

CORRESPONDENCES

COPD and IPF: it's all about regulation and balance

The dominant theory of Hippocrates was that of the four humours—that when the four humours were in balance health prevailed. Therefore, the main goal of the medical therapy was to restore humoral equilibrium. We read with great interest the article by Hou *et al.*,¹ where an imbalance between protective and detrimental subgroups of T regulatory (Treg) cells in patients with COPD is showed. On the contrary with previous studies reporting no significant differences in CD4 foxp3+ T cells between patients with COPD and smokers,² authors performed an elegant series of experiments and dissected Treg cells into three distinct subpopulations, denominated resting, active and cytokine-secreting Treg cells based on the intensity of foxp3+ expression and the secretion of proinflammatory cytokines including interferon γ and interleukin 17. As expected, subgroup analysis revealed an imbalance between different Treg subsets, including a downregulation of suppressive Treg cells and an increased proportion of the cytokine-secreting non-Treg subpopulation in patients with COPD compared with smokers with normal pulmonary function tests. Furthermore, a significant correlation between low suppressive:proinflammatory Treg ratio and indicators of disease severity (FEV₁%pred) locally (bronchoalveolar lavage fluid) and systemically support the notion of an uncontrolled airway inflammation that cannot be counterbalanced by defective protective immune mechanisms.¹ In accordance with these findings, our study group demonstrated a global Treg numerical and functional deficiency in patients with idiopathic pulmonary fibrosis (IPF) while a sound correlation of suboptimal Treg suppressive capacity with indices of functional severity was also noted. Furthermore, no effect of low doses of corticosteroids and antioxidants in the number of Tregs in patients with IPF was also reported.³

The above observations render Treg subsets as potential future therapeutic targets by restoring their disturbed homeostasis and yield them as promising prognosticators for chronic lung diseases. However, for these biomarkers to become truly valuable in the everyday clinical practice, longitudinal, carefully designed studies correlating circulating Treg phenotypical and functional profiles with prognosticators of disease outcome and treatment

responsiveness are sorely needed. Finally, given that COPD and IPF share significant pathogenetic similarities and may coexist under the umbrella of a newly defined, previously under-recognised entity denominated combined pulmonary fibrosis and emphysema,⁴ it would be of special interest to delineate Treg profiles in this specific subgroup of patients. Identification of a subset of patients with combined pulmonary fibrosis and emphysema that could benefit from immunomodulatory interventions is of paramount importance given the fact that the presence of autoimmunity has been suggested to be linked with more favourable prognosis.⁵

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