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Pulmonary dendritic cells from chronic obstructive pulmonary disease patients suppress lung immune responses through induction of regulatory T cells
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Defective Th immunity is considered to be implicated in the enhanced vulnerability of Chronic Obstructive Pulmonary Disease (COPD) patients to lower respiratory infections and lung cancer. Tolerogenic dendritic cells (DCs) and regulatory T cells (Tregs) are critical in the suppression of Th immunity. Their role in COPD is elusive. We hypothesized that pulmonary DCs in COPD exhibit tolerogenic properties and suppress lung Th responses through induction of Tregs. CD1c+ DCs and CD3+ T cells were isolated from the lungs of COPD patients (n=17), smokers (n=16) and never-smokers (n=4). DC maturation prior and upon LPS exposure were examined. The effects of pulmonary DCs on lung Th cell responses and on the induction of Tregs were investigated. Pulmonary DCs from COPD patients and smokers express decreased levels of co-stimulatory molecules (CD40/86) compared to never-smokers at baseline (p<0.01). Upon LPS exposure, only DCs from COPD patients fail to upregulate costimulatory molecules. Pulmonary DCs from COPD patients induce decreased proliferation of autologous lung CD4+ and CD8+ T cells compared to DCs from smokers (p<0.001). CD4+ T cells treated with DCs from COPD patients, but not from smokers, express increased levels of the immunosuppressive cytokine IL-10 (p<0.01) and suppress Th responses in in vitro suppression assays. Our results reveal that lung DCs from COPD patients suppress lung immune responses through induction of Tregs. This novel immunoregulatory circuit has important clinical implications for the enhanced vulnerability of COPD patients to respiratory infections and lung cancer.

*These authors contributed equally. Funded by Thorax.

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Regulatory T cells in healthy and asthmatic subjects challenged with rhinovirus
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Background: Allergic asthma is characterised by an imbalance in Th2/Th1 response and elevated secretion of Th2 cytokines. Regulatory T cells (Tregs), expressing FoxP3, are thought to play a prominent role in the suppression of Th1 lymphocytes in asthma patients.

Objectives: The aim was to address whether the number of Tregs differ between asthmatic patients and healthy controls and how these numbers are affected by a Th1 response, i.e. a provocation with rhinovirus type 16 (RV16).

Methods: Mild allergic asthma patients (n=9) and healthy non-allergic controls (n=14) were inoculated with RV16 (10 TCID50). One day before and six days after the provocation, blood was drawn and bronchoalveolar lavage (BAL) fluid was collected. Lymphocytes and peripheral blood mononuclear cells (PBMCs) were analysed by multi-colour flow cytometry to quantify the CD4+CD25+FoxP3+ Treg numbers.

Results: Mild asthma patients had more CD4+CD25+FoxP3+ Tregs (6.1±0.7%) in peripheral blood compared to the healthy controls (3.7±1.1%, p=0.003). FoxP3 was expressed in a larger proportion of CD4+ cells in the BAL than in peripheral blood of both asthmatic (7.9±3.0 in BAL and 5.1±1.4 in blood) and control subjects (7.5±2.6 in BAL and 3.9±1.6 in blood), but no difference between the prevalence in BAL lymphocytes from both groups was observed. RV16 provocation did not affect the CD4+CD25+FoxP3+ Treg numbers in blood and BAL in either patients with mild asthma or healthy controls.

Conclusion: There is a higher number of CD4+CD25+ cells expressing FoxP3+ in peripheral blood of mild allergic asthma patients. Rhinovirus challenge did not have an impact on PBMC and BAL Treg numbers in both healthy and asthmatic individuals.

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Methods: The circulating percentage of CD4+CD25high and CD4+FoxP3+ Treg in peripheral blood was estimated by flow cytometry analysis. We included 60 patients with COPD (57.8±1.09 years old), 20 patients with BA (54.7±2.2 years old) and 17 HD (54.0±2.5 years old).

Results: It was shown that COPD is associated with the increasing of percentage number of CD4+CD25high Treg (2.8±2.04%) in the peripheral blood in comparison to BA (1.8±0.47%, p = 0.004) and HD (1.36±0.24%, p = 0.005). The patients with BA had the decreasing CD4+FoxP3+ Treg (2.5±7.60, p = 0.001) compared to COPD (8.37±0.38, p < 0.001) and HD (8.10±0.48, p < 0.001).

Conclusions: We consider that the increase of regulatory blood CD4+CD25high Treg in COPD patients might be markers of disease severity. Our study suggests an association between differences in subpopulations of Treg in patients with BA and COPD with varying degrees of inflammation.

P1832

IL-17 and Th17-cells as markers of disease progression in pediatric allergic diseases. A therapeutic approach in an “in vitro” models

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Th17 cells and IL-17 play a role in allergy development and progression. We tested IL-17 in plasma (9, nasal wash (NW) and induced sputum (IS) from 12 healthy (HC), 14 intermittent asthma (IA) and 28 mild-moderate asthma (MA) with concomitant intermittent rhinitis (IR, n=16) or concomitant persistent rhinitis (PR, n=10) on the IL-8 release from nasal and bronchial epithelial cell lines pretreated with and without an anti-IL-17 receptor antibody and stimulated respectively with NW and IS from children with MA and PR (n=10), 2) on the IL-8 release from nasal and bronchial epithelial cell lines pretreated with and without an anti-IL-17 receptor antibody and stimulated respectively with NW and IS from children with MA and PR (n=10), 2) on the IL-8 release from nasal and bronchial epithelial cell lines pretreated with and without an anti-IL-17 receptor antibody and stimulated respectively with NW and IS from children with MA and PR (n=10).

In vitro experiments showed that Budesonide with Formoterol treatment significantly reduced 1) CD3+IL-17+ and CD3+ROG+R+ in peripheral blood (PB) T-cells from children with MA and PR; 2) the effect of IL-17 present in NW and IS from children with MA and PR.

IL-17 and Th17-cells are markers of disease progression in children with allergic asthma and concomitant PR. Budesonide with Formoterol might be useful for a therapeutic approach to control IL-17 mediated allergic disorders.

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P1833

Lung and blood Th1 and Th17 responses against mycobacterial antigens in patients with pulmonary sarcoidosis

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Sarcoidosis is an inflammatory disorder characterized by granulomas most commonly affecting the lungs. The presence of mycobacterial antigens, and recently a specific protein, M. tuberculosis catalase-peroxidase (mKatG), in sarcoidosis tissue has been reported. Th1 cell responses against mKatG have been observed in sarcoidosis lung and peripheral blood cells. In the present study, IL-17 and IFNγ production were evaluated by ELISPOT after stimulation of bronchoalveolar lavage (BAL) fluid and peripheral blood cells with mKatG and M. tuberculosis PPD proteins. Two groups of sarcoidosis patients were compared: HLA-DR3 positive (good prognosis) versus HLA-DR3 negative (bad prognosis). We also did immunohistochemistry on bronchial biopsies for further characterization of cytokine expression. Both mKatG and PPD stimulation of BAL cells resulted in higher frequencies of cells producing IFNγ compared to IL-17. We did not detect any significant difference between BAL and blood regarding IL-17 secretion after stimulation with both mKatG and PPD, while significantly more BAL cells produced IL-17 in comparison to blood stimulation with mKatG and PPD (p<0.05). The existence of IL-17+ cells in the granulomas also supports the role of IL-17 in sarcoidosis. The observed Th17 responses against mycobacterial antigens could contribute to the inflammation in sarcoidosis, although they generally occur at lower frequencies than corresponding Th1 responses.
Background: COPD is characterized by chronic inflammation in the lungs. CD8+ T cells but in more severe disease also CD4+ T cells, have been implicated in the pathogenesis of COPD. Different subpopulations of T-cells play a role in this disease.

Methods: Bronchoalveolar lavage (BAL) and biopsy were performed on 24 never-smokers, 20 smokers with normal lung function and 20 COPD patients (14 smokers and 6 ex-smokers). The frequencies of major lymphocyte subsets and the differentiation status of CD4+ and CD8+ T cells were analyzed by flow cytometry.

Results: There were higher percentages of CD8+ T cells in smokers and CD56+ T cells in smokers and COPD patients compared to never-smokers (p < 0.05). A higher frequency of CD27+CD45RA- cells and a lower frequency of CD27-CD45RA- cells was found in the CD4+ T cell population of COPD current smokers compared to never-smokers and COPD ex-smokers (p < 0.05). Smokers with normal lung function had a higher percentage of CD4+CD27-CD45RA+ cells compared to never-smokers (p < 0.05).

Conclusions: The higher percentages of cytotoxic T cells in smokers and COPD patients may be related to smoking-induced tissue damage. The increased percentage of central memory cells in COPD smokers suggests an ongoing immune response. Smoking cessation resulted in a normalization of CD4+ central/memory cell memory in BAL, indicating a reversibility of smoke-induced changes.

P1835 TCR rearrangement in patients with eosinophilic lung disease Nathalie Freymond1, Vincent Cottin1, Chahéra Khouatra1, Nathalie Lemoine1, Jean-François Corder1, National Reference Center for Rare Pulmonary Diseases, Louis Pradel Hospital, Lyon, France; 2Department of Internal Medicine, Hôpital Sénéan, Suresnes, France; 3Immunology Laboratory, University Hospital, Lille, France

Background: Expansion of monoclonal population of T-cells with T-cell receptor (TCR) rearrangements and aberrant cell surface immunophenotype produce IL-5 and contribute to the pathophysiology of the lymphocytic variant of the hypereosinophilic syndrome (HES).

Objective: To evaluate the expansion in eosinophilic lung disease.

Methods: T-cell expression profile was analysed by flow cytometry and TCR clonal gene rearrangements were studied by PCR in 45 consecutive patients with peripheral blood eosinophilia (greater than 1.0 × 10³/μL) and eosinophilic lung disease. Patients with myelodysplastic or lymphocytic variants of HES or any identified cause of eosinophilia were excluded.

Results: Monoclonal TCR rearrangements were detected in 11/45 patients (24%). No significant clinical or biological difference was found between patients with or without clonal TCR gene rearrangements. IL-5 serum level was normal in all patients.

Conclusion: Expansion of TCR-Vγ7 or TCR-Vγ9 populations are present in a proportion of patients with eosinophilic lung disease without aberrant cell-surface immunophenotype. Further study is needed to evaluate whether T-cell clonality might contribute to the pathophysiology of these conditions or is only a transient reactive phenomenon.

P1836 Reduced expression of PPAR-alpha in bronchoalveolar lavage CD4+ T cells of sarcoidosis patients Muntasar Abo Al Hayja, Anders Eklund, Johan Grunewald, Jan Wahlström. Karolinska Institute, Dept of Medicine, Solna, Stockholm, Sweden

Background: Sarcoidosis is a systemic inflammatory disease characterized by non-caseating granulomas affecting many organs, especially the lungs and intrathoracic lymph nodes. Activated CD4+ T cells with a type 1 cytokine profile are considered to be of central importance for the pathogenesis. The peroxisome proliferator-activated receptors (PPARs) are nuclear receptors that play important regulatory roles in numerous cellular processes, including inflammation. Three PPARs have been described, namely PPAR-alpha, -beta/delta and -gamma. They are expressed in many cell types, including macrophages and T cells. The purpose of this study was to investigate the expression of PPARs on CD4+ T cells in sarcoidosis patients.

Methods: Seventeen sarcoidosis patients and nine healthy controls underwent bronchoscopy with bronchoalveolar lavage (BAL) whereafter CD4+ and CD8+ T cells and alveolar macrophages (AMs) were sorted by flow cytometry and subjected to real-time PCR analysis for mRNA expression of PPARs. Immunofluorescence staining of BAL cytospin slides with anti-PPAR antibodies was also performed.

Results: PPAR-alpha relative gene expression was significantly downregulated in CD4+ T cells of sarcoidosis patients, but no differences were observed with regard to T cell expression of the other PPARs. PPAR expression in AMs did not differ between patients and controls. No differences were observed between patients with active vs. quiescent disease.

Conclusion: The observed downregulation of PPAR-alpha in T helper cells may contribute to ongoing inflammation in pulmonary sarcoidosis via the repression of proinflammatory genes.

P1837 Killer cells in asthma with incomplete airflow reversibility Carolyn Tubbby1, Tim Harrison2, Ian Todd1, Lucy Fairclough1. 1Department of Immunology, Nottingham Respiratory Biomedical Research Unit, The University of Nottingham, Nottingham, United Kingdom; 2Department of Respiratory Medicine, Nottingham Respiratory Biomedical Research Unit, The University of Nottingham, Nottingham, United Kingdom

Asthma with complete airflow reversibility (ACR) represents the majority of asthma cases, however recent attention has focussed increasingly on a small subset of asthmatics that display incomplete airflow reversibility despite optimal treatment (AIR), also a feature of COPD. A growing amount of literature has linked the three main types of killer cells, namely CD8 T cells, Natural Killer (NK) and NKT cells, to both ACR and COPD due to their cytotoxic and immunoregulatory functions. We aimed to study the expansion of these cells in ACR patients.

Objective: To evaluate the expansion of the three main killer cell subsets in CD4+ and CD8+ T cells and their expression of IFNγ and perforin in ACR and AIR patients.

Methods: A total of 11 ACR patients (8 with hypereosinophilic asthma, 2 with Churg-Strauss syndrome, 1 with Wegener's granulomatosis) and 10 AIR patients were recruited. Expansion of TCR-Vδ1, -Vδ2, -Vγ1, -Vγ2, -Vγ3 and -Vγ4 T cell clones was examined by tetramer staining and intracellular cytokine staining. Killer cell function of 3/11 ACR and 3/10 AIR patients was assessed by functional cytotoxicity experiments.

Results: Six of 11 ACR patients and 3 of 10 AIR patients expressed IFNγ and perforin in their CD4+ and CD8+ T cells. Killer cell subsets were more expanded in ACR patients compared to AIR patients, as quantified by perforin/granzyme B expression and functional cytotoxicity assays. This indicates killer cells may be recruited to the AIR lung and may have a subsequent role in the disease pathogenesis, as has been shown in COPD.

P1838 Collagen receptor α2β1 integrin is overexpressed on CD4 and CD8 peripheral blood T lymphocytes in long-lasting clinically stable asthma Joanna Zuk, Stanislaw Bazan-Socha, Jacek Misiol, II Department of Internal Medicine, Jagiellonian University Medical College, Cracow, Poland; 2Department of Internal Medicine, Jagiellonian University Medical College, Krakow, Poland; 3Department of Internal Medicine, Jagiellonian University Medical College, Cracow, Poland

Background: Recruitment of the inflammatory cells from blood to the airways in asthma is mediated by adhesive molecules – e.g. selectins and integrins. In cells trafficking the best known integrins are molecules containing α4 and β2 subunits. We hypothesized that also integrins α1 and β7 may play a role in asthma pathogenesis.

Objective, material and methods: The aim of the study was to assess expression of several very late antigen (VLA) integrin subunits (α1, α2, α4 and β1) on blood T lymphocytes involved in the airways during long-lasting asthma in two subgroups of asthmatics (mild to moderate persistent asthma in a stable clinical condition) and 15 healthy controls.

Methods: Expression of both α4 and β1 on CD4 T cells was significantly higher in asthma subjects than in controls. The α1 subunit was absent from blood lymphocytes. The α2 chain hardly detected on lymphocytes from healthy subjects was apparently present in asthmatics. Surprisingly, in subjects suffering from asthma for over 4 years (n=15) statistically significant overexpression of α2, α4 and β1 subunits on both CD4 and CD8 T cells was observed as compared to controls.

Conclusion: Expression of certain VLA integrin subunits on blood T cells may depend on asthma duration. In long-lasting disease α2 and β1 subunits are overexpressed on both CD4 and CD8 T lymphocytes. The biological role of α2β1 integrin in asthma is unknown. This integrin has been described as a stimulator of collagen accumulation in the airways and in chronic disease may be at least in part, responsible for asthma airway remodelling.

P1839 Different Th1, Th2, Th17 and Treg associated chemokine local pattern expression in lung in a murine model of allergic inflammation You Li, Carina Malmskål, Madeleine Rådinger, Margareta Sjöstrand, Helena Forsslund, Mikael Mikko, Johan Grunewald, Åsa Wheelock, Jan Wahlström, Magnus Sköld. 1Karolinska Institutet, Dept of Medicine, Solna, Stockholm, Sweden; 2Department of Respiratory Medicine, Jagiellonian University Medical College, Cracow, Poland; 3Immunology Laboratory, University of Gothenburg, Gothenburg, Sweden

We have reported that Th1, Th2, Th17 and Treg cells are differently distributed in the lung during airway allergic inflammation. T helper cells express different chemokine receptors and we hypothesize that Th1, Th2, Th17 and Treg cells distribution in the lung is a result by different local chemokine expression.

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Ovalbumin (OVA)-sensitized C57BL/6 mice were exposed intranasally to OVA or PBS on five days and lung tissue was pooled after final allergen exposure. Peribronchial (PB), perivascular (PV) and alveolar (A) tissue was selected from lung tissue sections using Laser Microdissection and Pressure Catapulting technology. Total RNA was extracted and each location was pooled from three OVA/OVA mice. Chemokine gene expression was performed using RT-PCR gene array. Tissue from which expression of an OVA/PBS mouse was used as control and results were expressed as fold change from control. Chemokine ligands for Th1-associated receptors; CCR2 (CCL2, CCL5, CCL7) and CCR3 (CCL3, CCL11) were increased in both A and Pb tissue, while CXCRL1 (CCL10) was increased in Pb followed by A and Pb tissue. In Th2-associated CCR8 (CCL8) was most highly induced in Pb (21.3 fold) followed by Pb and A tissue. In Th2/Treg-associated CCR4 (CCL17, CCL22) the pattern was A, Pb, Pb while in Treg/T17 CCRC (CCL19) was increased mainly in Pb then in Pb but not in A tissue. Allergen exposure increased gene expression of all Th1, Th2, Treg and Th17 associated chemokines in lung. However, the expression pattern shows differences in both tissue distribution and magnitude, arguing for a high complex local milieu that can regulate T-cell subsets distribution.

**P1840**

**T cell specific expression of a short splice variant of the tumor suppressor gene CYLD amplifies the development of allergic airway disease**

Sebastian Reuter, Marc Becker, Nina Dehzad, Helen Martin, Ari Waisman, Sebastian Reuter, Marc Becker, Nina Dehzad, Helen Martin, Ari Waisman, T cell specific expression of a short splice variant of the tumor suppressor in both tissue distribution and magnitude, arguing for a high complex local milieu that can regulate T-cell subsets distribution.

**P1841**

**Apoptosis of peripheral blood lymphocytes in different periods of asthma**

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**Background:** Resistance of lymphocytes to apoptosis can cause decrease of these cells elimination from respiratory ways and play a key role in persistence of inflammation in asthma. Objective: The aim of this study was to reveal the disturbances of blood lymphocytes apoptosis in different periods of asthma.

**Methods:** 25 steroid naive asthmatic adults with asthma exacerbation and 25 with asthma remission were randomly selected and 20 matched control subjects were included. All were submitted to detailed clinical history and examination, pulmonary function testing. Peripheral blood lymphocytes (PBLs) were stimulated by phytoagglutinin (PHA) and cultured for 72 hours. Apoptotic of PBLs was determined by flow cytometry by evaluating of Annexin V expression for detection of early apoptotic cells (Annexin V positive-PI negative).

**Results:** Our results showed that there were significantly lower values of early apoptotic cells in blood in subjects with asthma remission (20.29±1.69% vs 41.65±2.38%; p<0.001) and controls (20.29±2.38% vs 43.02±2.58%; p<0.001). But there were no differences in values of early apoptotic cells in subjects with asthma remission and controls (41.65±1.19% vs 43.02±1.54%; p=0.05). Conclusions: The value of early apoptotic cells in 72 hours cultures of stimulated by PHA lymphocytes is a sensitive marker for asthma exacerbation and remission and can be predictor for asthma exacerbation.

**P1842**

**Mechanism of long-lasting suppression against Th2 immune response in the lung by a novel antedrug TL7 agnostic**

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**Rationale:** To identify the mechanisms by which a novel antedrug Toli like receptor (TL7) agnostic, AZI1441970, mediates the long-lasting suppression of Th2 immune responses.

**Methods:** Long-lasting efficacy of AZI1441970 against bronchoalveolar lavage (BAL) eosinophilia was investigated utilizing OVA-sensitized mice or OVA-specific Th2 cells adoptively transferred into mice. The mechanism by which AZI1441970 mediated long-lasting efficacy was investigated utilizing T cell-deficient nude mice and several knock-out (KO) mice including type 1 IFN receptor KO mice, B cell KO mice and rag2 KO mice lacking B and T cells.

**Results:** Weekly lung doses of AZI1441970 for 6 weeks significantly inhibited BAL eosinophilia for at least 6 weeks following cessation of dosing. The long-lasting efficacy observed with the compound was largely abolished in type 1 IFN receptor KO mice, rag2 KO mice or nude mice, but maintained in B cell KO mice. T cells were shown to be involved in the mechanism of efficacy in a T cell reconstituted nude mouse model of allergic airways inflammation. Nose only exposure of AZI1441970 also resulted in long-term efficacy in the lung. **Conclusions:** We show that intranasal dosing of AZI1441970 to achieve lung dose in mice induced a long-lasting efficacy against Th2 immune responses in the lung. The efficacy in the lung is also achieved by nose only exposure of the TL7 agnostic. Furthermore, our mechanism studies demonstrate that the long-lasting inhibition of the Th2 immune responses is mediated by both T cell and Th2-dependent. These data suggest that novel antedrug TL7 agnostics may have potential in the treatment of allergic disease.

**P1843**

**Repeated intranasalTLR7 stimulation reduces allergen responsiveness in allergic rhinitis**

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**Background:** The TLR7 agonist AZD8848 was developed as a treatment for allergic airway disease with the rationale of suppressing allergic (Th2-like) immune responses by triggering innate immune responses through TLRs. Intranasal administration of AZD8848 has demonstrated protection against allergen challenge in animal models of asthma and allergic rhinitis. AZD8848 is rapidly hydrolysed in vivo to a metabolite that is over 100-fold less active, to minimise the risk of undesirable systemic effects.

**Methods:** Five once-weekly intranasal doses of AZD8848 (60 µg) were given in a randomised, placebo-controlled, double-blind, parallel group clinical trial to patients with allergic rhinitis (AR) off season (NCT00770003). Nasal symptoms were recorded during a 7-day nasal allergen challenge period starting 24 hours post last dose of AZD8848 to assess clinical effect. Biomarkers of TLR7 activation and plasma exudation were monitored in plasma and nasal lavage. Safety, tolerability and pharmacokinetics were also monitored.

**Results:** Successful stimulation of TLR7 was indicated by reversible reductions in blood lymphocytes and increased plasma levels of IL-1Ra 24 hrs after administration of AZD8848. Some patients reported transient flu-like symptoms, as expected based on mechanism of action. AZD8848 reduced total nasal symptoms of allergic rhinitis as recorded 10 minutes after allergen challenge on days 5, 6, 7 and 8 after the last dose of AZD8848. Levels of IL-1ra in nasal lavage were also reduced by AZD8848.

**Conclusion:** Repeated intranasal administration of AZD8848 activated TLR7 and this resulted in a sustained reduction in responsiveness to allergen in patients with AR.

**P1844**

**Farm dust decreases Th2 driven allergic airway inflammation in mice: A role for airway TL2 and TL4R?**

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**Exposure to farm dust is known to decrease allergic inflammation in an ovalbumin**
mouse model for asthma. However, the underlying mechanisms of this protection are not known. With the focus on the role of epithelium in this process, we investigated whether farm dust also protects against allergic airway inflammation in a more clinically relevant house dust mite (HDM) asthma mouse model. Dust from different farms in Germany was collected and pooled. BALB/c mice were exposed intranasally 4 times/week for 5 weeks to PBS or farm dust (1 mg/ml, 50 μl/day), followed by PBS or HDM (2.5 mg/ml, 10 μl/day). IgE levels, inflammatory cells, cytokines (CC chemokine ligand (CCL)20, thymic stromal lymphopoietin (TSLP) and Th2) and Toll-like receptor (TLR)2 and TLR4 expression on epithelial cells were assessed.

Farm dust+HDM exposed mice had lower levels of HDM-specific IgE in serum, eosinophilic inflammation, and Th2 cytokines in lungs than HDM exposed mice. Expression of TLR2 and 4 in epithelium, and CCL20 and TSLP levels in lung tissue were lower in farm dust exposed than HDM exposed mice. Additionally, we observed less spindle shaped CD68+ cells beneath the epithelial basement membrane in farm dust exposed mice.

Lower expression of TLR2 and 4 in epithelium after farm dust exposure may explain the lower levels epithelial cell-derived cytokines CCL20 and TSLP. These lower CCL20 and TSLP levels could have prevented the recruitment of antigen presenting cells as evidenced by the spindle shaped CD68+ cells, as well as the skewing towards a Th2 response. Hence, lower expression of TLR2 and 4 may contribute to the observed protection against HDM-induced allergic inflammation in farm dust-exposed mice.