

## 2012 Abstracts



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*The Role of Perivascular Adipose Tissue in  
Pulmonary Arterial Hypertension*

Pulmonary arterial hypertension (PAH) is a rare disease characterized by ever increasing pulmonary vascular resistance and significant vascular remodeling. Although the classic indicators of PAH progression are well recognized, the initiating factors involved in the pathogenesis of PAH are not well understood. Perivascular inflammatory cells have been shown to influence plexiform lesion development, leading to growing interest in the relationship between perivascular inflammation and pulmonary artery (PA) remodeling. Smaller visceral adipose depots are receiving increased attention for their localized inflammatory role in cardiovascular disease. We previously found complement proteins C3 and C4 [C3/C4] deposited at the external elastic lamina of the descending aorta extending through the perivascular adipose tissue (PVAT) in the absence of luminal deposition or plaque development. We determined that C3/C4 bind to collagen and elastin within the vascular wall of murine aorta, suggesting that complement may play a critical role in the pathogenesis of vascular stiffness and atherosclerosis through a mechanism initiated at the adventitia or the PVAT rather than the endothelial surface. The same pro-inflammatory environment may exist surrounding the PAs, contributing to PAH.

We hypothesize that the vascular remodeling due to PAH progression is associated with dysfunctional PA PVAT. We propose that a PAH rat model will have a greater volume of PA PVAT with more extensive C3/C4 deposition and pro-inflammatory protein expression than a control model.



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First we will quantify the volume of PA PVAT using microCT and correlate these findings with the extent of vascular remodeling and PA PVAT hypertrophy due to PAH progression as measured through morphological changes using scanning electron microscopy. Second, we will characterize the deposition of C3/C4 in the PA vascular wall and PA PVAT using established immunohistochemistry and histology techniques while evaluating the association with vascular remodeling. Finally, we will identify unique and novel pro-PAH proteins and inflammatory cell populations found in the PA PVAT using proteomics and molecular histology and we will correlate these findings with vascular remodeling at specified time intervals.