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Protease activated receptor 2 (PAR2) antagonism reduces pro-inflammatory cytokine production in bronchial epithelial cells

COPD, Epithelial cell, Inflammation

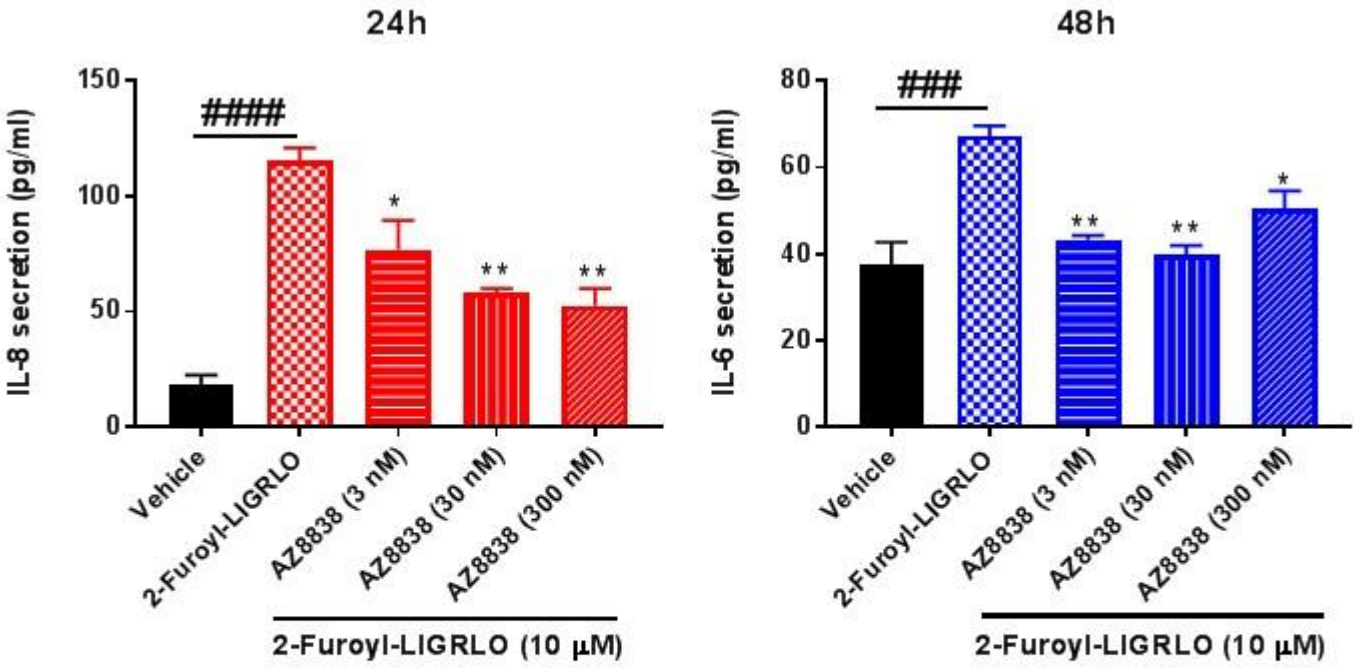
M. Bailo[1], L. Dunning[1], J. Brzeszczynska[1], K. Mcintosh[2], R. Plevin[2], S. L. Martin[3], G. P. Sergeant[4], C. S. Goodyear[5], G. S. Litherland[1], J. C. Lockhart[1], A. Crilly[1]

[1]University of the West of Scotland - Paisley (United Kingdom), [2]University of Strathclyde - Glasgow (United Kingdom), [3]Queen's University - Belfast (United Kingdom), [4] Dundalk Institute of Technology - Dundalk (Ireland), [5]University of Glasgow - Glasgow (United Kingdom)

PAR2 is a G-protein coupled receptor which modulates inflammation via pro-inflammatory cytokine release. Chronic obstructive pulmonary disease (COPD) is associated with an abnormal inflammatory response by the lungs (Barnes, P. J. *The Journal of allergy and clinical immunology* 2016; 138: 16-27). The aim of this study was to investigate a putative role for PAR2 in COPD.

Expression of PAR2 was evaluated in primary human bronchial epithelial cells derived from healthy controls and COPD patients (HBECs & DHBECs respectively) and bronchial epithelial cell lines (BEAS-2B) by immunofluorescence. Levels of secreted IL-6 and IL-8 were determined by ELISA. The role of PAR2 in BEAS-2B was investigated using the PAR2 agonist 2-Furoyl-LIGRLO-amide (10 μM) and the antagonist AZ8838 (Cheng R. *et al*. *Nature* 2017; 545: 112-115).

Immunofluorescent microscopy showed PAR2 expression in HBECs, COPD HBECs and BEAS-2B. Evaluation of spontaneous cytokine secretion revealed that both IL-6 and IL-8 were significantly increased ($p<0.01$) in DHBECs compared to HBECs and BEAS-2B. Inhibition of PAR2 activation in BEAS-2B by AZ8838 significantly reduced IL-8 (24 h) and IL-6 (48 h) secretion (figure below).



IL-6 and IL-8 level in the supernatant of BEAS-2Bs cells after 24h and 48h stimulation with AZ8838 (3 nM – 300 nM) + 2-Furoyl-LIGRLO-amide was examined using ELISA assay. Results are expressed in mean±SEM of 3 different replicates. One way ANOVA corrected with Bonferroni test for multiple comparison was performed to analyse the difference in secretion. *(####p<0.0001; ###p<0.001;**p<0.01; *p<0.05).*

Using a recently described antagonist (AZ8838), this study demonstrates a role for PAR2 in pro-inflammatory cytokine release in bronchial epithelial cells, suggesting PAR2 may contribute to the pathogenesis of COPD.