Potential role of nerve cells in pathogenic wound healing induced by stretching stimulation

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Cutaneous wound healing generally leads to mature scars. It involves precise and complicated interactions between multiple cell types, including fibroblasts, inflammatory cells, and vascular endothelial cells, and derangements in these processes can induce abnormally growing scars such as keloids. A possible cause of these derangements is mechanical tension on the wound/scar: this tension is thought to partly promote pathogenic scarring by stimulating fibroblasts to lay down abundant extracellular matrix. Another relevant cellular player in normal and abnormal cutaneous wound healing may be nerve cells, because nerve fibers are widely distributed in the superficial skin layer of skin and the factors that they produce are known to alter the behavior of other cells. However, the roles of nerves in wound healing and keloid formation/progression remain poorly understood. To investigate whether nerve cells can modulate the ability of mechanical tension to promote fibroblast activity, the neuronal PC12 cell line was co-cultured with rat dermal fibroblasts in a cyclic stretch chamber. Indeed, when the co-cultures were stretched, PC12 cells bearing neurites promoted the differentiation of dermal fibroblasts. Interestingly, the differentiated fibroblasts conversely promoted the elongation of the neural fibers of the PC12 cells. Thus, nerve cells and fibroblasts may interact to promote wound healing, and this interaction is mediated by stretching stimulation. Further research on the roles of nerves in wound healing is needed.