Modulation of release of Endothelin-1 in hypertrophic human endocardial and vascular endothelial cells

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As vascular endothelial cells (VECs) line the vascular walls, endocardial endothelial cells (EECs) line the cardiac cavities and constitute a barrier between the circulating blood and the adjacent cardiomyocytes. In addition, similar to VECs, EECs produce and release various cardioactive factors such as Neuropeptide Y (NPY) and Angiotensin II (Ang II). Theses peptides are implicated in various cardiac pathologies including hypertrophy of cardiomyocytes. However, it is not known whether EECs and VECs volume is also increased and whether this modulates excitation-secretion coupling of these cells. Using real 3D confocal microscopy imaging, immunofluorescence and various molecular biology techniques, we found that NPY and Ang II induce an increase in the volume of human EECs and VECs. This increase in cell volume is accompanied by an increase in hypertrophic markers such as the DNA/protein ratio and ANP mRNA. We also found that Ang II-induced hypertrophy of EECs and VECs is primarily mediated via AT_1 receptor activation whereas the NPY-induced hypertrophy is mediated via activation of the Y_1, Y_2 and Y_5 receptors. In addition, NPY and Ang II modulate the release of Endothelin-1 from normal and hypertrophic human EECs and VECs. Thus, similar to cardiomyocytes, cardiac hypertrophy is associated with EECs and VECs hypertrophy and modulates the secretory capacity of these cells. Modulation of secretion may in turn contribute to the cardiac remodelling that occurs in hypertrophy and heart failure. The work was supported by the Canadian Institutes of Health Research (CIHR) and the Heart and Stroke Foundation of Quebec (HSFQ). The authors thank Quebec Transplant and the donors for the donated tissues.