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

We thank Tzouvelekis and Bouros[1] for their interest in our recent article in *Thorax*.[2] The theory of Hippocrates reminds us of the balance theory informing traditional Chinese medicine. Ancient Chinese scholars believed there were two natural, complementary yet contradictory forces in our universe: yin and yang, with the former being feminine or negative and the latter masculine or positive. Both of them are always in a state of dynamic balance. A balanced state of yin and yang means health whereas an excess or deficiency of one or the other usually indicates disease. Ancient scholars in China therefore treated this phenomenon as the universal law. The delicate balance of anti-inflammatory (yang) or proinflammatory (yin) power plays a pivotal role in maintaining lung homeostasis.[3] Based on our findings and previous studies, we believe that this imbalance exists in COPD and idiopathic pulmonary fibrosis (IPF) and in other immune-mediated disorders.

According to the theory of yin and yang, the main goal of medical therapy was to restore the delicate balance. Glucocorticoids are the most effective anti-inflammatory treatments available for many inflammatory and immune diseases, including asthma, rheumatoid arthritis, inflammatory bowel disease and autoimmune diseases. Glucocorticoids inhibit the activation and proliferation of inflammatory cells by chromatin remodelling and gene expression. On the other hand, glucocorticoid treatment promotes or initiates differentiation of CD4 T cells to regulatory T (Treg) cells by a FOXP3-dependent mechanism.[4] It seems that glucocorticoids are trying to restore the homeostasis between inflammatory and regulatory cells. However, no effect of glucocorticoids on the number of Tregs in patients with IPF[5] and COPD[2] was reported, probably due to the glucocorticoid resistance characterising these two diseases. Anyway, further studies are still needed to clarify whether glucocorticoids or other immunomodulating agents have any effects on the different subpopulations of Treg cells in COPD or IPF. Finally, we agree with Tzouvelekis and Bouros that an exploration of the Treg profiles in combined pulmonary fibrosis and emphysema is of great importance, as it could contribute to our understanding of adaptive immunity in the pathogenesis of both diseases.

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