

# Angiogenesis in wound healing.

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## Abstract

During wound healing, angiogenic capillary sprouts invade the fibrin/fibronectin-rich wound clot and within a few days organize into a microvascular network throughout the granulation tissue. As collagen accumulates in the granulation tissue to produce scar, the density of blood vessels diminishes. A dynamic interaction occurs among endothelial cells, angiogenic cytokines, such as FGF, VEGF, TGF-beta, angiopoietin, and mast cell tryptase, and the extracellular matrix (ECM) environment. Specific endothelial cell ECM receptors are critical for these morphogenetic changes in blood vessels during wound repair. In particular, alpha(v)beta3, the integrin receptor for fibrin and fibronectin, appears to be required for wound angiogenesis: alpha(v)beta3 is expressed on the tips of angiogenic capillary sprouts invading the wound clot, and functional inhibitors of alpha(v)beta3 transiently inhibit granulation tissue formation. Recent investigations have shown that the wound ECM can regulate angiogenesis in part by modulating integrin receptor expression. mRNA levels of alpha(v)beta3 in human dermal microvascular endothelial cells either plated on fibronectin or overlaid by fibrin gel were higher than in cells plated on collagen or overlaid by collagen gel. Wound angiogenesis also appears to be regulated by endothelial cell interaction with the specific three-dimensional ECM environment in the wound space. In an in vitro model of human sprout angiogenesis, three-dimensional fibrin gel, simulating early wound clot, but not collagen gel, simulating late granulation tissue, supported capillary sprout formation. Understanding the molecular mechanisms that regulate wound angiogenesis, particularly how ECM modulates ECM receptor and angiogenic factor requirements, may provide new approaches for treating chronic wounds.

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