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Title: Roles of circulating and resident myeloid cell subpopulations in bronchopulmonary remodeling and pulmonary hypertension

Ms. Kelley 1080 Colvin kelley.colvin@ucdenver.edu [1,2,3], Dr. Kurt 1081 Stenmark kurt.stenmark@ucdenver.edu MD [1,3] and Dr. Michael 1082 Yeager michael.yeager@ucdenver.edu [1,2,3]. [1] Pediatrics Critical Care, University of Colorado Denver, Aurora, CO, United States, 80045 ; [2] Bioengineering, University of Colorado Denver, Aurora, CO, United States, 80045 and [3] Cardiovascular Physiology, University of Colorado Denver, Aurora, CO, United States, 80045 .

Body: Rationale: Pulmonary hypertension (PH) is characterized by vascular remodeling and the presence of myeloid cells. A clearer understanding of the myeloid cell phenotypes contributing to pulmonary vascular remodeling seems a pre-requisite for anti-inflammatory therapy for patients with PH. Methods: We used immunohistology, qPCR, cell sorting, and immunoblot on lung tissue and peripheral blood derived from rat (green fluorescent protein [GFP] bone marrow transplanted) PH models and humans with PH. Results: In human blood, we found increased fibrocytes in PH vs. controls, assessed as CD45+/procollagen+ (PH 1.2% of total white blood cells, WBC vs. controls 0.45% WBC) or vimentin+ (PH 1.9% vs. controls 1.35% WBC) or smooth muscle actin+ (PH 2.2% vs. controls 0.3% WBC) or heat shock protein 47+ (PH 0.27% vs. controls 0.078% WBC). No differences in myeloid derived suppressor cell (CD45+/CD33+/CD11b+/MHCII-) numbers were observed. PH patients expressed Fc gamma receptors (FcgR) CD16, CD32, and CD64 more robustly vs. controls. We found positive correlation between fibrocytes and cardiac output, and strong positive correlation between fibrocytes and expression of CD16 and CD32 FcgRs. Similar results were obtained using blood from rats with PH. FACS analysis of PH rat lungs confirmed increases in fibrocytes, as well as cells positive for CD68+, or CD163, or CD11c, CD103, CD206, and CD11b. Only CD11b cells were co-positive for GFP, a result confirmed by immunofluorescence of tissue sections. Conclusion: A clearer understanding of how myeloid cells impact the pathobiology of PH may have profound therapeutic significance.