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

COPD, Epithelial cell, Inflammation

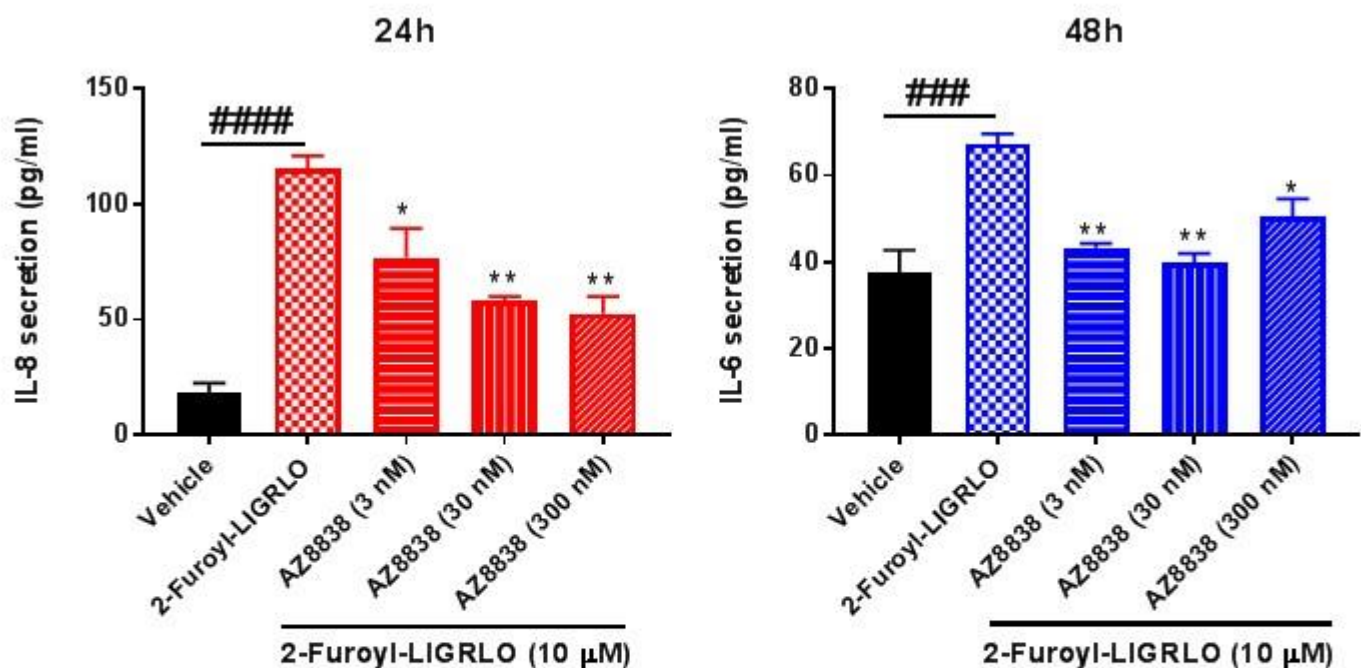
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PAR2 is a G-protein coupled receptor which modulates inflammation via pro-inflammatory cytokine release. Chronic obstructive pulmonary disease (COPD) is associated with an abnormal inflammatory response by the lungs (Barnes, P. J. *The Journal of allergy 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.