European Respiratory Society
Annual Congress 2013

Abstract Number: 2001

Publication Number: P626

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: COPD - mechanism **Keyword 2:** Monocyte / Macrophage **Keyword 3:** Bacteria

Title: Increased expression of sphingosine-1-phosphate and S1PR2 are associated with attenuated macrophage phagocytosis in COPD

Mr. Tankut G. 4274 Guney Tankut.guney09@imperial.ac.uk [1], Dr. Rebecca 4275 Holloway r.holloway@imperial.ac.uk [1], Dr. Abigail 4276 Taylor A.Taylor2@wellcome.ac.uk [1], Dr. Catherine 5374 Thomas cmrthomas@doctors.org.uk MD [1], Prof. Peter 4277 Barnes p.j.barnes@imperial.ac.uk [1] and Prof. Louise 4278 Donnelly l.donnelly@imperial.ac.uk MD [1]. [1] Airway Disease, National Heart and Lung Institute, Imperial College London, London, United Kingdom, SW3 6LY .

Body: Sphingosine-1-phosphate (S1P) is a lipid mediator that may alter macrophage polarisation and function. S1P is synthesised by SPHK1 and SPHK2 and acts via S1P receptors. Its role in COPD is unclear and so this study examined S1P levels in induced sputum and its role using monocyte-derived macrophages (MDM). Induced sputum was collected from non-smokers (NS), smokers (S) and COPD patients. MDM were generated from monocytes. S1P was measured by ELISA and gene expression of SPHK1-2 and S1PR1-5 measured by qPCR and Western blotting. MDM phagocytosis of Haemophilus influenzae (HI) or Streptococcus pneumoniae (SP) was assessed by fluorimetry. S1P was elevated in induced sputum from COPD patients compared with NS (NS 6.2±2μM; S 11.1±2μM; COPD 15.4±3μM; n=8-9, $p<0.05$). There was no difference in expression of SPHK1 or SPHK2 between the groups (Table 1). However, expression of only one receptor (S1PR2) was significantly increased in COPD MDM (Table 1). Inhibition of SPHK increased phagocytosis of HI and SP by COPD MDM (138±11% and 122±4% respectively) as did a selective S1PR2 antagonist, JTE-013 (144±7% and 137±7% respectively). Exogenous addition of S1P suppressed phagocytosis of HI by NS MDM by 19±7%. These data suggest that S1P may suppress phagocytosis and inhibition of synthesis or blockade of S1PR2 might improve bacterial clearance in COPD.

Enzyme and S1P receptor gene expression levels.

	NS n=13	S n=12	COPD n=23
SPHK1	1172±426	2253±854	1317±445
SPHK2	352±88	51±122	2808±1155
S1PR1	16±12	51±19	56±40
S1PR2	526±118	1463±268*	1545±320*
S1PR3	86±69	21±15	216±180

S1PR4	251±83	186±48	393±80
S1PR5	1±0	3±2	6±2

Table 1: Data are mean±SEM of % ratio gene:HPRT1; *p<0.05