**Background**

- Pulmonary Hypertension (PH) is a progressive disorder characterized by inflammatory cell recruitment, including T & B lymphocytes, & altered pro-inflammatory cytokine profiles
- Pathogenesis involves vascular injury, cell death, & persistent inflammation, yet details of this process are still relatively unknown
- Vascular remodeling & inflammation of the right ventricle (RV) has been documented in the monocrotaline (MCT) rat models of PH
- Cardiac fibrosis causes increased stiffness & induces pathological signaling within cardiomyocytes, resulting in progressive cardiac failure; excessive extracellular matrix (ECM) impairs mechano-electric coupling of cardiomyocytes & increases risk of arrhythmias
- Myocardial inflammation & edema likely compromise cardiac function
- The **objective** of this study was to investigate the extent of fibrotic remodeling & excess fluid accumulation in hearts of rats with PH

**Hypothesis**

- We hypothesized that PH is associated with the accumulation of excess fluid in the ventricles & fibrosis of cardiac tissue that may contribute to diminished cardiac output and ventricular failure

**Materials & Methods**

- Rat heart sections & those derived from experimental PH induced by MCT injection, were stained & compared to controls to identify morphology & organization of cardiac vessels
- Antibodies:
  - Lycopersicon Lectin & ULEX Lectin labels rodent endothelial cells green (FITC)
  - α-Actinin antibody (1α) labels myocytes
  - mouse anti-Aquaporin-1 antibody (1α) labels lymphatic vessels & some blood vessels

**Results**

**Figure 1.** Significant RV and LV Edema in MCT-Induced PH. Expanded fluid compartment likely causes an increased O2 diffusion distance in the tissue

**Figure 2. Upper Panels:** Trichrome stain of Normoxic (Nx) and MCT-induced PH rats. Pervascular and transmural fibrosis is evident as collagen deposition (blue stain, yellow arrows) **Middle & Lower Panels:** Fluorescent stains of Normoxic and MCT-induced PH rats. Lectins outline the vessels. No co-localization between α-Actinin and ULEX Lectin. RV, Right Ventricle

**Figure 3.** Cardiac output at the left atrial pressure of 15 mm Hg. expressed as a percent of control, plotted as a function of extracellular fluid. W, wet weight; D, dry weight. As myocardial edema accumulates, the heart’s ability to maintain cardiac output at LAP of 15mm Hg diminishes (REF 2)

**Discussion**

**Figure 4.** Mechanisms that potentiate myocardial edema formation. Myocardial edema compromises cardiac function directly, or indirectly by altering the matrix. (Adapted from Ref 2)

**Conclusions**

- Fluid accumulation is evident in RV & LV MCT rats; may contribute to constrictive loss of cardiac function
- The degree of PH is directly proportional with the degree of RV fibrosis, so we speculate myocardial edema and fibrosis may contribute to ventricular dysfunction and ultimately RV failure
- **Future Studies:** We intend to further understand the impact of fibrosis and edema upon the lymphatic vessels of the heart in PH

**References**


**Acknowledgements**

- Department of Pulmonary & Critical Care Medicine, University of Colorado Denver Health Sciences, Aurora, Colorado 80045
- NIH HL-084823-02 & HL-014985-01 (K.R.S.)
- Webb-Waring Center, School of Medicine, University of Colorado Denver Health Sciences, Aurora, Colorado 80045
- Dr. John Repine, Director, Webb-Waring Center
- David H. Wagner, PhD, Assistant Director for Summer Program
- Regina Richards, MSW, BA, Director, Office of Diversity and Inclusion, School of Medicine, University of Colorado Denver Health Sciences
- North Foundation
- Colorado Leaders, Interns, Mentors in Business
- Colorado University Summer Program (CUSP) – NIH funded