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Title of Presentation: Identifying Keratinocyte Derived Collagen Inhibitory Factors to Treat Hypertrophic Scar and Keloid

Abstract

Two extremes of the wound healing process represent serious pathologic conditions: non-healing and over-healing. There exist a multitude of strategies that effectively address early stages of wound healing; however, there are no specific modalities to target or signal wound healing cessation. Consequently, patients continue to deposit matrix long after the wound has technically healed. Over healing such as post-burn hypertrophic scarring (HSc) and keloid are disfiguring and devastating, resulting in bulky, itchy and inelastic scars that pose serious functional and cosmetic problems for recovering burn patients. Our working hypothesis has been that mesenchymal-epithelial communication is critical in exchanging information between keratinocytes and fibroblasts. Keratinocyte releasable factors function as either stop signals at the late-stage of wound healing or by modulating the expression of key Extra-Cellular Matrix (ECM) components.

Our working hypothesis has been that keratinocyte releasable factors should function as either stop signals at the late-stage of wound healing or by modulating the expression of key ECM components (collagen type I and type III) and proteolytic enzymes (such as collagenase (MMP-1)) in dermal fibroblasts.

To test this hypothesis, we established a keratinocyte/fibroblast co-culture in-vitro model, and have since identified two sets of keratinocyte releasable anti-fibrogenic factors for dermal fibroblasts. The 1st set of these factors stimulate the expression of MMPS (MMP-1, 3, 8 and 24) while the 2nd set of the factors suppresses the expression of key ECM components such as type I and III collagen.

In tandem these two sets of factors stand to elucidate a clear picture of how to regulate, slow down or stop wound healing in such a way to improve/prevent hypertrophic scars and keloid. As such, the main goal of this study is to identify these keratinocyte releasable anti-fibrogenic factors, their motifs, functionality and their therapeutic benefits in wound healing.