Oxidative stress driven inflammatory responses in lung epithelial cells


Published in: THORAX

DOI: 10.1136/thorax-2020-BTSabstracts.55

Published: 21/01/2021

Document Version
Peer reviewed version

Link to publication on the UWS Academic Portal

Citation for published version (APA):

General rights
Copyright and moral rights for the publications made accessible in the UWS Academic Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
If you believe that this document breaches copyright please contact pure@uws.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.
Oxidative Stress Driven Inflammatory Responses in Lung Epithelial Cells

COPD, Inflammation, Epithelial cell


1University of the West of Scotland - Paisley, Scotland (United Kingdom), 2Queens University Belfast - Belfast, Northern Ireland (United Kingdom), 3Dundalk Institute of Technology - Dundalk, Ireland (Ireland), 4University of Glasgow - Institute of Infection, Immunity & Inflammation (United Kingdom). This study was funded by the EU under the Interreg VA Programme, managed by the Special EU programmes body (SEUPB).

Cigarette smoke stimulates an inflammatory response and produces oxidants that cause oxidative stress in the lung, promoting pathophysiological changes related to chronic obstructive pulmonary disease (COPD). Hydrogen peroxide (H$_2$O$_2$) is an important oxidant detected in breath condensate of COPD patients. We aim to understand how chronic exposure to H$_2$O$_2$ alone or in combination with other inflammatory mediators influences epithelial cell responses relevant to COPD lung pathology.

BEAS-2B cells were exposed chronically to H$_2$O$_2$ for 2 h/day for 3 days at different concentrations, alone or in combination with TGF-β (10 ng/ml) or LPS (100 or 500 ng/ml). Cell viability was assessed by MTT assay. Cytokines were measured by ELISA. Intracellular ROS production was detected by CM-H$_2$DCFDA assay. Data were analysed using one-way ANOVA, followed by Multiple Comparison Test.

Cells tolerated a repeated exposure of H$_2$O$_2$ (up to 15 μM) ± TGF-β or LPS without significant loss of viability. Intracellular ROS was significantly elevated in the presence of LPS (mean ± SEM; 217±17 %; p<0.0001) or H$_2$O$_2$ (331±13 %; p<0.0001), with an additive effect of combined treatment (H$_2$O$_2$, 444±12 vs. LPS + H$_2$O$_2$, 604±35 %; p<0.0001). H$_2$O$_2$ stimulated modest release of IL-8 (38±2 pg/ml) and IL-6 (84±13 pg/ml). However, repeated 15 μM H$_2$O$_2$ exposure synergistically enhanced TGF-β induced IL-8 (TGF-β, 194±13 vs. TGF-β+ H$_2$O$_2$, 279±10 pg/ml; p<0.0001) but not IL-6 (TGF-β, 431±22 vs. TGF-β+ H$_2$O$_2$, 449±2 pg/ml). H$_2$O$_2$ synergistically enhanced LPS secretion of both IL-8 (LPS, 2487±21 vs. LPS+ H$_2$O$_2$, 2898±109 pg/ml; p<0.0001), and IL-6 (LPS, 2469±72 vs. LPS+ H$_2$O$_2$, 3277±62 pg/ml; p<0.0001).

Oxidative stress appears to be generated in BEAS-2B cells by LPS or H$_2$O$_2$ alone, and increased in combination. Repeated exposure to H$_2$O$_2$ induced minimal inflammatory response, but synergistically enhanced the effect of TGF-β and LPS on cytokine production. These data suggest combined exposure models may be useful to study the effects of epithelial cell challenges relevant to COPD pathology.