IJAE
Vol. 116, n. 1 (Supplement): 32, 2011
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Endothelial cells and the complement component C1q as novel therapeutic tools for the treatment of chronic ulcers

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One of the major limitation of the current treatments for burns and chronic ulcers is the absence of a rapid functional vascular plexus formation. The impaired angiogenic condition leads to a poor nutritional intake and to increased microbial contamination. To evaluate novel potential therapeutic strategies to improve new vessel formation we set up a method for the isolation of human adult dermal endothelial cells (ADMEC) from skin biopsies. We then evaluated the ability of ADMEC to adhere and to grow into a tridimensional matrix of collagen and of human decellularized dermis. A wound healing model was established in rats to investigate the role of endothelial cells in an in vivo angiogenic process. The data show an increase of vascular structures in the wounds treated with endothelial cells compared to the controls. Several soluble factors can be produced by endothelial cells and promote angiogenesis. We have recently showed that decidual endothelial cells are able to synthesize C1q and express surface-bound C1q under physiological conditions. Since decidua is a site of active angiogenesis, we sought to ascertain whether C1q can play a role in this process. To confirm our hypothesis we used different approaches such as permeability, cell migration and proliferation assay, besides wound healing and aortic ring assay. C1q acts as a permeabilizing factor inducing the FITC-BSA leakage through a monolayer of endothelial cells (ECs). Next, we found that C1q was able to promote motility of ECs in a wound healing assay, and to recruit ECs acting as a chemotactic factor, furthermore C1q was also found to have an additional effect on EC inducing cell proliferation. To confirm and extend these data, we used the rat aortic ring assay to evaluate the ex vivo effect of C1q. C1q was also found to stimulate the formation of tubular structures in a matrigel assay and to promote sprouting formation in the aortic ring assay. The presence of both ECs and pericytes were documented in the sprouts indicating that complete new vessels are being formed. The in vivo proangiogenic activity of C1q was evaluated in rats using a wound healing assay. C1q, VEGF or saline was topically applied to the wounds and the skin lesions removed after 14 days were examined for vessel formation. The wounds treated with C1q exhibited a number of new vessels increased to that of saline treated wounds and comparable to that of VEGF. The results suggest that the topical application of endothelial cells or C1q are of potential therapeutic interest as a pro angiogenic treatment of chronic ulcers.

Keywords: endothelial cells, angiogenesis, wound healing, C1q