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NGF involvement in vascular formation and its applications in therapeutic angiogenesis of experimental critical limb ischemia

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Abstarct

Critical limb ischemia (CLI) is a severe form of peripheral artery disease caused by a poor supply of blood to the affected muscle. The ultimate failure of surgical revascularization in patients has led to attempts to develop alternative angiogenic therapies, including administration of angiogenic growth factors either as recombinant protein or as gene therapy. Vascular Endothelial Growth Factor (VEGF), is crucial for new blood vessels formation and Nerve Growth Factor (NGF) has been also reported to play an important role in angiogenesis although, less investigated. Based on these observations, we hypothesized that NGF may induce the formation of functional blood vessels in a hindlimb ischemic rabbit model. Results: Hindlimb ischemia was induced in 34 rabbits bilaterally, by endovascular embolization of femoral arteries. On the 7th, 14th, and 20th post-embolization days, NGF was injected intramuscularly, in one ischemic limb, and vehicle was injected in the contralateral control limb. On the 40th day, newly developed collateral vessels were quantified by trans-auricular, intra-arterial subtraction angiography. Perfusion analysis of an in vivo dynamic computed tomography (CT) study was performed, to investigate the hemodynamic recovery of the distal ischemic tissues. Functional estimation of limb perfusion showed a statistically significant increase of blood flow and blood volume upon NGF therapy. However, the increase of the collateral vessels was not detectable angiographically, explaining NGF-stimulated, capillary angiogenic network formation but not increase of arteriogenesis. The combination of NGF with either tropomyosin-related kinase type A receptor or vascular endothelial growth factor receptor 2 antagonists, abolished the NGF-induced hemodynamic recovery. Conclusions: These findings provide new insights into understanding the involvement of NGF in vascular formation and its applications in therapeutic angiogenesis of CLI.

Biography:

Lazarovici graduated in pharmacology and toxicology at the Hebrew University, post graduated on neurobiology at the Weizmann Institute of Science and conducted neurochemical and molecular research at the National Institutes of Child Health and Human Development, NIH, Bethesda, USA. He was a visiting professor in the School of Biomedical Engineering, Science and Health Systems, Drexel University and Faculty of Engineering, Temple University, Philadelphia, USA. He is a member of 15 international and national academic societies, published about 250 scientific articles and reviews and edited six books.