Abstract Group: 4.3. Pulmonary Circulation and Pulmonary Vascular Disease

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Title: Pulmonary lymphoid neogenesis in idiopathic pulmonary arterial hypertension

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Body: Background: Idiopathic pulmonary arterial hypertension (IPAH) patients present circulating autoantibodies against vascular wall components. Pathogenic antibodies may be generated in tertiary (i.e. ectopic) lymphoid tissues (tLTs). Aims and objectives: To assess how frequent are tLTs in IPAH lungs as compared to controls and flow-induced PAH (Eisenmenger syndrome -ES-) and to identify local mechanisms responsible for their formation, perpetuation and function. Methods: tLTs composition and structure were studied by multiple immunostainings. Cytokines/chemokines and growth factor expression was quantified by real-time PCR and localized by immunofluorescence. The systemic mark of pulmonary lymphoid neogenesis was investigated by flow cytometry analyses of circulating lymphocytes. Results: As opposed to controls and ES, IPAH lungs contained perivascular tLTs, comprising B and T cell areas with high endothelial venules and dendritic cells. Lymphocyte survival factors, such as IL-7 and PDGF-A, were expressed in tLTs as well as the lymphorganogenic cytokine/chemokines, lymphotoxin-α/β, CCL19, CCL20, CCL21 and CXCL13, which might explain depletion of circulating CCR6+ and CXCR5+ lymphocytes. The presence of germinal center centroblasts, follicular DCs, activation-induced cytidine deaminase and IL21+PD1+ T follicular helper cells in tLTs together with CD138+ plasma cells accumulation around remodeled vessels in areas of Ig deposition argued for local immunoglobulin (Ig) class switching and ongoing Ig production. Conclusions: We highlight the main features of lymphoid neogenesis specifically in
the lungs of patients with IPAH providing new evidence of immunological mechanisms in the evolution of this fatal condition.