

European Respiratory Society Annual Congress 2012

Abstract Number: 2137

Publication Number: 3117

Abstract Group: 5.3. Allergy and Immunology

Keyword 1: COPD - mechanism **Keyword 2:** Animal models **Keyword 3:** No keyword

Title: Role of ADAM19 and neuregulin-1 in Muc5ac expression in lungs of cigarette smoke-exposed mice

Lisa 16316 Dupont lisa.dupont@ugent.be ¹, Prof. Dr Guy 16317 Joos guy.joos@ugent.be MD ¹, Prof. Dr Guy 16318 Brusselle guy.brusselle@ugent.be MD ¹ and Dr. Ken 16319 Bracke ken.bracke@ugent.be ¹. ¹ Respiratory Medicine, Ghent University Hospital, Ghent, Belgium .

Body: Mucus hypersecretion is an important feature of COPD, resulting in chronic cough and contributing to dyspnea by obstructing the airway lumen. Signalling through the epidermal growth factor receptor (EGFR) plays an ubiquitous role in the production of mucins. We hypothesize that A Disintegrin And Metalloproteinase 19 (ADAM19) stimulates mucin production by shedding of the EGFR-ligand neuregulin-1. C57BL/6 mice were exposed to air or cigarette smoke (CS) for 4 or 24 weeks. IHC for ADAM19 on lung tissue sections showed intense staining in bronchial and vascular smooth muscle cells, as well as in endothelium, and a faint staining in bronchial and alveolar epithelial cells. Quantification of ADAM19 protein expression in the airway wall showed a significant increase upon 4 weeks of CS-exposure, but not upon 24 weeks. Accordingly, protein levels of neuregulin-1 were significantly elevated in BAL fluid of mice exposed to CS for 4 weeks, but not for 24 weeks. Finally, pulmonary Muc5ac mRNA expression was significantly increased upon both 4 and 24 weeks of CS-exposure, while we found no differences in the mRNA expression of Muc5b. These data demonstrate that 4 weeks of CS-exposure leads to increased expression of ADAM19 and enhanced shedding of neuregulin-1. Binding of neuregulin-1 to EGFR may contribute to the increased expression of Muc5ac. However, especially upon chronic CS-exposure, other EGFR-ligands or alternative mechanisms may be involved in mucin production.