European Respiratory Society
Annual Congress 2012

Abstract Number: 2738

Publication Number: 386

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: COPD - mechanism **Keyword 2:** Inflammation **Keyword 3:** Experimental approaches

Title: Effect of neutrophil supernatants on ex vivo small airway contractility in COPD

Ms. Natasha J. 10989 Madge natasha.madge10@imperial.ac.uk , Dr. Louise E. 10990 Donnelly l.donnelly@imperial.ac.uk and Dr. Duncan F. 10991 Rogers duncan.rogers@imperial.ac.uk . [1] Airway Disease, National Heart & Lung Institute, Imperial College London, United Kingdom .

Body: Airway neutrophilia is a significant feature of COPD. Neutrophils release a variety of cytotoxic products (e.g. proteases) that degrade components of extracellular matrix. This may result in destruction of the lung and impedance of airflow characteristic of COPD. Small airways are the main site of airflow obstruction in COPD. Our aim was to study the effects of products from activated neutrophils on the contractility of small airways. Rat precision cut lung slices (PCLS) were obtained and videomicroscopy used to assess contractility of small airways. Neutrophils were isolated from whole blood from non-smokers, smokers and COPD patients, stimulated with fMLP (100µM) and supernatants collected. PCLS were incubated overnight in neutrophil supernatants, and the contractility of small airways assessed by addition of increasing concentrations of carbachol. PCLS incubated in supernatants from COPD patients caused a significant leftward shift in $EC_{50,}$ compared with untreated controls (13±2 vs 34±8µM, n=6, $p<0.01$). Conversely, PCLS incubated in supernatants from smokers had no effect on EC_{50}, but significantly reduced maximal contraction compared with untreated controls (65±1% vs 88±3%, n=4, $p<0.05$). PCLS incubated in supernatants from non-smokers showed small but significant reductions in both EC_{50} (16±3 vs 32±8µM, n=6, $p<0.05$) and maximal contraction (79±4 vs 87±2%, n=6, $p<0.05$), compared with untreated controls. Elastase content of supernatants correlated with maximal contraction, but not with EC_{50}. We conclude that neutrophil supernatants from COPD patients increase the sensitivity of small airways to cholinergic stimulation, which may contribute to the airflow limitation characteristic of the disease.