

# European Respiratory Society Annual Congress 2013

**Abstract Number:** 2145

**Publication Number:** P628

**Abstract Group:** 3.2. Airway Cell Biology and Immunopathology

**Keyword 1:** Inflammation **Keyword 2:** COPD - mechanism **Keyword 3:** No keyword

**Title:** Presence of progranulin in airway inflammation associated with COPD

Dr. Michael 16645 Ungurs m.ungurs@bham.ac.uk<sup>1</sup>, Dr. Nicola 16646 Sinden n.sinden@bham.ac.uk MD<sup>1</sup> and Prof. Rob 16647 Stockley Rob.Stockley@uhb.nhs.uk MD<sup>2</sup>. <sup>1</sup> Clinical and Experimental Medicine, University of Birmingham, Birmingham, West Midlands, United Kingdom, B15 2TT and <sup>2</sup> Lung Investigation Unit, Birmingham & Black Country Comprehensive Local Research Network, Birmingham, West Midlands, United Kingdom, B15 2WB .

**Body:** Background Progranulin (PGRN) inhibits neutrophil (PMN) degranulation, however PMN proteinases convert PGRN into pro-inflammatory granulin-peptides (GRNs). PGRN may therefore be central to dysregulated neutrophilic inflammation associated with COPD. The objectives of this study were to study the presence of PGRN and its conversion into GRN-peptides in sputum sol phase samples from patients with COPD. Methods Western blots were used to identify PGRN and GRN-peptides in sputum sol phase obtained from patients with a clinical diagnosis of COPD in a clinically stable state. PGRN concentrations in sputum sol phase were measured by ELISA. The proteinase inhibitors A1AT, SLPI and EDTA were added with human recombinant PGRN to sputum sol phase samples to identify the proteinases responsible for PGRN conversion activity. Results PGRN and GRN-peptides were present in sputum sol phase and PGRN (nM) correlated negatively with bacterial load (CFU/ml) ( $r=-0.446$ ,  $p=0.003$ ,  $n=43$ ) and markers of neutrophilic inflammation including neutrophil elastase (NE) (nM) ( $r=-0.562$ ,  $p=0.008$ ,  $n=21$ ) and proteinase-3 (PR3) (nM) ( $r=-0.515$ ,  $p=0.017$ ,  $n=21$ ). The PGRN converting activity was blocked by A1AT, but not EDTA and only with SLPI when PR3 activity was absent. Conclusion PGRN and GRN-peptides are present in sputum sol phase, conversion is driven by PR3 and NE. The concentration of PGRN in the airways is associated with the increased inflammation seen with bacterial colonisation as assessed by markers of neutrophilic inflammation.