Chemists find new compounds to curb staph infection

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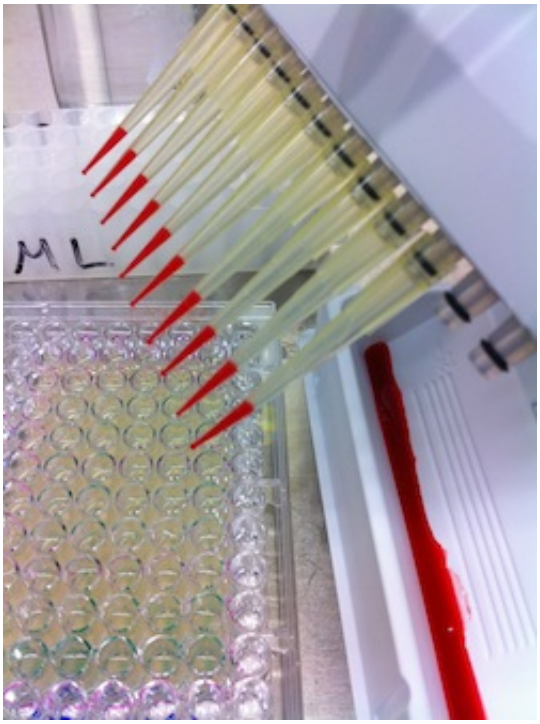

These assays were used to assess the effects of new agents to disrupt communication among pathogenic staph bacteria. Research shows promise for a new approach to thwarting staph infections, which are increasingly resistant to conventional antibiotics. Credit: Blackwell Lab

(Phys.org) —In an age when microbial pathogens are growing increasingly resistant to the conventional antibiotics used to tamp down infection, a team of Wisconsin scientists has synthesized a potent new class of compounds capable of curbing the bacteria that cause staph

infections.

Writing online in the *Journal of the American Chemical Society*, a group led by University of Wisconsin-Madison chemistry professor Helen Blackwell describes agents that effectively interfere with the "quorum sensing" behavior of Staphylococcus aureus, a bacterium at the root of a host of human infections ranging from acne to life-threatening conditions such as pneumonia, toxic shock syndrome and sepsis.

"It's a whole new world for us," says Blackwell, whose group identified peptide-based signaling molecules that effectively outcompete the native molecules the bacterium uses to communicate and activate the genes that cause disease.

Bacteria use quorum sensing to assess their population density and coordinate certain behaviors. They do so through the use of pheromone-like chemicals, which bind to receptors either in the bacterial cell or on its surface and tell it if there are enough companion bacteria around to switch on genes that perform certain functions. In the case of Staphylococcus aureus, quorum sensing activates toxin production, manifesting disease in the host.

Interfering with bacterial quorum sensing to stymie disease is considered a promising new antibiotic strategy, says Blackwell. Staph, she adds, is an excellent target as the bacterium is not only a prevalent pathogen, but some strains, notably methicillin-resistant Staphylococcus aureus or MRSA, have developed resistance to commonly used antibiotics such as penicillin and its derivatives.

The new compounds synthesized by Blackwell and her colleagues are peptides that work at very low concentrations by blocking the chemical receptors the bacterium uses to regulate quorum sensing. The new agents devised by Blackwell and her group work on the four subtypes of staph,

all of which use different quorum sensing signals and are found in different infection types.

"We had not worked much in this area because the (signaling molecules) are somewhat challenging to synthesize," explains Blackwell. "We now have developed methods to make these molecules and analogs much more efficiently, which helped fuel this new study."

For now, the compounds devised by the Wisconsin team will have their greatest impact in the lab as research probes to further study the role of quorum sensing in Staphylococcus aureus. In addition, the gritty details of how these synthetic agents work in the cell need to be determined in order to optimize their potential use in both the lab and clinic. Such studies are ongoing.

"The impact of these new peptides could be significant because staph is an important and increasingly scary pathogen. There is plenty of scope," notes Blackwell.

Provided by University of Wisconsin-Madison