Bioactive peptides found to promote wound healing

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Newly-created bioactive peptides promote wound healing through the growth of new blood vessels and epithelial tissue, such as skin. These wound-healing peptides, synthesized by researchers at the Tufts Center for Innovations in Wound Healing Research, increased angiogenesis in vitro by 200 percent. The discovery, reported online in advance of print this week in *Wound Repair and Regeneration*, provides a better understanding of the mechanisms regulating wound healing and may lead to new therapies for acute and chronic wound healing.

"We identified specific bioactive peptides that are produced from collagenase treatment of extracellular matrix, which stimulate the healing process within a wound. By creating combinations of several key peptide fragments, we were able to synthesize an entirely novel class of wound-healing peptides that promote the fundamental response to injury: blood vessel formation and epithelialization," said senior author Ira Herman, PhD, a professor of molecular physiology and pharmacology at TUSM; member of the cell, molecular & developmental biology, and cellular & molecular physiology program faculties at the Sackler School of Graduate Biomedical Sciences; and director, Tufts Center for Innovations in Wound Healing Research.

"This is the first time these peptides have been identified and synthesized and we hope that these discoveries and new technologies will have broad implications for acute, chronic, burn, and scarless wound healing," Herman continued.

The team from Tufts used a three-dimensional wound model to examine the effect of the bioactive peptides on wound healing. After three days, wounds treated with the peptides showed signs of robust repair, while controls did not.

"We found that collagenase enzyme derived from Clostridium histolyticum bacteria releases biologically active fragments – peptides – from extracellular mammalian proteins. These peptides stimulate proliferation of capillary endothelial cells, enhance microvascular remodeling in the 2-D model, and induce endothelial sprouting in a 3-D model of injury repair, and therefore are likely to have potential to stimulate blood vessel formation and promote healing in response to injury in animals and humans," said first author Tatiana Demidova-Rice, BS, a PhD candidate in the cell, molecular and developmental biology program at the Sackler School of Graduate Biomedical Sciences at Tufts.

Angiogenesis, the formation of new blood vessels from existing vessels, is a key step in all types of wound healing from knee scrapes to venous stasis ulcers, pressure sores and diabetic foot ulcers. In order for tissues to be repaired, there must be an adequate blood supply bringing nutrients, oxygen, and signaling molecules to the site of the injury. Collageneses are enzymes that remodel extracellular matrix by cleaving one of its key components, collagen.

"The most potent wound-healing peptide is a 'combinatorial' peptide synthesized from bioactive fragments derived from the collagenase treatment of biosynthesized matrix. Outcomes of these studies suggest that it could be possible to create personalized regenerative medicine-based wound healing therapies and platforms that would be tailored to individuals. We are currently testing the efficacy of these fragments in an effort to develop better treatments for wound healing. Formulation of the bioactive peptides into heat-stable and portable materials could be of

extreme value to soldiers injured in combat," said Herman.

As director of the Tufts Center for Innovations in Wound Healing Research (TIWR), Herman brings together investigators from a broad range of disciplines to advance wound healing research and therapeutics. Researchers combine recent insights and advances in wound-healing biology, materials sciences, and bioengineering to create fully-vascularized organ constructs for personalized regenerative medicine, while offering new and innovative opportunities for drug screening, discovery and development. TIWR investigators are currently developing cutting-edge technologies in biomaterials sciences and nano-fabrication processing to create personalized wound healing therapeutics, including "next generation" wound care products for civilian and soldier use.

More information: Demidova-Rice TN, Geevarghese A, Herman IM. Wound Repair and Regeneration. " Bioactive peptides derived from vascular endothelial cell extracellular matrices promote microvascular morphogenesis and wound healing in vitro." Published online December 6, 2010, doi:10.1111/j.1524-475X.2010.00642.x

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