



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Anti-infective Studies

Novel Antimicrobial Peptides as Topical Anti-infectives Against Combat-related Bacterial and Fungal Wound Infections

Therapeutic interventions for ballistic wound infections (BWIs) are limited by the increasing number of multidrug resistant pathogens, antibiotic/antimycotic side effects and poor wound penetration. Thus, investigators at Riptide Biosciences, Inc. (Mare-Island-Vallejo, CA) developed designed antimicrobial peptides (dAMPs) to address the challenges present in the treatment of BWIs (*D'Avignon et al., 2008; Horvath EE, et al., 2007*).

dAMPs are based on naturally occurring antimicrobics. Over 30 dAMPs were synthesized and evaluated for their antimicrobial potency against several bacterial and fungal strains. Time-kill assays against bacteria *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Staphylococcus aureus* (*S. aureus*) were utilized as an early screen for microbial reduction by the peptides. Promising dAMPs were then evaluated to determine the lowest concentration required to inhibit growth of the strains. The time-kill assays illustrated that the dAMPs successfully destroy pathogens, and toxicity assays demonstrated that therapeutic levels were not toxic (*Clemens et al., 2017*). The curative potential of three dAMPs (RP504, RP554, and RP557) was evaluated in a pig burn wound model infected with *P. aeruginosa* and *S. aureus* with RP557 yielding remarkable activity. RP557 is now entering Investigative New Drug (IND)-enabling studies.

The clinical implementation of dAMPs could be an innovative method of dealing with antibiotic resistance while providing a new broad-spectrum treatment against biofilms, fungi, and drug-resistant bacterial and fungal infections associated with BWIs, thus reducing the chances for systemic and fatal infections in patients.

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