Human Coronary Micro-artery Dysfunction is Associated with Structural and Smooth Muscle Cell Phenotypic Alterations

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Autoregulation is compromised in patients with coronary heart disease. Little is known how coronary arterial smooth muscle structure and phenotype links to vascular reactivity.
Right atrial appendage biopsies from consented patients undergoing valve replacement surgery, and from pigs were collected at clinical standards under general anesthesia. Human and porcine arteries from right atrial appendage samples were isolated and mounted for pressure myography. Confocal imaging established vasomotor responses, cellular viability, and immunohistochemical localization of proteins.
We compared the structural features of human patient intra-myocardial coronary arteries (IMCAs) with equivalently handled porcine IMCAs. More than half the human IMCAs failed to develop ≥10% myogenic tone. 3D confocal imaging revealed a novel, distinct layer of longitudinally-arranged SMCs (l-SMCs) between the endothelium and the expected circumferentially-arranged SMCs responsible for radial contraction (r-SMC) in the majority of human and porcine IMCAs.
Contractile function strongly correlated with SMC phenotype, with the synthetic markers L-caldesmon and vimentin highly expressed in SMCs with poor contractile function, namely the human r-SMCs and the porcine l-SMCs. Thus, we propose that l-SMCs retain an immature, synthetic phenotype in healthy vessels with functional r-SMCs but, with loss of r-SMC function in aged patients, l-SMCs may play a reparative role and can adopt a contractile phenotype in an attempt to restore function and control myocardial perfusion. The role of l-SMCs in maintaining the integrity of arterial function warrants further investigation