

COMBATting FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

Limiting Biothreat Exposure With A Novel Purified Bioactive Lactoferrin As A Multifunctional Countermeasure In Battlefield Wounds

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Battlefield exposure to biological agents is exacerbated by open wounds, polytrauma, and human orifices. We suggest key factors of the mammalian innate immune system can be used to develop host-directed medical countermeasures by utilizing their multifunctional modes of action. These activities promote wound repair and regeneration through immunomodulatory and anti-inflammatory actions while also displaying broad anti-virulent activities by inhibiting the formation of bacterial and fungal biofilms and limiting viral cellular entry. Lactoferrin is one of the most potent mammalian immune proteins and has shown promise through extensive publication, however its translation and commercialization has been fundamentally limited by a lack of suitable industrial-scale isolation and purification technologies to develop a pharmaceutical-grade effective active ingredient. Lactea Therapeutics and its affiliates have developed a novel, patent-pending technology to purify naturally derived bovine lactoferrin (Lactea-Lf) in a native ultrapure active state for use as a medical countermeasure. In biofilm studies, Lactea-Lf demonstrates potent *in vitro* activity against *E. coli*, *P. aeruginosa*, *K. pneumonia*, MRSA, *Candida spp.* and *C. neoformans*. Interestingly, for all tested species, Lactea-Lf exhibits a lower dosage dependence for biofilm inhibition than total growth elimination allowing it to potentially synergize with other antimicrobials. In addition to this anti-biofilm efficacy, Lactea-Lf was found to expedite wound repair and regeneration versus standards of care (Bacitracin and Silver sulfadiazine) in a large-scale partial-thickness comparative wound study. Pigs treated with Lactea-Lf approached stage 3 wound progression within 24hrs while the standards of care remained in stage 2 at day 7. In early clinical testing, Lactea-Lf has been used successfully to treat and heal multiple chronic wounds, including in patients with comorbidities, and those with chronic *P. aeruginosa* infections. Lactea's research has been strengthened by further *in vitro* bacterial biothreat (*F. tularensis* and *B. mallei*) and *in vivo* viral biothreat (EEV) research at USAMRIID which has preliminarily demonstrated dose dependent success in potentially treating these major biothreats. Future studies have been planned with USAMRIID for their priority pathogens, as well as with USAMRICD, to evaluate ocular wound repair from chemical threats. Based on the data to date, Lactea-Lf has the potential to be distributed in a shelf-stable, safe, self and buddy application to broadly reduce biological biothreat infiltration of battlefield wounds while expediting wound closure to enhance the rapid recovery of the warfighter.

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