Thoracic Aortic Disease: A Multi-layered Problem and Solution in Perivascular Oversight of Vessel Homeostasis

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The tri-layered anatomy of blood vessels (endothelium, smooth muscle and adventitia) underscores the importance of understanding inter-layer communication in cardiovascular disease. Foundational studies by Dr. Phillippi and colleagues investigate the impact of medial smooth muscle cell responses to oxidative stress on the unique extracellular matrix architecture distinguishing the pathophysiology of the aortopathy associated with the congenital heart anomaly of bicuspid aortic valve from that of idiopathic aneurysms of the thoracic aorta. More recently, her laboratory has centered attention on the adventitia as an adaptive and dynamic player in aortic disease and as a local source of oxidative stress. The vasa vasorum (*Latin*: the vessels of the vessels) is a network of microvessels infiltrating the adventitia of large blood vessels to provide oxygen and nourishment. Dr. Phillippi's group identified pathological features of the vasa vasorum that are known to compromise blood flow and nourishment to the host vessel such as reduced vessel density, less neovascularization, wall thickening, occlusion and dilatation associated with deficiency of hypoxia-triggered targets in aneurysmal patients. Dr. Phillippi's lab is also the first, to their knowledge, to uncover a phenotypic diversity of resident progenitor-like cells localized to the vasa vasorum. In the setting of thoracic aortic disease, the approach to characterize perivascular oversight of vessel homeostasis employs several tissue-engineered models of disease using human aortic specimens and primary cells from all three blood vessel cell layers. It is anticipated that this work will lead to refinement of risk assessments and thus, improve clinical management and care of patients. Enhanced understanding of perivascular progenitor cells' governance of blood vessel health could enable their regenerative potential to be harnessed for treatment of aortic disease in a minimally-invasive manner.