Abstract:

Hypothesis and Objective: Tissue injury leads to extensive extracellular matrix (ECM) changes throughout the wound healing process. MFAP5 is a 25 kD serine and threonine rich small microfibril-associated protein, involved in the regulation of major ECM pathways and microfibril function. Interestingly, the role MFAP5 plays in the wound healing process is currently unknown. This study was undertaken to identify the genes that are most differentially expressed between skin and oral mucosa as related to wound healing and fibrosis. **Methods:** Previously available human gene array data from scar-forming skin wounds and minimally scarring oral wounds was utilized to investigate the differential expression of genes that are closely related to wound healing and fibrosis in these alternate healing phenotypes. In addition, MFAP5 was directly examined to investigate its role in wound healing. A murine model of full-thickness excisional skin wounds was employed, and the effect of MFAP5 neutralization on healing was assessed. Mice were randomly assigned to three wound treatment groups: phosphate-buffered saline (PBS), immunoglobulin G (IgG), and anti-MFAP5 antibodies. Histologic wound samples were stained with Masson's Trichrome and Picrosirius stains, and AxioVision software was used to quantify collagen deposition and the ratio of mature/immature collagen, respectively. Data was analyzed by 2-way ANOVA and multiple t-test. **Results:** It was found that in humans, MFAP5 expression was significantly higher in skin versus oral wounds at baseline and throughout the course of wound healing. Furthermore, in the murine model, antibody neutralization of MFAP5 *in vivo* led to decreased collagen deposition with lower mature collagen and significantly higher immature collagen when compared to the control groups. **Conclusion:** These results suggest that MFAP5 promotes collagen deposition during wound healing in skin *in vivo*. Therefore, the production of MFAP5 may have significant implications for scar formation in skin and other fibrotic conditions.