REGULATION OF VASCULOGENESIS AND ANGIOGENESIS IN THE HUMAN BODY

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The research was supported by the FEFU Science Foundation under the state task 17.5740.2017/6.7.

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RELEVANCE

Relevance According to the opinion Ahluwalia A, Jones MK, Brzozowska I, Tarnawski AS. (2017), regeneration of blood vessels (neovascularization) is critical for tissue injury healing. The contribution of bone marrow-derived endothelial progenitor cells (BMD-EPCs) to neovascularization during tissue injury healing is not fully elucidated and it is not clear whether BMD-EPCs can form new capillary blood vessels independently or jointly with fully differentiated endothelial cells (ECs) [1].

The most studied is the relationship between vasculogenesis and osteogenesis in birds. So, in the studies Huang SC, Zhang LH, Zhang JL, Rehman MU, Tong XL, Qiu G, Jiang X, Iqbal M, Shahzad M, Shen YQ, Li JK. (2018) tibial dyschondroplasia (TD) is the most-prevalent leg disorder in fast-growing chickens; it is intractable and characterized by abnormal endochondral bone formation of proximal tibial growth-plates (TGPs) [2].

Tanaka R. and co-authors (2018) was showed that autologous endothelial progenitor cell (EPC) therapy is commonly used to stimulate angiogenesis in ischemic repair and wound healing. However, low total numbers and functional deficits of EPCs make autologous EPC therapy ineffective for diabetes. Currently, none of the known ex vivo culture techniques can expand and/or ameliorate the functional deficits of EPCs for clinical usage [3]. It is possible that, the process of vascular formation in endochondral bone appears to initiate the pathological changes in TD, and improvement of this process during coupling with osteogenesis may be a potential therapeutic approach to treat this intractable disease.

Vasculogenesis is a complex process by which endothelial stem and progenitor cells undergo de novo vessel formation. Quantitative assessment of vasculogenesis has become a central readout of endothelial progenitor cell functionality [4].

The growth and formation of vessels in the pre- and postnatal period of the development of the body is through vasculogenesis, angiogenesis and arteriogenesis. Angiogenesis is the formation of new capillaries from postcapillary venules, which is carried out through activation of endothelial cells, expression of proteases in them, extracellular matrix degradation, proliferation and migration of these cells, the formation of primary high-permeability vascular structures, the subsequent stabilization and "maturation" of these structures through the involvement of pericytes and smooth muscle cells (GMC) and their organization in a complex three-dimensional vasculature. Knowledge about factors regulating vasculogenesis remains limited. The cellular repressor of E1A-stimulated gene (CREG) has been reported to be involved in maintaining cellular differentiation and endothelial homeostasis [3]. The main stimulus to angiogenesis in physiological and pathological conditions is a lack of oxygen (hypoxia or ischemia), which, through the activator of the transcription of angiogenesis factors - hypoxia-induced factor-1 (HIF-1), induces the expression of many angiogenic factors and primarily the regulator of angiogenesis in both

the embryonic and postnatal period of the body - VFF and its receptors VEGF selectively stimulates the proliferation and migration of endothelial cells (EC), their precursors and monocytes that express receptors to it, increases vascular permeability, promoting the swelling of plasma proteins into the circulatory space that is necessary for EC migration, induces the expression of endothelial NO synthase and the formation of NO, which contributes to vasodilation and stimulates the expression of proteases that destroy the bonds between the EC and the extracellular matrix, which is necessary for directional cell migration.

In the process of stabilization and "maturation" of newly formed immature vascular network involved: 1) angiopoietin-1, suppressing EC proliferation, reducing vascular permeability, which helps to attract pericytes; 2) platelet FR (PDGF), which attracts pericytes and GMC; 3) transforming FR-beta 1 (TGF-beta 1), stimulating the synthesis of matrix proteins. The process of angiogenesis is strictly regulated by RF in time and space, and this must be taken into account when planning the tactics of therapeutic angiogenesis. In the postnatal organism, the stable state of the vessels is maintained by a balance between the activators of angiogenesis (mainly PD and cytokines) and its inhibitors (thrombospondin, inhibitors of matrix metalloproteases and plasminogen activators, endostatin, etc.) and the shift of this balance towards the activators, as a rule, a short-term, leads to the activation of angiogenesis, for example, in inflammation, wound healing, ischemia. Insufficient physiological angiogenesis due to insufficient production of FF or expression of their receptors, or increased production of its inhibitors, can contribute to the increase in the severity of ischemic diseases (CHD, chronic lower limb ischemia). Angiogenesis leads to an increase in the density of the capillary network in ischemic tissues and a decrease in peripheral vascular resistance, which is necessary to ensure tissue perfusion, but without arteriogenesis, it is insufficient for complete revascularization.

Comşa Ş, Ceauşu RA, Popescu R, Cîmpean AM, Raica M. was found (2017) hMSC stimulated the CAM mesenchymal cells (cMSC) to acquire endothelial and pericyte-like features and to generate cord/capillary-like structures (CLS) in the chorionic epithelium and the mesoderm, but they also entered these structures (CD34+/SMA (smooth muscle actin)+ hMSC). Simultaneously, hMSC induced a process of sprouting angiogenesis in the mesoderm, CD105+ hMSC being identified in the proximity of the angiogenic areas and was shown, that hMSC and CAM establish a genuine hotspot of vasculogenesis, which may evolve to a valuable experimental model for this research field. [5].

Arteriogenesis - the formation of collateral vessels from non-functioning arteriolar compounds - is the most effective revascularization process, providing blood flow around the occlusion site. The most important stimulator of arteriogenesis is an increase in the shear stress above the occlusion site, caused by an increase in blood flow, which promotes the expression of adhesion molecules by endothelial cells and subsequent accumulation of monocytes in the vessel wall secreting a large amount of RF, of which the main regulators of arteriogenesis are FGF fibroblasts, as well as PDGF, VEGF and CXC-chemokines [6].

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