European Respiratory Society
Annual Congress 2012

Abstract Number: 753

Publication Number: P791

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: Biomarkers **Keyword 2:** Inflammation **Keyword 3:** COPD - mechanism

Title: Enhanced IL-6 and CCL3 activity in COPD

Dr. Arjun 2982 Ravi ARavi@meu.org.uk MD [1], Dr. Shruti 2983 Khurana SKhurana@meu.org.uk MD [1], Dr. Jonathan 2984 Plumb Jonathan.Plumb@manchester.ac.uk [1], Mr. George 2985 Booth GBooth@meu.org.uk [1], Dr. Matthew 3185 Catley Matthew.Catley@UCB.com [2], Dr. Emma 3186 Smith Emma.Smith@UCB.com [2], Dr. Louise 3189 Healy Louise.Healy@UCB.com [2], Prof. Dr Jørgen 3190 Vestbo Jorgen.Vestbo@manchester.ac.uk MD [1] and Prof. Dr Dave 6882 Singh DSingh@meu.org.uk MD [1]. [1] Medicines Evaluation Unit, University of Manchester, Greater Manchester, United Kingdom and [2] UCB Celltech, UCB S.A, Slough, Berkshire, United Kingdom .

Body: Rationale IL-6 is a pleiotropic cytokine that is involved in the regulation of inflammation. Increased serum IL-6 levels are associated with reduced FEV1 in COPD patients independent of age or smoking status. Elevated levels of sputum IL-6 in COPD patients have been associated with increased exacerbation frequency. The mechanism by which IL-6 may mediate inflammation in COPD is uncertain. We sought to determine levels of IL-6 and its soluble receptor (sIL-6R) in COPD sputum. IL-6 signaling can alter the levels of the neutrophil chemoattractant CCL3 and the monocyte chemoattractant CCL2; we also investigated the levels of these chemokines. Methods 70 patients with GOLD stage I-IV COPD and 30 healthy controls comprising of 15 healthy smokers (HS) and 15 healthy non-smokers (HNS) underwent sputum sampling with PBS processing. Levels of IL-6, sIL-6R, CCL2, CCL3 were determined by multiplex analysis (MSD® platform) of sputum supernatant. Results Healthy smokers expressed the highest levels of sputum IL-6. COPD patients expressed the highest levels of sIL-6R. COPD patients also expressed the highest levels of sputum CCL3. In contrast, CCL2 expression was significantly reduced in COPD patients.

	COPD	HS	HNS	ANOVA
IL-6 (pg/ml)	116.8 (84.5)	258.3 (214.1)	80.87 (74.34)	p=0.0016
sIL-6R (pg/ml)	256.6 (260.9)	98.84 (44.33)	136.2 (90.31)	p=0.019
CCL2 (pg/ml)	26.7 (51.2)	207.8 (104)	162.4 (142.6)	p<0.0001
CCL3 (pg/ml)	182.1 (164)	8.12 (6.83)	58.75 (63.17)	p<0.0001

Data expressed as mean (SD)

Conclusion We report evidence of enhanced IL-6 signaling and CCL3 activity in COPD sputum. We have observed that there is reduced CCL2 activity and enhanced CCL3 activity in COPD sputum. IL-6 may

therefore promote neutrophillic inflammation in COPD through up-regulation of CCL3 expression.