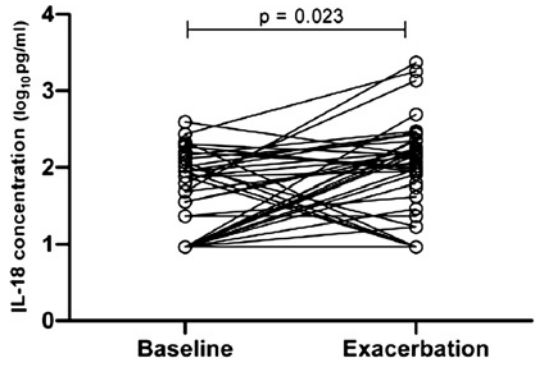

Abstract P119 Figure 1 Paired sputum IL-18 levels at baseline and exacerbation.

REFERENCE

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P120 COMPARISON OF CELLULAR INFLAMMATION AND TLR EXPRESSION PROFILES BETWEEN HEALTHY AND COPD SUBJECTS

doi:10.1136/thoraxjnl-2011-201054c.120

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Introduction and Objectives Chronic obstructive pulmonary disease (COPD) is a complex inflammatory disease of the lungs Initiated by inhalation of toxic particles or gases. Periodic exacerbations triggered by respiratory pathogens are a major cause of morbidity/mortality in these patients. Microbial pathogens are recognised by pattern recognition receptors such as the toll-like receptors (TLRs), initiating innate immune defences. We hypothesised that abnormal TLR expression, and not resident inflammatory cell load in the lung parenchyma, contributes to exacerbation in COPD.

Methods Human lung tissue, distant from tumour margins, was taken from ex-smoker patients undergoing lobectomy for lung cancer. Patients were classified according to GOLD guidelines as healthy control subjects (HC) or those with COPD. Resected tissue was digested and cells analysed by flow cytometry for phenotypic markers of epithelial cells and inflammatory cell subtypes (macrophages, CD8 + and CD8− T lymphocytes) and the TLR2 and four expressions on these subtypes. Quantitative data of cell numbers and TLR staining intensity were compared using Mann–Whitney U tests.

Results Seven COPD patients and nine age-matched HC were analysed. No significant differences in the numbers of inflammatory or epithelial cells in the parenchymal tissue of these groups were observed, although a trend was observed to a reduction in macrophage numbers in the COPD group (median HC=4.2, median COPD=3.2 p=0.17). Similarly, no significant difference was found in the level ofTLR2 or TLR4 expression on any of the cell types examined. However, a trend was observed towards a decrease in TLR2 expression on epithelial cells in the COPD patients (median sMFI 3399 (HC) vs 2462 (COPD), p=0.094).

Conclusions This preliminary analysis has demonstrated that, as hypothesised, there was no significant difference in inflammatory cell load in parenchymal tissue between the two groups. The trend towards a reduced expression of TLR2 in the epithelial cells may reflect an abnormal down regulation of this receptor due to constant exposure to bacterial pathogens. The lack of surveillance of microbial pathogens by TLRs is a potential mechanism by which patients with COPD are more susceptible to infection by new bacterial strains and thus could contribute to exacerbation frequency.

P121 DIFFERENTIAL RESPONSES OF M1 AND M2 MONOCYTE-DERIVED MACROPHAGE PHENOTYPES IN COPD

doi:10.1136/thoraxjnl-2011-201054c.121

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Introduction Inflammation in chronic obstructive pulmonary disease (COPD) is associated with increased numbers of highly activated macrophages with a reduced phagocytic capacity. Macrophages may exist as M1 "classically activated" or M2 "alternatively activated" with different phagocytic and inflammatory mediator profiles, suggesting in COPD a more persistent, M1 macrophage predominates. It is unknown whether circulating monocytes in COPD patients predetermine whether M1 macrophages will be preferentially activated, thus driving an inflammatory phenotype.

Objectives This study investigated differences between monocyte-derived macrophages (MDM) from non-smokers, smokers and COPD patients driven towards M1and M2 phenotypes.

Methods Monocytes were isolated from whole blood and cultured with GM-CSF (2 ng/ml) or M-CSF (100 ng/ml) for 12d to generate M1 and M2 MDM respectively. Cells were stimulated with LPS (0.01–100 ng/ml) for 24 h and TNFα, CXCL8 and IL-10 measured by ELISA. Phagocytosis was measured fluorimetrically following exposure to fluorescent beads, *H influenzae* or *S pneumoniae* for 4 h.

Results There were no differences in baseline release of any of the cytokines measured between subject groups. Cells released cytokines in response to LPS in a concentration-dependent manner. M1MDM derived from non-smokers and COPD patients released greater concentrations of LPS-stimulated (10 ng/ml) TNFα compared to M2 MDM. (Non-smokers: 7.4±2.3 vs 1.5±0.2 ng/ml, n=4; p<0.01; COPD: 7.0±1.8 vs 2.1±0.9 ng/ml, n=4) and significantly less IL-10 (Non-smokers: 0.4±0.2 vs 3.0±0.6 ng/ml, n=4; p<0.05; COPD: 0.3±0.04 vs 1.5±0.5 ng/ml, n=3) than M2 MDM. These differences were not apparent in cells from smokers. Both M1 and M2 MDM released LPS-stimulated CXCL8 similarly with no difference between subject groups. Phagocytosis of polystyrene beads was similar by both MDM phenotypes in all subject groups. However, there was a trend for M2 MDM to phagocytose more bacteria compared with M1 MDM which reached significance in healthy subjects (p<0.05).

Conclusions M1 and M2 MDM from non-smokers and COPD subjects showed distinct differences with respect to LPS-stimulated cytokine release and phagocytosis, however these differences were not apparent in cells from smokers without COPD. This suggests that smokers without COPD have altered circulating monocytes that do not differentiate into the pro-inflammatory M1 macrophage and may be protective against the development of COPD.

P122 NO ABSTRACT ASSIGNED TO THIS NUMBER

doi:10.1136/thoraxjnl-2011-201054c.122

Challenges in smoking cessation

P123 A RETROSPECTIVE COHORT STUDY OF THE LONG TERM EFFECTIVENESS OF SMOKING CESSATION COUNSELLING

doi:10.1136/thoraxjnl-2011-201054c.123

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Introduction and Objectives A regional smoking cessation counselling service provides one-to-one counselling with follow-up by telephone and appointments for up to 1 year. Previously, no long-term