European Respiratory Society
Annual Congress 2012

Abstract Number: 4658

Publication Number: P3151

Abstract Group: 1.5. Diffuse Parenchymal Lung Disease

Keyword 1: Interstitial lung disease **Keyword 2:** Biomarkers **Keyword 3:** Immunology

Title: Frequencies and dynamics of peripheral immune cell subsets in idiopathic pulmonary fibrosis: Preliminary results and clinical implications

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Body: Involvement of the immune response in the pathogenesis of idiopathic pulmonary fibrosis (IPF) is not well clarified. Emerging T cell subsets including IL-17 secreting T helper cells (TH17) and regulatory T lymphocytes (Treg) expressing TGF-beta may exert antithetical actions. Distribution and phenotype characteristics of peripheral immune cells along with TH17/Treg dynamics were investigated by multi-parametric flow cytometry in 15 IPF patients (mean age 63 yrs; 13 men) and 10 age- and sex-matched healthy subjects. Proportions of $CD4^+$ and $CD8^+$ T cells and of B ($CD20^+$) lymphocytes were similar in the two groups. Frequencies of NKT ($CD3^+CD56^+$) and NK cells ($CD3^-CD56^+CD16^+$) were reduced in IPF ($p<0.0001$ for NK cells), the 24% of the latter co-expressing CD161 and CD152a (versus 4.2±3.3; $p=0.001$). IPF patients displayed higher Treg proportions ($CD4^+CD25^{high}FoxP3^+$) (0.71±0.4 vs 0.3±0.13; $p<0.05$). No differences in the distribution of highly suppressive Treg ($CD13^+$) cells were found. Upon stimulation, Treg expression of TGF-beta was similar in the two groups. Conversely, frequencies of IL-17-espressing $CD4^+$ cells were significantly lower in IPF (0.92±0.56 vs 0.21±0.11; $p<0.001$). This finding was associated with an increased TGF-beta/IL-17 ratio in IPF (2.18±1.15 vs 0.38±0.2; $p=0.001$). This study first provides evidence in IPF of a peripheral Treg/TH17 functional imbalance along with a depletion of NK cells which display an inhibitory phenotype. Dynamics of Treg/TH17 cells may represent a non invasive tool for disease severity assessment and treatment monitoring. Efforts are requested to thoroughly delineate these observations at the lung level.