

European Respiratory Society Annual Congress 2012

Abstract Number: 2294

Publication Number: 4538

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: Infections **Keyword 2:** Smoking **Keyword 3:** COPD - exacerbations

Title: Impact of cigarette smoke exposure on Pseudomonas clearance in serpinB1^{-/-} mice

Ms. Tiziana Patrizia 15814 Cremona tiziana.cremona@tki.unibe.ch¹ and Dr. Charaf 15815 Benarafa charaf.benarafa@tki.unibe.ch¹. ¹ Theodor Kocher Institute, University of Bern, Switzerland, 3012 .

Body: Opportunistic pathogens colonize the lungs of COPD patients and contribute to exacerbations. Cigarette smoke exposure induces pulmonary inflammation and is associated with increased incidence and morbidity of pulmonary infections but specific mechanisms linking smoke exposure to defective microbial clearance remain to be defined. Knock-out mice for serpinB1 (sB1^{-/-}), a potent inhibitor of neutrophil proteases, have a severe defect in Pseudomonas clearance associated with increased inflammation, neutrophil death and proteolysis of antimicrobial molecules. In this study, we investigated the combined effects of cigarette smoke exposure and excess neutrophil proteases on Pseudomonas clearance. sB1^{-/-} and wild-type mice were exposed to cigarette smoke or room air (control) for 6 weeks and infected intranasally 24h later. As shown previously, control sB1^{-/-} mice had a severe defect in bacterial clearance compared to control wild-type mice 20h post infection. Surprisingly, clearance was dramatically improved in smoke-exposed sB1^{-/-} mice, which had very low bacterial counts similar to smoke-exposed and control wild-type mice. At earlier time points (4 & 9h post infection), smoke-exposed wild-type mice also had lower bacterial counts than control wild-type mice. All groups of mice had similar bacterial counts 30min after infection suggesting no effect of prior smoke exposure on initial Pseudomonas survival. No increase in Pseudomonas-specific serum antibodies or neutrophil numbers was seen in smoke-exposed compared to their respective control mice. Our findings indicate that protease:inhibitor imbalance and acute cigarette smoke exposure differentially affect the kinetics of Pseudomonas clearance in the lung.