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Title: M2 chemokines during acute exacerbations of IPF

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Body: Background: Alternative activation of macrophages is a well-recognized phenomenon in patients with IPF and is associated with poor prognosis. The most common cause of death in IPF is Acute Exacerbations (AEs). Objectives: Evaluation of the alternative activation state of macrophages during acute exacerbations in patients with IPF. Methods: 61 patients with IPF and 14 healthy volunteers underwent bronchoscopy with bronchoalveolar lavage, one million BAL cells were cultured for 24 hours without further stimulation and the conditioned medium was harvested. Spontaneous M2 chemokine production (CCL2, CCL17, CCL18, CCL22 and IL-1Ra) was measured by ELISA. AEs were defined according to the criteria of Collard et al. (Collard, HD et al. AJRCCM 2007; 176:636-643). Results: BAL cells of patients with IPF produced significantly more CCL2, CCL17, CCL18, CCL22 and IL-1Ra as compared to cells of healthy volunteers. Seventeen patients suffered from an AE at the time point of bronchoscopy. The spontaneous production of CCL2, CCL18, CCL22 and IL-1Ra were significantly increased of BAL cells from patients with AE in comparison to patients without AE (all p<0.05). Furthermore, 5 patients underwent bronchoscopy before and during an AE and showed a significant increase in CCL18 (p=0.04). Of note, M2 chemokine production was elevated despite a decrease in the percentage of alveolar macrophages during AE. Conclusion: We could show a further increase of M2 chemokines during AEs in patients with IPF. High state of alternative activation of macrophages is associated with an increased risk for AEs and might therefore be a therapeutic target for AE prophylaxis.