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Published in:
European Respiratory Journal

DOI:
10.1183/13993003.congress-2020.2292

Published: 28/10/2020

Citation for published version (APA):

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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).
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.