The Role of VEGF-B and NRP-1 Axis in Regulating Mitochondrial Homeostasis in Ischemic Heart Disease

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Ischemic heart disease takes 17.9 million lives each year. Vascular endothelial growth factors (VEGFs) and their receptors are key in angiogenesis and vascular remodeling. VEGF-B was found to play a key role in regulating metabolism, blood vessel growth during development, and is a defense mechanism against oxidative stress. The main objective is to determine the role of VEGF-B/NRP-1 signaling pathway in cardiac function and regeneration in ischemic heart disease. Both in vitro cell culture studies and in vivo zebrafish model were exposed to hypoxia to mimic myocardial infarction (MI). Endothelial cells and cardiomyocytes were treated with hypoxia, VEGF-B, VEGF-B+hypoxia. RTPCR was performed to analyze the mRNA expressions tested cardiac genes, and inflammatory markers. Zebrafish larvae were treated with hypoxia, VEGF-B, and hypoxia+VEGF-B, looking at cardiac function and chamber development. It was determined that hypoxia upregulates inflammatory genes in endothelial cells and downregulates essential cardiac genes in cardiomyocytes. Hypoxia also decreases zebrafish survivability, heart rate, and heart chamber size. VEGF-B overexpression is not harmful. VEGF-B overexpression in hypoxic conditions prevents the upregulation of inflammatory markers in endothelial cells and the downregulation of selective cardiac genes in cardiomyocytes. It increased survivability and heart rate in zebrafish. VEGF-B has a protective effect against hypoxia. The VEGF-B/NRP-1 axis improves cardiac function and cardiac regeneration in pathological situations such as hypoxia. By confirming VEGF-B and NRP-1 axis maintains mitochondrial homeostasis in the ischemic heart, VEGF-B was identified as a strong target gene for therapies for myocardial infarction and heart failure.

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