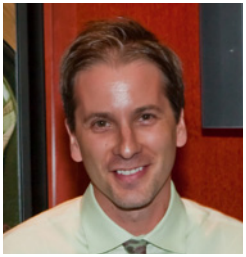

Michael Eric Yeager, PhD

University of Colorado School of Medicine
Aurora, Colorado

Circulating Mesenchymal Precursors in Severe PAH and the Role of Endothelin-1 in their Recruitment and Differentiation into Fibrocytes

Vascular remodeling in chronic hypoxic pulmonary artery hypertension (PAH) occurs throughout all three layers in resistance and main pulmonary arteries. Following hypoxia, fibroproliferative change is evident in the adventitial layer and is characterized by the presence of monocyte lineage cells derived from circulating mesenchymal precursors. The vascular remodeling observed is causally related to the influx of mesenchymal precursors because: 1) depletion of these precursor cells ameliorates the vascular change, and 2) both hypoxia and endothelin-1 (ET-1) are required for neovascularization of rat pulmonary arteries by activated fibroblasts. For this proposal, it is hypothesized that circulating mesenchymal precursors are increased in severe PAH and correlate with poor prognosis. Furthermore, it is hypothesized that endothelin-1 is a critical homing signal for the recruitment and differentiation of mesenchymal precursors that drive the remodeling process. The successful conclusion of this work will result in a clearer picture of the vascular remodeling associated with monocyte infiltration and provide the potential for a novel therapeutic approach for PAH.