

EFFECT OF A RECOMBINANT SOLUBLE Dll4-Fc ON FUNCTIONAL ACTIVITY OF ENDOTHELIAL CELLS *IN VITRO* AND VASCULARIZATION *IN VIVO*

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It is well known, that the restoration of the microvasculature system is obligatory during of wound healing processes. Increased angiogenesis in damaged tissue can positively affect the speed and quality of its recovery. In this study, the role of soluble recombinant protein Dll4-Fc in functional activity of HUVEC, HUVEC-56 and ECV-304 in a two-dimensional (2D) and three-dimensional (3D) culture system *in vitro* and capillary network formation during wound healing in rats *in vivo* was investigated. The aim is the possible use of Dll4-Fc in the development of biomedical cell-based products, which could stimulate the growth of blood vessels in damaged organs and tissues. It was shown that in 2D-cultivation system Dll4-Fc does not affect the proliferative and migratory activity of endothelial cells. However, the positive effect of Dll4-Fc on the morphology of the endothelial cell layer and the formation of capillary-like structures was revealed in 3D-cultivation system with ECV-304 cells on the surface of a collagen gel. For the first time, the positive effect of the use of "Equivalent dermal ED" in a composition with HUVEC and Dll4-Fc on the formation of vessels *in vivo* during the healing process was shown.

Keywords: Notch signaling, Dll4-Fc protein, angiogenesis, endothelial cells, dermal fibroblasts, dermal equivalent, tissue engineering