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The Role of Classical Dendritic Cells in Pulmonary Hypertension

INTRODUCTION:

Pulmonary hypertension (PH) is often fatal and is characterized by elevated right ventricle pressures and increased vascular remodeling and resistance.

BACKGROUND:

Dysregulated immunity underlies the pathophysiology of PH, which is demonstrated by elevated numbers of inflammatory cells around the remodeled vessels, as well as high levels of inflammatory cytokines present in the plasma of patients from different PH groups. Notably, there is a substantial body of evidence indicating that dendritic cells are orchestrators in this process; however, there are few studies that address the pathogenic mechanisms through which these cells could participate in PH.

HYPOTHESIS AND SPECIFIC AIMS:

Our goal is to determine the mechanistic role of dendritic cells driving inflammation in the context of hypoxia, which leads to vascular disease. This project will unravel pathophysiological mechanisms of classical dendritic cells (cDCs) in hypoxia-PH by using recombinant murine animals and single-cell RNA sequencing. We propose that the activation of these cells by a hypoxic stimulus can trigger secretion of cytokines, chemokines, and growth factors by the vascular bed, driving the remodeling and changing of the perivascular environment and potentially leading to recruitment of dendritic cells and macrophage/ monocyte influx into the lung perivascular compartment. We have supportive preliminary data revealing that classical dendritic cells are pathogenic in hypoxia-induced PH, are increased in lungs of hypoxia-challenged mice, and are probably involved in monocyte/macrophage recruitment into the lung. This project will be highly innovative in pulmonary vascular diseases and will open an unexplored and rich investigative research field.