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Title: Enhanced neutrophilic inflammation in IL-10-deficient mice exposed to cigarette smoke via TNF-α regulation

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Body: BACKGROUND We established a mouse model of short-term cigarette smoke (CS) exposure, which shares common molecular features with COPD patients. Interleukin (IL) -10 has a suppressive effect on inflammatory reactions and we previously presented that nasal administration of IL-10 attenuated CS-induced neutrophil recruitment to the lung (Higaki et al., ERS 2011). The effect of IL-10 on cigarette smoke-induced inflammation was investigated, using IL-10-deficient mice. METHODS Both IL-10-deficient mice and wild-type mice were exposed to CS. Total cell counts, as well as cell differentiations, in bronchoalveolar lavage (BAL) fluid were determined. TNF-α GM-CSF, and KC mRNA levels in lung tissue were estimated using quantitative RT-PCR. MMP-9 expression in lung tissue was investigated by immunohistochemical analysis. RESULTS & DISCUSSION CS exposure significantly enhanced recruitment of neutrophils and macrophages to the lung (p<.01). CS exposure also increased the mRNA levels of TNF-α, KC, and GM-CSF in lung tissues in both genotypes (p<.01). IL-10 deficient mice revealed further enhancement in neutrophilic recruitment (p<.05) in comparison with wild-type mice, in parallel with the elevation in TNF-α levels (p<.05). Immunohistochemical analysis revealed that more MMP-9 positive cells were recruited to the lung in IL-10 deficient mice with CS exposure. CONCLUSION Our result indicated that anti-inflammatory effect of IL-10 on CS-induced inflammatory reactions, especially neutrophilic recruitment to the lung, is probably via reducing TNF-α levels.