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Exploring the Role of T-Cell Associated Pulmonary Vasculature Injury and Right Ventricular Dysfunction

INTRODUCTION:

The immunologic contribution to the pathogenesis of pulmonary vasculature disease (PVD) will likely play a significant role in future therapeutic considerations. Immune checkpoint inhibitors (ICIs) are commonly used immunotherapies, and through their direct modulation of T-cell activity, serve as a potential direct translational model for immune mediated pulmonary vascular injury.

BACKGROUND:

Immune cell abnormalities contribute to the pathogenesis of PVD. Flow cytometric analysis of the peripheral blood of patients with pulmonary arterial hypertension identified increased frequencies of effector memory T cells relative to healthy controls. Moreover, animal models have demonstrated a reduction in the development of PAH after Treg T-cell subset immune reconstitution prior to vascular injury. However, blockade of the PD-1 pathway-with ICI therapy reversed this protection. The use of ICI therapies can result in significant immune-related adverse events (irAEs) including cardiopulmonary toxicity. The development of PVD, as a potential consequence of ICI induced autoimmunity, is not well understood. One study demonstrated increased median pulmonary artery to aorta ratio (PA/Ao) in patients treated with anti-PD-1 therapy. Another study showed increased thoracoabdominal aorta inflammation by 18-FDG PET/CT scan after a mean of 4.4 months of therapy. Recently, we reported a correlation between exposure to ICI's and right ventricular dysfunction as measured by speckle-tracking echocardiography. We also confirmed that exposure to ICI's results in an increased PA/Ao ratio. Taken together these findings support a potential role ICI's may play in pulmonary vascular disease and have important implications on right ventricular function. We propose to prospectively explore the impact of ICI therapy induced T-cell modulation on pulmonary vascular injury and right ventricular function. Transthoracic echocardiography, 18-FDG PET/CT imaging, and serologic analysis will be performed to highlight this potential novel immune related adverse event.

HYPOTHESIS AND SPECIFIC AIMS:

We hypothesize that ICI therapy induced T-cell modulation is associated with the development of pulmonary vascular injury. This study may provide insight into pathophysiologic mechanisms of PVD and shed light on potential novel therapeutic pathways.