Synopsis of Original Research Paper

Comprehensive studies on the expression and working mechanisms of angiogenic cytokines in human skin

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Background: Vascular endothelial growth factor (VEGF) induces proliferation of endothelial cells and in vivo angiogenesis. The regulation of the secretion of VEGF from human skin fibroblasts has not been well investigated, although paracrine interactions between fibroblasts and endothelial cells have been suggested to play a key role in granulation tissue formation. Objective: To explore the significance of human skin fibroblasts as a source of VEGF in granulation tissue formation. Methods: VEGF secreted from cultured human skin fibroblasts was measured by ELISA. VEGF mRNA expression was examined by real-time polymerase chain reaction analysis. Results: Transforming growth factor-β1, platelet-derived growth factor-BB and interleukin-1α strongly up-regulated VEGF secretion from human skin fibroblasts. Epidermal growth factor, transforming growth factor-α, basic fibroblast growth factor, tumor necrosis factor-α and interferon-γ had no significant effects on VEGF secretion. Transforming growth factor-β1, platelet-derived growth factor-BB and interleukin-1α acted synergistically each other. The levels of secreted VEGF after the stimulation of these cytokines were high enough to exert its biological activities. Interferon-γ enhanced interleukin-1a-induced VEGF production but diminished the effect of transforming growth factor-β1. The results of ELISA were confirmed at the mRNA level by real-time polymerase chain reaction analysis, except for the synergistic effect of interferon-γ with interleukin-1α. Conclusions: Fibroblasts could be an important source of VEGF during wound healing. Paracrine interactions between fibroblasts and endothelial cells via VEGF may play a key role in the formation of granulation tissue.