The Role of VEGF and FGF21 in Restoring the Hypotrophic Response of Endostatin in Neonatal Rat Ventricular Myocytes

Puttamraju, Nikhil (School: Paradise Valley High School)

Endostatin, a fragment of collagen XVIII, is a potent anti-angiogenic factor with strong therapeutic potential in liver cancer by inhibiting tumor blood vessel formation. However, its clinical use has been limited by cardiovascular side effects, particularly its impact on cardiomyocyte growth. This study investigates the effects of Endostatin on cardiomyocytes under proteostatic stress and evaluates whether protective factors can mitigate its adverse effects. After primary neonatal rat ventricular myocytes (NRVMs) were cultured and treated with Endostatin (0.2 µg/mL) by the Qualified Scientist, either alone or following pre-treatment with vascular endothelial growth factor (VEGF) or fibroblast growth factor 21 (FGF21), the Finalist evaluated cardiomyocyte growth by measuring cell size via microscopy. Hypertrophic gene expression (Nppa and Nppb) was then quantified using RT-qPCR and normalized against housekeeping genes. Endostatin treatment significantly reduced both cell size and hypertrophic gene expression, indicating suppression of growth pathways. Pre-treatment with VEGF or FGF21 reversed these effects, restoring both molecular and structural markers of cardiomyocyte growth. These findings demonstrate that Endostatin negatively regulates cardiomyocyte growth under stress but that its harmful effects can be mitigated through activation of protective signaling pathways. This suggests a potential strategy for improving the safety of Endostatin-based therapies. By combining Endostatin with protective factors such as VEGF or FGF21, it may be possible to preserve its anti-cancer benefits while minimizing cardiovascular risk. This approach could enhance the clinical viability of Endostatin and contribute to more effective treatments for liver cancer.

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