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Title: The IL-2-dependent Th1 response to bacterial infections is suppressed in COPD

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Body: Susceptibility to bacterial infections is enhanced in COPD, which promotes exacerbations. IL-2 triggers proliferation of Th1 cells important for infection defence. We elucidated modulation of IL-2 release from Th1 cells by LPS and in COPD. Peripheral blood CD4+ cells of n=10 age-/gender-matched never-smokers (NS), smokers without (S) and with COPD were ex vivo activated towards Th1 by αCD3/αCD28 antibodies and IL-12. IL-2 release (ELISA) and cell count/death was analyzed after 24-96h of cultivation. Activation towards Th1 increased IL-2 release and cell count. IL-2 release was increased in COPD and negatively correlated to FEV_1 [% pred.]. Nonetypeable H. influenzae extract suppressed IL-2 release from Th1 cells of NS, which was abolished by Polymyxin B or CLI095 (LPS/TLR4 inhibitors). LPS reduced IL-2 release and cell count of Th1 cells, these effects were enhanced in COPD. LPS effect on IL-2 negatively correlated with FEV_1 [% pred.] and was abolished by CLI095. In the presence of LPS, blocking MyD88/IRAK was more efficient in restoring IL-2 release in NS vs. COPD, whereas blocking TRIF/IKKε was more efficient in COPD, and moxifloxacin (MXF) increased IL-2 release and cell count of Th1 cells. MXF effect on IL-2 was enhanced in COPD and correlated to the IL-2-inducing effect of p38MAPK inhibitor SB203580. All effects were $p<0.05$. LPS and MXF did not induce Th1 cell death. Th1 response to bacterial infections is impaired in COPD due to a shift from MyD88/IRAK to TRIF/IKKε signalling, which enhances suppression of IL-2 and Th1 growth by LPS. MXF might reinforce IL-2 expression and Th1 growth by blocking p38MAPK signalling. Targeting TLR4 signalling combined with MXF might reduce exacerbation rates.