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Wnt signaling modulation in chronic wounds

Abstract

Wnt signaling is activated following acute cutaneous injury and promotes fibrotic wound healing. Topical application of Wnt signaling inhibitor promotes regenerative cutaneous repair. We utilized STZ-induced type I diabetes C57Bl/6J mouse model to study chronic wound repair. Full thickness excisional wounds activated Wnt signaling in both dermal and epidermal layers identified by beta-catenin immune-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 model. 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 human, we studied Wnt signaling in de-identified human wound biopsies obtained from Vanderbilt. Human chronic wound pathologies including diabetic ulcer, keloids, hypertrophic scars, and melanoma were screened for beta-catenin immunostaining. We found variability in the level of Wnt signaling activation in different chronic wound pathologies. This understanding is crucial to establish a correlation between Wnt signaling activation and chronic non-healing wounds. Our studies will pave the way to use Wnt signaling inhibitors for **selective personalized therapy** for chronic wounds.