037

Wnt signaling modulation in chronic wounds

Canonical Wnt signaling pathway is quiescent in many mammalian organs and gets activated in response to injury. Wnt signaling promotes fibrotic wound healing following acute cutaneous injury by epithelial migration, differentiation and myofibroblast activation. Topical application of Wnt signaling inhibitor promotes regenerative cutaneous repair. To study Wnt signaling modulation in chronic wound repair, we created wounds in STZ-induced type I diabetes C57Bl/6J mouse model. Full thickness excisional wounds activated Wnt signaling in both dermal and epidermal layers identified by beta-catenin immunohistological staining and axin2 transcript levels. Topical application of a small molecule Wnt signaling inhibitor significantly promoted regenerative wound healing in full thickness excisional wound injury models. We provided strong positive implications of Wnt pathway inhibition during chronic cutaneous wound repair in animal models. However, there is a large gap in our understanding of Wnt signaling activation in chronic non-healing human wounds. To understand chronic wound pathologies in humans, we obtained de-identified human wound biopsies from Vanderbilt University Medical Center. Human chronic wound pathologies which include diabetic ulcer, keloids, hypertrophic scars, and melanoma re-excision wounds to screen for fibrosis, collagen deposition and beta-catenin (Wnt signaling) activation. We aim to identify Wnt dependent or independent chronic wound pathologies. Our preliminary results identified that not all chronic wounds are driven by Wnt activation. While hypertrophic scars and decubitus ulcers showed significant Wnt activation, beta catenin activity was not identified in wounds such as keloids. This understanding is crucial to establish a correlation between Wnt signaling activation and chronic non-healing wounds. Our future studies are focused on the identification of the cell types regulated by Wnt activation in vivo and in vitro. Our studies will pave the way to use Wnt signaling inhibitors for selective personalized therapy for chronic wounds.