Therapeutics & Vaccines

Treating Staph Infections, Toxic Shock Syndrome by Disrupting Bacteria Quorum Sensing

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WARF: P130070US02

Inventors: Helen Blackwell, Danielle Wittenwyler, Yiftah Tal Gan

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing compounds that weaken the infectivity of *Staphylococcus* bacteria by targeting their AgrC receptors.

Overview

'Staph' infections, particularly by *Staphylococcus aureus* strains, can cause skin ailments and more serious conditions like heart valve inflammation and toxic shock syndrome. These strains also are the leading cause of infections caught in hospitals. The pathogen's resistance to antibiotics, including the 'last resort' drug vancomycin, is very troubling.

An alternative strategy to fight these strains targets their quorum sensing (QS) ability. QS is a chemical signaling process used by many types of bacteria that allows them to 'count' themselves and behave as a group. The process involves bacteria secreting and detecting signal molecules that then bind to their cellular receptors and spur them to express genes involved in sporulation, conjugation, biofilm formation and the production of virulence factors.

S. aureus uses QS to launch an infection. Specifically, the job of regulating tissue-degrading enzymes, toxins and other weapons involves four AgrC signal receptors. Interfering with these receptors would undermine bacteria coordination and thereby inhibit virulence. Such anti-virulence strategies are some of the most exciting new ways to control bacterial infection that have emerged over the past decade.

The Invention

UW–Madison researchers have synthesized new peptide-based compounds that can strongly inhibit or activate the AgrC receptors of *Staphylococcus*.

The compounds are structural variants of the AIP-III cyclic peptide that are produced naturally by the bacteria. The compounds interfere with quorum sensing by inhibiting the AgrC receptor. *S. aureus* strains can be categorized into four groups depending on the different AgrC receptor that they possess; these different groups are found in different infection types.

Several of the new cyclic peptides are capable of inhibiting all four of the known AgrC receptors, and thereby represent pan-active quorum sensing inhibitors in all groups of staph. Antibiotics may be combined with the compounds to further augment their ability to help treat infections.

Applications

- Treating *Staphylococcus* infections, including those strains that produced toxic shock syndrome (group-III)
- Inhibiting or dispersing *Staphylococcus* biofilms

Key Benefits

- Uniquely targets the QS pathway and inhibits AgrC receptors with picomolar IC_{50} values
- Reduces production of virulence factors and toxins involved in infection, including the toxin responsible for toxic shock syndrome, by more than 80 percent
- Increases the susceptibility of bacteria to antibiotics by targeting biofilm formation
- Could decrease cost of treating bacterial infections involving biofilms, which exceeds $1 billion per year in the U.S.

Additional Information

For More Information About the Inventors

- Helen Blackwell

Related Technologies

- For more information about targeting bacteria quorum sensing to fight biofilm and infection, see WARF reference number P05282US.
- For more information about novel antimicrobial agents that modulate quorum sensing and are effective at physiological pH, see WARF reference number P09045US02.

Publications

- Tal-Gan et al. 2013. Highly Potent Inhibitors of Quorum Sensing in Staphylococcus aureus Revealed Through a Systematic Synthetic Study of the Group-III Autoinducing Peptide. J. Am. Chem. Soc., 135, 7869–7882.

Tech Fields

- Therapeutics & Vaccines : Anti-infectives (antibacterials, antifungals, antivirals)

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847