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Title: Upregulation of myeloid derived suppressor cells (MDSCs) in chronic obstructive pulmonary disease and its relationship with disease severity

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Body: MDSCs have received growing interest as suppressors of immune responses in cancer, induced in the attempt to escape immune surveillance. MDSCs have been recently implicated in immune modulation in chronic inflammatory diseases, particularly autoimmune. Since we proposed an autoimmune component in COPD, we examined the induction of MDSCs in peripheral blood of smokers with COPD with or without lung cancer. In particular, we evaluated the α chain of the IL-4 receptor (IL4Rα, which has been proposed as a marker for MDSCs) in patients with COPD (n=32, 8 with concomitant cancer) compared to subjects with a similar smoking history who did not develop COPD (n=8) and non-smokers (n=10). The expression of IL-4Rα was increased in monocytes from smokers with COPD (17±2%) compared to smokers without COPD (10±1%) and non-smokers (9±1%; $p<0.05$ for both). This increase was particularly evident in COPD patients with concomitant cancer (23±3%) but was also present in those without cancer (16±1%). A similar IL-4Rα pattern was observed in the granulocytic fraction of blood leukocytes (8±1 vs 3±2 vs 4±2%). Of note, IL4Rα expression was not linked to smoking status or cumulative history, but was correlated with the degree of airflow limitation ($p=0.0003, r=0.55$). In conclusion, our study shows that IL4Rα expression is upregulated in smokers with COPD, either with or without lung cancer, but not in smokers who despite a similar smoking history did not develop the disease. These results indicate that the upregulation of MDSCs observed in patients with COPD is not due to smoking itself, but is rather related to the severity of the disease. Funded by Padua University.