European Respiratory Society
Annual Congress 2013

Abstract Number: 6002

Publication Number: OP05

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keywords: no keyword selected

Title: LSC 2013 abstract - Role of CXCL13 in cigarette smoke-induced lymphoid follicle formation and COPD

Dr. Ken Bracke ken.bracke@UGent.be [1], Fien Verhamme [1], Mootoosamy Cunoosamy [2], Ronald Herbst [3], Hamida Hammad [4], Bart Lambrecht [4], Guy Joos [1] and Guy Brusselle [1]. [1] Department of Respiratory Medicine, Ghent University Hospital, Ghent, Belgium ; [2] R& I IMed, AstraZeneca, Molndal, Sweden ; [3] Department of Research, MedImmune, Gaithersburg, United States and [4] Department for Molecular Biomedical Research & Department of Respiratory Medicine, Flanders Institute for Biotechnology (VIB) & Ghent Universtity Hospital, Ghent, Belgium .

Body: Rationale: The B-cell attracting chemokine CXCL13 is an important mediator in the formation of tertiary lymphoid organs (TLOs). Increased numbers of ectopic lymphoid follicles have been observed in lungs of patients with severe COPD. However, the role of these TLOs in the pathogenesis of COPD remains unknown. Objectives: By neutralizing CXCL13 in a mouse model of chronic cigarette smoke (CS)-exposure, we aimed at interrogating the link between lymphoid follicles and development of pulmonary inflammation, emphysema and airway wall remodelling. Methods: We first quantified and localized CXCL13 in lungs of air- or CS-exposed mice and in lungs of never smokers, smokers without airflow obstruction and patients with COPD by RT-PCR, ELISA and immunohistochemistry. Next, CXCL13 signaling was blocked by prophylactic or therapeutic administration of anti-CXCL13 antibodies in mice exposed to air or CS for 24 weeks (chronic exposure) and several hallmarks of COPD were evaluated. Results: Both mRNA and protein levels of CXCL13 were increased in lungs of CS-exposed mice and patients with COPD. Importantly, expression of CXCL13 was observed in CD20+ B-lymphocytes within lymphoid follicles. Prophylactic and therapeutic administration of anti-CXCL13 antibodies completely prevented the CS-induced formation of pulmonary lymphoid follicles in mice. Interestingly, absence of these TLOs attenuated inflammation in bronchoalveolar lavage, but did not influence the development of emphysema and airway wall remodelling. Conclusion: CXCL13 is produced by B-lymphocytes within lymphoid follicles of patients with COPD and is crucial for the formation of TLOs and for inflammatory responses in bronchoalveolar lavage of CS-exposed mice.