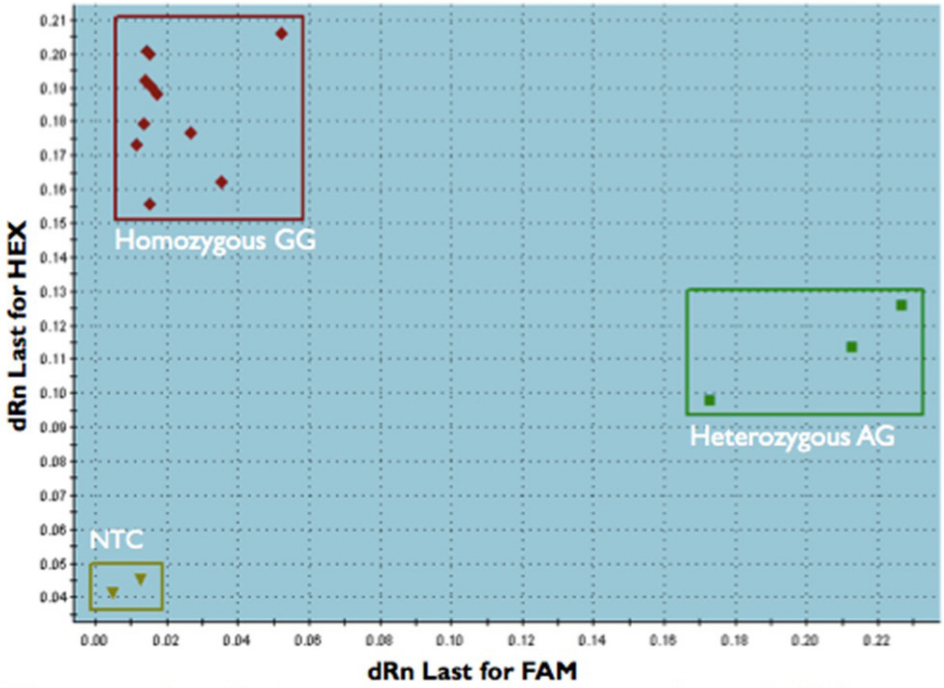

FIGURE 1: A sample TaqMan® assay of 16 samples (including 2 negative controls, NTC). Fluorescence of the different allele-specific fluorophores used (HEX and FAM) allows differentiation between genotypes GG, GA, AA.

Abstract P249 Figure 1 A sample TaqMan® assay of 16 samples (including 2 negative controls, NTC). Fluorescence of the different allele-specific fluorophores used (HEX and FAM) allows differentiation between genotypes GG, GA, AA.

P250 ASSOCIATION BETWEEN PGRN AND AIRWAY INFLAMMATION IN COPD

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Background Progranulin (PGRN) is an anti-inflammatory protein, which is converted into pro-inflammatory granulin peptides (GRNs) by neutrophil elastase (NE) and proteinase-3 (PR3) (1). Neutrophilic inflammation is implicated in the pathophysiology of COPD, therefore the influence of PGRN on mechanisms of neutrophilic inflammation may be of great relevance to understanding and treating inflammation in the disease.

Methods Sputum and serum samples were obtained from COPD patients with chronic bronchitis at exacerbation and in the subsequent clinically stable state. Sputum samples were graded by purulence and cultured for quantitative microbiology. PGRN was measured in sputum sol phase together with leukotriene B4 (LTB4), interleukin 8 (IL-8), myeloperoxidase (MPO), tumour necrosis factor α (TNFα), NE and PR3. PGRN and C-reactive protein (CRP) were measured in the serum.

Results PGRN was lower in purulent sputum (median=38.91 ng/ml (IQR=1.55–89.71 ng/ml)) than mucoid (median=79.78 ng/ml (IQR=51.57–111.24 ng/ml)) (p=0.024, n=69). In purulent sputum PGRN correlated negatively with bacterial load and markers of inflammation (Table 1). Serum PGRN did not correlate with CRP, but was higher in stable COPD patients (median=65.71 ng/ml (IQR=0–86.46 ng/ml)) than healthy controls (median=38.55 ng/ml (IQR=36.11–44.82 ng/ml)) (p=<0.001, n=20), and increased further during purulent exacerbations (median=75.43 ng/ml (IQR=64.83–85.28 ng/ml)) (p=0.010, n=25).

Conclusion The concentration of PGRN in the lung is associated with the increased inflammation seen with bacterial infection and exacerbation as assessed by markers of inflammation. The conversion of PGRN to GRNs may provide a mechanism by which neutrophil proteases regulate inflammation in COPD. Elevated circulating PGRN may reflect systemic inflammation associated with COPD.

1. Kessenbrock K, et al. J Clin Invest. 2008 Jul; 118(7):2438–47.

Abstract P250 Table 1 Correlations and their significance between PGRN and markers of inflammation measured in sputum sol phase

	Correlations	n
IL-8 (nM)	r=–0.512, p=<0.001	44
MPO (units/ml)	r=–0.543, p=<0.001	36
LTB4 (nM)	r=–0.438, p=0.003	44
TNF (pM)	r=–0.647, p=0.032	11
NE (nM)	r=–0.614, p=0.002	22
PR3 (nM)	r=–0.737, p=<0.001	22
Bacterial load (CFU/ml)	r=–0.418, p=0.005	44

P251 THE ROLE OF REACTIVE OXIDATIVE SPECIES WITHIN CIGARETTE SMOKE EXTRACT ON APOPTOSIS AND INFLAMMATION IN PRIMARY NASAL EPITHELIAL CELLS

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Introduction The responses of the bronchial epithelium to cigarette smoke (CS) are well characterized, but effects on the nasal epithelium, also important in respiratory disease, are not as well defined. The mechanism of cell death due to cigarette smoke extract (CSE) exposure is controversial. As there is convincing evidence that cigarette smoke decreases levels of protective antioxidants, we hypothesised that reactive oxidative species contained within CSE contribute to its immunomodulatory and cytotoxic properties.

Methods Nasal brushings were obtained from 16 healthy volunteers from the medial aspect of the inferior turbinate as previously