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Novel extracellular matrix-derived peptides promote wound healing and tissue regeneration

Ira M Herman
Tufts University School of Medicine, USA

Recently, our work has revealed that clostridial collagenase stimulates extracellular matrix remodeling along with epithelial and vascular cell injury responses while promoting impaired wound healing *in vivo*. Herein, we will review published findings and preliminary work yet to be published, which demonstrate that bacterial collagenase promotes wound healing responses by elaborating bioactive matrix fragments that stimulate epithelial, fibroblastic and angiogenic responses to injury. To these ends, we performed limited digestions of defined human dermal capillary-derived endothelial (HMVEC) and human fibroblast (HF)-derived extracellular matrices while MS/MS mass spectrometry was used to reveal several collagenase-generated matrix fragments derived from collagen and or collagen-associated proteins. Chemical synthesis and re-combination of some of these bioactive peptides were then used in several cells and animal-based wound healing assays to ascertain whether one or another peptide could activate cellular responses to injury *in vitro* and impaired wound healing *in vivo*. Results reveal that several peptides discovered significantly promote cell proliferation and angiogenesis *in vitro* and stimulate impaired wound healing *in vivo*. These findings indicate that collagenase indirectly possesses wound healing activity by the creation of bioactive peptides and that these wound healing peptides can convert non-healing wounds into those capable of closure.

ira.herman@tufts.edu