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LIPS

Title: Wnt signaling inhibition promotes wound healing and inhibits fibrosis in chronic wounds

Wnt signaling is activated following acute cutaneous injury and promotes fibrotic wound healing. Topical application of Wnt signaling inhibitors promote regenerative cutaneous repair following acute injury. However, there is a gap in our understanding of Wnt signaling activation in chronic non-healing human wounds. This work is focused on delineating the impact of canonical Wnt signaling modulation in chronic wounds. Preliminary studies in our lab have shown that full thickness excisional wounds in Streptozotocin (STZ)-induced type I diabetic mice activated Wnt signaling in both dermal and epidermal layers identified by β-catenin immunostaining and AXIN 2 transcript levels. Treatment with Wnt signaling inhibitors promoted regenerative repair following excisional wound. Analysis of a panel of human chronic wound pathologies demonstrated differential expression of β-catenin in different chronic wounds. To understand the cellular mechanism of Wnt signaling modulation in Wnt-responsive chronic wounds, we treated human diabetic fibroblasts with Wnt signaling inhibitors and performed Western blot analysis for active β-catenin protein. Wnt signaling inhibitors ICG-001 and XAV-939 inhibited the expression of a pro-fibrotic protein, Collagen 1α1 together with active β-catenin. Future work will focus on analyzing the functional effect of Wnt signaling inhibitors on diabetic fibroblasts. These results suggest that Wnt signaling inhibitors could be utilized for the treatment of Wnt-responsive chronic wounds. Our goal is to identify the cellular and molecular players of fibrotic wound healing that can be modulated by Wnt signaling inhibitors. Our studies will pave the way to use Wnt signaling inhibitors for selective personalized therapy for chronic wounds.