P113 ANTIMICROBIAL PEPTIDES IN INFLAMMATORY PHENOTYPES OF COPD

¹JL Cane, ¹SJ Thulborn, ²SC Piper, ²DK Finch, ¹M Bafadhel. ¹University of Oxford, Oxford, UK; ²MedImmune, Cambridge, UK

10.1136/thoraxjnl-2017-210983.255

Introduction Antimicrobial peptides act to defend the host from microbial action and colonisation. Patients with COPD and neutrophilic inflammation experience bacterial colonisation more frequently than other COPD phenotypes. Here we assess the levels of five antimicrobial peptides in peripheral blood and sputum in relation to their inflammatory phenotype. We hypothesise that patients with neutrophilic inflammation have lower antimicrobial peptide levels than other COPD inflammatory phenotypes and that the presence of non-typeable haemophilus influenzae (NTHi) is associated with low antimicrobial peptide levels.

Method Plasma and sputum supernatants from 8 healthy donors, 18 COPD patients and 10 non-eosinophilic asthmatics were tested for SLPI, osteopontin, lysozyme, elafin and beta defensin-1 by ELISA. Patients were stratified into eosinophilic and neutrophilic groups with a 3% sputum eosinophil cut-off. NTHi was measured in sputum plugs by qPCR of the *Omp P6* gene.

Results Levels of antimicrobial peptides in plasma and sputum showed no difference between those with eosinophilic and neutrophilic COPD. Between disease groups, beta defensin-1 levels are higher in plasma of COPD patients (median: 10.92 ng/ml (IQR: 4.137–18.09)) than healthy individuals (median: 3.665 ng/ml (IQR: 2.59–4.549), $p=0.0033$) and non-eosinophilic asthmatics (median: 4.984 ng/ml IQR: 3.334–7.208), $p=0.0442$) (figure 1). No antimicrobial peptide correlated with NTHi levels in the sputum plug.

Conclusions Similar levels of SLPI, osteopontin, lysozyme, elafin and beta defensin-1 in sputum and plasma between COPD phenotypes suggests that defence against pathogens by these antimicrobial peptides is not lacking in differential inflammatory COPD phenotypes. The role antimicrobial peptides play in NTHi colonisation remains to be determined.

Abstract P113 Figure 1 Concentrations of beta defensin-1 in plasma from healthy individuals, asthmatics and COPD patients.

P114 GLUCOCORTICOID RECEPTOR α AND β EXPRESSION IN BRONCHIAL EPITHELIAL CELLS INFECTED WITH NTHI

LJ Parker, JL Cane, SJ Thulborn, M Bafadhel. University of Oxford, Oxford, UK

10.1136/thoraxjnl-2017-210983.256

Introduction Steroids act through the glucocorticoid receptor (GR), of which the alpha-isoform (GR α) is most abundant. Neutrophilic COPD is associated both with resistance to steroids and with airway bacterial infection, most commonly by non-typeable Haemophilus influenzae (NTHi). We hypothesised that NTHi downregulates GR α or upregulates its inhibitory beta-isoform (GR β) in bronchial epithelial cells, thereby inhibiting their response to steroids.

Method Bronchial epithelial cell line Beas-2B were treated with the corticosteroid Fluticasone propionate (0, 1 nM or 100 nM) for 2 hours prior to infection with 1.5×10^4 , 1×10^6 and 1.5×10^7 CFU/ml NTHi (low, medium and high load respectively). 6 hours post-infection supernatants were collected and RNA extracted from cells. RNA was reverse transcribed to cDNA in which levels of GR α , GR β and GAPDH were determined by SYBR Green PCR and expression calculated using the Pfaffl method relative to untreated cells.

Results GR α expression in Beas-2B was enhanced by corticosteroid treatment in a stepwise manner for 1 nM (median fold increase from untreated: 1.491, IQR: 1.305–1.668), and 100 nM (median: 1.742 fold, IQR: 1.51–1.9) ($p \geq 0.05$ for both). Increasing load of NTHi showed no effect on GR α expression. GR β expression showed little fluctuation from levels of untreated cells upon infection with NTHi alone or high dose corticosteroid, however the two showed a trend to synergistically decrease in GR β expression when treated with high corticosteroid and high load of NTHi (median fold change from untreated cells: 0.542 (IQR: 0.453–0.578) ($p=0.25$) (figure 1).

Conclusions Corticosteroid treatment shows a trend to increased GR α expression on Beas-2B cells. Increased NTHi load has no effect on GR α expression of Beas-2B cells. GR β expression appears not to be affected by NTHi infection alone, however with corticosteroid shows a trend to decreased expression. The experiments are to be repeated in primary bronchial epithelial cells to determine whether they follow the trend seen here in a cell line.

Abstract P114 Figure 1 Expression of GR β in Beas-2B cells relative to untreated cells normalised to GAPDH.