HUMAN RHINOVIRUS INFECTION OF ASTHMATIC AIRWAY EPITHELIAL CELLS CAUSES TIGHT JUNCTION DISASSEMBLY RESULTING IN INCREASED PERMEABILITY.

K LOOI[1,2], A LARCOMBE[2], G ZOSKY[2], P RIGBY[3], DA KNIGHT[4], SM STICK[1,2,5] & A KICIC[1,2,5]

[1]School of Paediatrics & Child Health, UWA, WA [2]TICHR, Centre for Child Health Research, WA [3]CMCA, UWA, WA [4]School of Biomedical Sciences & Pharmacy, University of Newcastle, Callaghan, NSW [5]Department of Respiratory Medicine, PMH, WA

Introduction: Human rhinovirus (HRV) has been identified as a major contributor of asthma exacerbations in children and has been suggested to occur by epithelial tight junction (TJ) protein modification and barrier integrity disruption. This study aimed to directly correlate live viral infection with TJ disassembly and whether this leads to barrier compromisation.

Methods: Polarised human epithelial colorectal adenocarcinoma cells (Caco-2), modified human airway epithelial cell (NuLi-1) and primary human airway epithelial cells (pAECs) were infected with HRV-1B at various multiplicity of infection (MOI) over 24 hours. HRV receptor and viral replication were assessed via qPCR while cell viability and apoptosis was assessed via proliferation and apoptotic assays. TJ protein expression of occludin, claudin-1 and zonal occludin-1 (ZO-1) was assessed using in-cell western assays. Transepithelial permeability assays were performed to assess effects on barrier integrity.

Results: Elevated basal LDL receptor expression was observed in asthmatic pAECs compared to healthy, but no significant change was seen in both cohorts following HRV-1B infection. Interestingly, viral replication was significantly higher in asthmatic pAECs compared to the healthy. A MOI-dependent effect on cell viability was observed in both healthy and asthmatic pAECs. Despite a significant 400-fold increase in apoptosis, no significant difference was detected in the apoptotic response between healthy and asthmatic pAECs 24h post infection. Although disassembly of tight junctions occurred with increasing MOI in the pAECs, a greater effect occurred within the asthmatic cohorts. A marked increase in transepithelial permeability was concurrent with this disassembly following infection.

Conclusion: Primary airway epithelial cells more susceptible to HRV-1B infection. At lower MOI, this causes a disassembly of TJ proteins, especially exaggerated in the asthmatic pAECs that is concomitant with increased transepithelial permeability. This may facilitate trafficking of small sized aeroallergens into the sub-epithelial space which could lead to the initiation of asthma exacerbation.