A MODIFIED COLLAGEN GEL DRESSING PROMOTES ANGIOGENESIS IN A PRE-CLINICAL SWINE MODEL OF CHRONIC ISCHEMIC WOUNDS

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Introduction: We recently performed proteomic characterization of a modified collagen gel (MCG) dressing and reported promising effects of the gel in healing full-thickness excisional wounds. In this work, we test the translational relevance of our aforesaid findings by testing the dressing in a swine model of chronic ischemic wounds recently reported by our laboratory. Full thickness excisional wounds were established in the center of bi-pedicle ischemic skin flaps on the backs of animals. Ischemia was verified by Laser Doppler imaging and MCG was applied to the test group of wounds. Seven days post-wounding, macrophage recruitment to the wound was significantly higher in MCG-treated ischemic wounds. In vitro, MCG up-regulated expression of Mrc-1 (a reparative M2 macrophage marker) and induced the expression of anti-inflammatory cytokine IL-10 and of β-FGF. Furthermore, analyses of wound tissues 7 days post wounding showed up-regulation of TGF-β, VEGF, vWF, and collagen type I expression in MCG-treated ischemic wounds. At 21 days post-wounding, MCG-treated ischemic wounds displayed higher abundance of proliferating endothelial cells that formed mature vascular structures and increased blood flow to the wound. Fibroblast count was markedly higher in MCG-treated ischemic wound-edge tissue. In addition, MCG-treated wound-edge tissues displayed higher abundance of mature collagen with increased collagen type I:III deposition. Taken together, MCG helped mount a more robust inflammatory response which resolved in a timely manner, followed by an enhanced proliferative phase, angiogenic outcome and post-wound tissue remodeling. Findings of the current study warrant clinical testing of MCG in a setting of ischemic chronic wounds.