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Repeated exposure to hydrogen peroxide enhances TGF-β and LPS dependent inflammatory responses in BEAS-2B cells

COPD, Inflammation, Epithelial cell

F. Tarhini¹, L. Dunning¹, A. Crilly¹, J. Brzeszczynska¹, L. Mcearvey², K. Thornbury³, C. S.Goodyear⁴, J. C.Lockhart¹, G. J.Litherland¹

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)

Cigarette smoke stimulates an inflammatory response and produces oxidants that cause oxidative stress in the lung, which promotes pathophysiological changes related to chronic obstructive pulmonary disease (COPD) (Kirkham, P. Pharmacol Ther 2006; 111: 476-94). Hydrogen peroxide (H₂O₂) is one of the oxidants detected in the breath condensate of COPD patients (Montuschi, P. Clin Chim Acta 2005; 35: 22-34). We aim to understand how chronic exposure to H₂O₂ alone or in combination with other inflammatory mediators influences epithelial cell responses relevant to COPD lung pathogenesis.

BEAS-2B cells were exposed to H₂O₂ (2 h/d for 3 days) at different concentrations, alone or in combination with TGF-β (10 ng/ml) or LPS (500 ng/ml). Cell viability was assessed. IL-8 and IL-6 were measured by ELISA. Data was analysed using Multiple Comparison Test.

Cells tolerated a repeated exposure of H₂O₂ (up to 15 µM) ± TGF-β or LPS without significant loss of viability. H₂O₂ stimulated modest release of IL-8 (mean ± SEM; 38±2 pg/ml) and IL-6 (84±13 pg/ml). However, repeated 15 µM H₂O₂ exposure significantly enhanced TGF-β induced IL-8 (TGF-β, 194±13 vs. TGF-β+ H₂O₂, 279±10 pg/ml; p<0.0001) but not IL-6 (TGF-β, 431±22 vs. TGF-β+ H₂O₂, 449±2 pg/ml). H₂O₂ enhanced LPS secretion of both IL-8 (LPS, 2487±21 vs. LPS+ H₂O₂, 2898±109 pg/ml; p<0.0001), and IL-6 (LPS, 2469±72 vs. LPS+ H₂O₂, 3277±62 pg/ml; p<0.0001).

Repeated exposure of BEAS-2B cells to H₂O₂ induced minimal inflammatory response, but enhanced the effect of TGF-β and LPS on cytokine production. These data suggest such combined exposure models may be useful to study the effects of epithelial cell challenge relevant to COPD pathology.