WOUND HEALING – NEW TREATMENT

Researchers in Lund have developed a treating gel using natural mechanisms to prevent and treat wound infections. This study has been published in Science Translational Medicine and has already been highly noticed.

A dual-action peptide-containing hydrogel targets wound infection and inflammation.

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Abstract

There is a clinical need for improved wound treatments that prevent both infection and excessive inflammation. TCP-25, a thrombin-derived peptide, is antibacterial and scavenges pathogen-associated molecular patterns (PAMPs), such as lipopolysaccharide, thereby preventing CD14 interaction and Toll-like receptor dimerization, leading to reduced downstream immune activation. Here, we describe the development of a hydrogel formulation that was functionalized with TCP-25 to target bacteria and associated PAMP-induced inflammation. *In vitro* studies determined the polymer prerequisites for such TCP-25-mediated dual action, favoring the use of noncharged hydrophilic hydrogels, which enabled peptide conformational changes and LPS binding. The TCP-25-functionalized hydrogels killed Gram-positive Staphylococcus aureus and Gram-negative *Pseudomonas aeruginosa* bacteria *in vitro*, as well as in experimental mouse models of subcutaneous infection. The TCP-25 hydrogel also mediated reduction of LPS-induced local inflammatory responses, as demonstrated by analysis of local cytokine production and *in vivo* bioimaging using nuclear factor κB (NF-κB) reporter mice. In porcine partial thickness wound models, TCP-25 prevented infection with *S. aureus* and reduced concentrations of proinflammatory cytokines. Proteolytic fragmentation of TCP-25 *in vitro* yielded a series of bioactive TCP fragments that were identical or similar to those present in wounds *in vivo*. Together, the results demonstrate the therapeutic potential of TCP-25 hydrogel, a wound treatment based on the body's peptide defense, for prevention of both bacterial infection and the accompanying inflammation.

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