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Regulatory T cells expressing Toll-Like Receptor 2 in Blood from Smokers with Stable Chronic Obstructive Pulmonary Disease

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Background. Long-term exposure to tobacco smoke is an important risk factor for COPD, and it does impair immunity. Recent findings indicate the involvement of regulatory T cells (Treg) in COPD, and Toll-Like receptor (TLR)-2 is known to mediate down-regulation of the immunosuppressive capacity in Treg. However, it is unclear whether Treg from long-term smokers (LTS) with or without COPD express TLR2, and this study addressed this matter.

Materials and methods: The LTS were interviewed (smoking, morbidity & medication), and lung function was determined (spirometry after bronchodilation). Venous blood was obtained, and leukocyte differential cell counts plus cytospin slides of PBMC were established. These slides were stained for FOXP3, the master transcription factor for Treg and TLR2 expression. TLR2 +FOXP3+, TLR2-FOXP3+, and TLR2+ monocytes were quantified (median (range)).

Results: Ten LTS with COPD (62(47-68) years); FEV1 58 (30-106) % predicted; FEV1/FVC 47 (29-68) %; 60% males) and 8 LTS without COPD (57 (40-68) years; FEV1 114 (95-129) % predicted & FEV1/FVC 76 (71-85) %; 50% males). The respective tobacco load was 32 (21-75) and 33 (17-46) pack-years. We detected no substantial difference in total leukocyte, monocyte or lymphocyte counts, whereas Treg (FOXP3+) counts tended to be increased (data not shown). The number of TLR2+FOXP3+ lymphocytes (0.06 (0.03-0.11) was higher ($p< 0.05$, Mann-Whitney) in LTS with COPD than in those without COPD (0.04 (0.02-0.07). However, the number of TLR2-FOXP3+ lymphocytes did not differ markedly. The number (x 106 cells/mL) of TLR2+ monocytes was higher ($p<0.05$, Mann-Whitney) in LTS with COPD (0.42 (0.30-0.83)) than in those without COPD (0.26 (0.16-0.58).

Conclusions: Systemic Treg TLR2+ lymphocytes are increased in COPD. Because stimulation of TLR2 by Gram-positive bacteria can inhibit the suppressive function of Treg, these findings are suggestive of a pathogenic mechanism contributing to impaired control of immunity in COPD.