

P004 Neurotrophins Promote Angiogenesis. Potential Implications for Curing Limb Ischaemic and Myocardial Infarction.
Costanza Emanuelli

Bristol Heart Institute, University of Bristol, Bristol, UK

NTs stimulate three receptor tyrosine kinases (trkA, B, and C) and also a p75 receptor (p75NTR), whose role is still controversial, but appear to be associated with apoptosis. Although neurotrophins (NTs) were initially studied for their trophic effect on neural cells, we recently discovered an unexpected role for the NT nerve growth (NGF) in reparative neovascularisation. NGF is released by and acts on endothelial cells (ECs) in culture to promote proliferation, migration, and survival, via trkA-Akt-eNOS-NO and via Erks. Furthermore, we found that NGF promotes angiogenesis and arteriogenesis in ischaemic hind-limbs, diabetic wounds, and the infarcted heart. Moreover, in the same clinical conditions, NGF prevented the apoptotic death of ECs and myocytes. Importantly, neutralisation of endogenous NGF by a blocking antibodies impaired the spontaneous angiogenic response to limb ischaemia. The NT brain derived neurotrophic factor (BDNF), acting on its trkB receptor, was similarly shown to promotes angiogenesis and vasculogenesis in vitro and in a mouse model of limb ischaemia. We found that muscle ischaemia up-regulates NGF and trkA, and that type 1 diabetes and ischaemia synergistically up-regulate p75NTR. In our models, NGF supplementation up-regulated trkA and down-regulated p75NTR. The potential of trkC on angiogenesis has not been tested, yet.

We propose that NTs may be envisage as potential valuable tools to combat cardiovascular ischaemic disease.