
“This is an author-submitted, peer-reviewed version of a manuscript that has been accepted for publication in the European Respiratory Journal, prior to copy-editing, formatting and typesetting. This version of the manuscript may not be duplicated or reproduced without prior permission from the copyright owner, the European Respiratory Society. The publisher is not responsible or liable for any errors or omissions in this version of the manuscript or in any version derived from it by any other parties. The final, copy-edited, published article, which is the version of record, is available without a subscription 18 months after the date of issue publication.”
Protease activated receptor 2 (PAR2) antagonism reduces pro-inflammatory cytokine production in bronchial epithelial cells

COPD, Epithelial cell, Inflammation


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