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Title: Alteration of the immune response to streptococcus pneumoniae during COPD exacerbation in mice

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Body: Background: Acute episodes of bacterial exacerbations mark the progression of chronic obstructive pulmonary disorder (COPD). These exacerbations often result in an increased inflammation of the respiratory tract causing death in many cases. Streptococcus pneumoniae is one of the most commonly isolated bacteria during these episodes. Mechanisms responsible for the increased susceptibility to this pathogen are unknown. Objectives: Our aim is to define the alteration of the immune response to Streptococcus pneumoniae infection by using a mouse model of COPD. Methods: C57BL/6 wild type mice were chronically exposed to cigarette smoke for 12 weeks. The mice were subsequently intranasally challenged with a sub-lethal dose of Streptococcus pneumoniae (4x10⁴cfu; serotype 1) and sacrificed at 1 and 3 days post-infection. Systemic and local inflammation and immune responses, bacterial burden and histopathological changes were evaluated. Results: Our results revealed that naïve mice are able to clear the bacteria within 24 hour post-infection, whereas COPD mice develop a strong lung infection. COPD mice show an increased bacterial load in their lung compartment as well as an increased inflammatory reaction (higher recruitment of neutrophils in the BAL). COPD mice show also a defect in NKT cell activation, in dendritic cell maturation, and in IL17 and IL22 production in response to Streptococcus pneumoniae. Conclusions: An increased susceptibility to Streptococcus pneumoniae infection was observed in COPD mice. The observed decrease in IL17 and IL22 production might be involved in the increased susceptibility of COPD mice to Streptococcus pneumoniae infection.