Asthma is a complex heterogeneous disease characterised by variable airflow obstruction, bronchial hyper-responsiveness, airway inflammation and remodelling. The heptadecapeptide nociceptin/orphanin FQ (N/OFQ) is the endogenous ligand for the N/OFQ peptide (NOP) receptor, a non-opioid member of the opioid receptor family. The role of N/OFQ-NOP system in asthma is uncertain. We sought to evaluate N/OFQ-NOP expression in healthy and asthmatic human airway tissues and relate this to an established animal model of asthma.

NOP expression in human airway cells was investigated predominantly by qRT-PCR. The functional role of N/OFQ on human airway structural and immune cells was then interrogated using a range of functional assays including proliferation, migration, collagen gel contraction and wound healing. We further investigated the functional role of N/OFQ in vivo using ovalbumin-sensitised mice.

NOP expression was detected in human airway smooth muscle cells (HASM; mean ± C2 = 11 ± 0.7, n = 13), bronchial epithelial cells (HBEC; mean ± C2 = 10 ± 0.49, n = 12), lung mast cells (mean ± C2 = 7 ± 0.64, n = 5) and peripheral blood eosinophils (mean ± C2 = 10.4 ± 1.2, n = 16). N/OFQ inhibited chemoattractant-induced migration of mast cells and eosinophils (see Figure). N/OFQ stimulated significant HBEC wound closure with 49.62 ± 3.58% (p < 0.001, n = 8) of the wound area.
Conclusion CRTh2 expression is upregulated in the epithelium of asthmatic patients compared to healthy controls. This is a novel finding, suggesting that CRTh2 antagonists may exert therapeutic effects on the bronchial epithelium as well as blocking inflammatory cell chemotaxis in asthma.

Abstract S19 Table 1.

<table>
<thead>
<tr>
<th>% +ve Area of Epithelium</th>
<th>Intensity of Epithelial Staining</th>
<th>Overall IHC Score</th>
<th>% Positive Cells in Submucosa/mm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>30.3* (12.6)</td>
<td>2.3 (4.6)</td>
<td>74.3* (46.9)</td>
</tr>
<tr>
<td>Healthy</td>
<td>16.6 (16.3)</td>
<td>1.7 (4.1)</td>
<td>38.8 (47.7)</td>
</tr>
</tbody>
</table>

Statistical analysis by unpaired T-test between Asthma and Healthy controls *p<0.05.

S20 CRTH2 IS EXPRESSED BY THE BRONCHIAL EPITHELIUM AND ITS ACTIVATION DRIVES EPITHELIAL DIFFERENTIATION

Background The chemoattractant receptor-homologous molecule expressed on Th2 cells (CRTh2) is implicated in the pathogenesis of asthma, but its expression in the bronchial epithelium and potential role in airway remodelling is unknown.

Methods CRTh2 protein expression was assessed in bronchial biopsies (n = 24) and primary epithelial cells (n = 16) using immunohistochemistry, and using flow cytometry, immunofluorescence, and quantitative RT-PCR (QT-PCR) respectively. The effects of 13, 14-dihydro-15-keto Prostaglandin D2 (DK-PGD2) on epithelial cell migration and differentiation was determined.

Results The number of submucosal CRTh2 positive inflammatory cells was increased in asthma compared to healthy controls 27.47 ± 0.0049). CRTh2 expression was identified on normal and asthmatic epithelial cells, but its expression was decreased in bronchial biopsies from asthmatics 21.43 per 10 mm² epithelial area (7.85) versus healthy controls 62.34 (36.41) (p = 0.0071) and similar findings were observed in primary epithelial cells. Squamous metaplasia of the bronchial epithelium was increased in asthma and related to decreased CRTh2 expression. DK-PGD2 promoted epithelial cell migration 12-fold increase (p = <0.0001) and in air-liquid interface cultures increased the number of MUC5AC + and involucrin - cells, which were blocked with a CRTh2 specific antagonist.

Conclusions CRTh2 is expressed by the bronchial epithelium and its activation drives epithelial differentiation suggesting that in addition to its well characterised role in inflammatory cell migration CRTh2 might contribute to airway remodelling in asthma.

S21 TYPE-2 INNATE LYMPHOID CELLS INDUCE CD4 T HELPER CELL TYPE-2 IMMUNE FUNCTIONS

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Introduction Type-2 innate lymphoid cells (ILC2) are a novel subset of immune cells characterised by their responsiveness to...
S18 Activation of nociceptin orphanin FQ (N/OFQ) – N/OFQ peptide (NOP) receptor system plays a key immunomodulatory role in asthma


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