INFLAMMATORY SKIN DISEASES (OTHER THAN ATOPIC DERMATITIS & PSORIASIS)

THE ANTIMICROBIAL PROTEIN REG3A IN INFLAMMATORY SKIN DISEASES

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A well-controlled and coordinated balance between immune defense and epithelial cell proliferation is essential to normal wound healing. Our group has identified the antimicrobial protein regenerating islet-derived protein 3A (REG3A) as a key coordinator of skin homeostasis and revealed that aberrant expression of REG3A leads to delayed wound healing in diabetes or the skin disorder psoriasis. REG3A is induced by IL-17, IL-36 and IL-33 after skin injury and feeds back on keratinocytes to inhibit terminal differentiation and increase cell proliferation, thus promoting wound healing. However, the profound expression of IL-17 and IL-36 in lesional skin of psoriasis patients leads to excessive expression of REG3A, which induces the epidermal hyperproliferation in psoriasis. In contrast, the decreased IL-17-induced IL-33 by hyperglycemia reduces REG3A in skin wounds of diabetes. The reduction in REG3A is associated with lower levels of SHP-1, which normally inhibits TLR3-induced JNK2 phosphorylation, thereby increasing inflammation in skin wounds and delaying wound healing in diabetes. Altogether, these data support that REG3A is a crucial modulator for epidermal homeostasis, repair, and disease. The aberrant expression of REG3A amplifies cell proliferation in psoriasis or inflammation in diabetic skin wounds, and may be a previously unknown key element in the pathogenesis of psoriasis and unhealed wounds of diabetic individuals.