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Polarised Release Of Mediators By Differentiated Primary Bronchial Epithelial Cells From Normal And Asthmatic Donors In Response To Grass Pollen

C. Blume[1], E. J. Swindle[1], P. Dennison[1], N. P. Jayasekera[1], H. Behrendt[2], C. B. Schmidt-Weber[3], S. T. Holgate[4], P. H. Howarth[1], C. Traidl-Hoffmann[3], D. E. Davies[1],

[1]University of Southampton, Southampton, United Kingdom, [2]ZAUM - Center of Allergy and Environment, Munich, Germany, [3]ZAUM - Center of Environment and Allergy, Munich, Germany, [4]University of Southampton, School of Medicine, Southampton, United Kingdom

Corresponding author's email: C.Blume@soton.ac.uk

Rationale: Airway epithelial cells form the first line of defence against environmental substances like pollen. On the apical surface of the airway epithelium, tight junctions control paracellular permeability to ions and macromolecules and define the polarity of the epithelium. The aim of this study was to analyse the polarised release of mediators by bronchial epithelial cells after exposure to grass pollen derived substances.

Methods: Primary human bronchial epithelial cells from normal or severe asthmatic donors were differentiated at the air-liquid interface (ALI) and stimulated apically with timothy grass pollen extract. Apical and basolateral release of IL-8, eotaxin, GM-CSF, IP-10, I-TAC, MCP-1, MDC, MIP-3α, RANTES, TARC and TNF-α were analysed by immunoassay. The integrity of the epithelial barrier was monitored by measuring transepithelial resistance (TER) and immunofluorescent staining for the tight junction proteins, ZO-1 and occludin. Involvement of ERK1/2, p38 and JNK mitogen-activated protein kinase (MAPK) pathways was assayed using specific inhibitors.

Results: At baseline, the concentrations of cytokines released by ALI cultures varied over three orders of magnitude, depending on the mediator. Although the rank order of cytokine secretion was similar for the both compartments, levels of RANTES and GM-CSF were atypical and were substantially lower in the basolateral compartment. Apical release of MIP-3α at baseline was significantly higher in cultures from severe asthmatic donors. Following exposure of the cultures to grass pollen extract, the integrity of the bronchial epithelial barrier was not impaired, however cytokine responses were either up or down regulated, especially in the apical compartment. Apical release of MIP-3α, TNFα and MDC was increased in severe asthma cultures, while MDC was reduced; MDC, eotaxin and IP-10 were reduced in normal cultures. Apical and basolateral IL-8 release was dose-dependently increased in response to pollen extract, with preferential release to the apical compartment but there was no significant difference between responses from cultures derived from non-asthmatic and severe asthmatic donors. Apical release of IL-8 was mediated by activation of the ERK1/2 and p38 MAPK pathways, whereas basolateral release was unaffected by any of the MAPK inhibitors.

Conclusion: The epithelial barrier modulates vectorial release of mediators in response to pollen without direct effects on the physical barrier properties of the epithelium. Since secretion of mediators to the apical and basolateral compartments is differentially regulated, a detailed analysis of the mechanisms of polarised mediator release may contribute to our understanding of the role of the epithelial in immune dysfunction in asthma.

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