European Respiratory Society
Annual Congress 2013

Abstract Number: 243

Publication Number: P559

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: Inflammation **Keyword 2:** Asthma - mechanism **Keyword 3:** Infections

Title: The NLRP3 inflammasome is not activated in airway smooth muscle upon TLR2 ligation

Ms. Hanna 1915 Im zhannaz89@hotmail.com [1], Dr. Jeremy 1916 Hirota Jeremy.Hirota@hli.ubc.ca [2], Mr. Md. Mostafizur 1917 Rahman mrah7373@uni.sydney.edu.au [1], Ms. Nowshin 1918 Rumzhum nrum3025@uni.sydney.edu.au [1], Dr. Melanie 1919 Manetsch MManetsch@ccia.unsw.edu.au [1], Mr. Chris 1920 Pascoe Chris.Pascoe@hli.ubc.ca [2], Dr. Brian 1921 Oliver Brian.Oliver@sydney.edu.au [3] and Prof. Alaina 1922 Ammit alaina.amit@sydney.edu.au [1]. [1] Respiratory Research Group, Faculty of Pharmacy, University of Sydney, Sydney, NSW, Australia, 2006 ; [2] UBC James Hogg Research Centre Heart + Lung Institute, St Pauls Hospital, Vancouver, BC, Canada, V6Z 1Y6 and [3] Woolcock Institute of Medical Research, University of Sydney, Sydney, NSW, Australia, 2006 .

Body: Inflammasomes have emerged as playing key roles in inflammation and innate immunity. A growing body of evidence has suggested that the nucleotide-binding domain and leucine-rich repeat protein 3 (NLRP3) inflammasome is important in chronic airway diseases such as asthma and COPD. Inflammasome activation results, in part, in pro-IL-1β processing and secretion of the pro-inflammatory cytokine IL-1β. Because asthma exacerbations are associated with elevated levels of secreted IL-1β we addressed whether the NLRP3 inflammasome is activated under in vitro conditions that mimic infectious exacerbation in asthma. Primary cultures of airway smooth muscle (ASM) cells were treated with infectious stimuli (mimicked using the TLR2 agonist Pam3CSK4, a synthetic bacterial lipopeptide). While Pam3CSK4 robustly upregulated ASM cytokine expression in response to TNFα and significantly enhanced IL-1β mRNA expression, we were unable to detect IL-1β in the cell supernatants. Thus, IL-1β was not secreted and therefore unable to act in an autocrine manner to promote amplification of ASM inflammatory responses. Moreover, TLR2 ligation did not enhance NLRP3 mRNA expression in ASM cells, nor was NLRP3 protein detected in the airway smooth muscle layer of tracheal sections from human donors. In conclusion, these data demonstrate that enhanced synthetic function of ASM cells, induced by infectious exacerbation of airway inflammation, is NLRP3 inflammasome and IL-1β-independent. Activation of NLRP3 inflammasome by invading pathogens may prove cell-type specific in exacerbation of airway inflammation in asthma.