate into "biofilms." To do this, it uses a microbial trick called quorum sensing, where chemical signals are used by the bacterium to gather and sense a critical mass of cells, which then act in unison to exert virulence, which in human patients can manifest itself in the form of pneumonia as well as urinary tract and blood infections.

Interfering with the quorum sensing behavior, some scientists think, may prove to be the Achilles heel of *A. baumanni* and other microbial pathogens, and new research by chemists at the University of Wisconsin-Madison now gives traction to that idea.

In a study by UW-Madison chemistry Professor Helen Blackwell and her

colleagues, and published online in the journal *ACS* Chemical Biology, certain small molecule chemicals that can disrupt quorum sensing in *A. baumanni* have been identified, providing a glimmer of hope that the stubborn pathogen can be tamed.

"Right now, there are no approved drugs out there to modulate (quorum sensing), explains Blackwell, a leading expert on the phenomenon in microbes. "The strategy is not to kill the bacterium, but to keep it from behaving badly."

Blackwell explains that *A. baumanni* and other bacterial pathogens behave differently once a certain population threshold is crossed: "When working as a group, they initiate behaviors different from those observed in an individual cell. They have the ability to take on more complex tasks, and many pathogens use quorum sensing to initiate certain group behaviors."

In *A. baumanni* and other troublesome microbes, those behaviors include increased virulence and the ability to form biofilms, a state that in *A. baumanni* is linked it its ability to persist on surfaces, sometimes for weeks at a time, and withstand antibiotic treatment.

Quorum sensing is governed by chemical signaling, notes Blackwell. Bacteria can get a sense of how many cells have gathered by assessing the concentration of chemical signals that they emit. By interfering with those signals, it may be possible to control behaviors such as biofilm formation and movement and thereby limit the virulence of *A. baumanni*.

"The way a quorum sensing modulator would work is that it wouldn't kill (the microbes), it would just just keep them from behaving badly," says Blackwell.

Combing libraries of potential quorum sensing modulators, Blackwell and her colleagues have identified a handful of compounds that effectively disrupt the signaling pathway *A. baumanni* depends on.

Although the compounds look promising, Blackwell emphasizes that they will likely find their first use in the lab as research tools. Quorum sensing is still not well understood, she explains, and much more research needs to be done before these compounds or others can be deployed in hospitals and other settings to disrupt deadly pathogens.

However, Blackwell expressed confidence that more such quorum sensing compounds remain to be found and next-generation agents may then be ready to tackle pathogens that are rapidly evolving resistance to our best drugs.

Provided by University of Wisconsin-Madison

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