European Respiratory Society
Annual Congress 2013

Abstract Number: 225
Publication Number: P3381

Abstract Group: 1.5. Diffuse Parenchymal Lung Disease
Keyword 1: Idiopathic pulmonary fibrosis Keyword 2: Bronchoalveolar lavage Keyword 3: Biomarkers

Title: Biomarkers of fibroproliferative healing in fibrosing idiopathic interstitial pneumonias

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Body: Aims: The main feature of fibrosing idiopathic interstitial pneumonias (fIIPs) is the fibroproliferative potential of underlying pathogenetic process. We hypothesize that the concentration of potential markers of fibroproliferative healing, PAR-2, TGF-β1, TNF-α and IL-4Rα in bronchoalveolar lavage fluid (BALF) differ in patients with fIIPs compared to controls (C). Patients and methods: 10 patients with fIIPs and 9 controls (C) were included to the study. Concentrations of CD124 (IL4Rα), PAR-2, TGF-β1 and TNF-α in BALF were determined using the ELISA method. Results: We observed higher concentrations of IL4Rα (fIIPS 1499.4 pg/ml vs. C 255.5 pg/ml; p < 0.05), PAR-2 (fIIPS 1807.9 pg/ml vs. C 421.0 pg/ml; p < 0.05) and TGF-β1 (fIIPS 283.0 pg/ml vs. C 197.1 pg/ml; p < 0.01) in BALF in fIIPs versus C. The values of TNF-α in BALF did not differ significantly in fIIPs compared to controls. The ratios also showed differences in fIIPS and C: IL4Rα/TGF-β1 (fIIPS 6.19 vs. C 0.68; p = 0.0143); TNF-α/IL4Rα (fIIPS 0.84 vs. C 7.93; p = 0.043); TGF-β1/TNF-α (fIIPS 0.21 vs. C 0.16; p = 0.0179) and protein/PAR-2 (fIIPS 0.06 vs. C 0.28; p = 0.0033). Conclusions: Increased values of TGF-β1 and PAR-2 in the BALF of fIIPs support the hypothesis regarding interactions of alveolar damage, the coagulation cascade and fibroproliferative healing in fIIPs. We found that PAR-2, TGF-β1 and IL-4Rα are significantly up-regulated in the BALF of fIIPs compared to controls, therefore we suppose that they could become suitable biomarkers of fibrosing interstitial lung diseases (i.e. the markers of fibroproliferative healing). The study was supported by grant NS10423-3/2009 and NT 13433-4/2012, IGA MZCR.