DISASSEMBLY OF EPITHELIAL TIGHT JUNCTIONS IN WELL-DIFFERENTIATED AIR-LIQUID INTERFACE (ALI) CULTURES FOLLOWING HUMAN RHINOVIRUS INFECTION RESULTS IN AIRWAY EPITHELIAL PERMEABILITY CHANGES.

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Introduction: Tight junctions (TJ) provide a physical barrier against external insults and although TJs have been extensively assessed in general terms, few studies have directly addressed the consequence on barrier function following the disassembly of TJ protein post human rhinovirus (HRV) infection. This study aimed to assess TJ expression and barrier function prior to and post HRV infection in well-differentiated cultures of both healthy and asthmatic epithelium.

Methods: Primary airway epithelial cells from healthy and asthmatic children obtained via bronchial brushings and cultured as previously mentioned (Kicic *et al.* 2006), were differentiated into air-liquid interface (ALI) and subsequently infected with HRV-1B over 24h. Barrier integrity was assessed by protein expression of occludin and zonula occluden-1 (ZO-1) via in-cell western (ICW) and confocal microscopy, while barrier function was assessed via transepithelial electrical resistance (R_T) measurement and a permeability assay.

Results: Semi-quantitative assessment of occludin and ZO-1 protein expression via confocal microscopy corroborated with ICW findings demonstrating reduced basal membrane TJ expression in asthmatic compared to healthy controls. A greater effect on TJ disassembly was observed within the asthmatic epithelium post infection and this was concurrent with a significant decrease in R_T and a marked increase in transepithelial permeability.

Conclusion: This study demonstrated significant differences in basal membrane TJ protein expression between healthy and asthmatic epithelium, suggesting intrinsic differences between healthy and mild-asthmatics. Furthermore, post HRV infection, an exaggerated disassembly in the asthmatic cohorts, which is concomitant with increased transepithelial permeability suggests elevated trafficking of small sized aeroallergens into sub-epithelial space, contributing to asthma exacerbations.

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