

Allergy Research

## **Response to House Dust Mites is Age-Dependent**

Neuherberg, August 26, 2016. **In adults with house dust mite allergy, a cascade of inflammatory signals on the airway epithelium leads to airway remodeling. This process cannot be influenced by standard cortisone therapy. Researchers at Helmholtz Zentrum München and Technical University Munich have reported these findings in the latest issue of the 'Journal of Allergy and Clinical Immunology'.**

Worldwide more than 300 million people suffer from asthma. A common symptom in this context is airway remodeling: a pathological remodeling of the airway structure due to misdirected repair processes.\* Depending on the age of the patient, messenger substances called leukotrienes play an important role here, as researchers led by Dr. Julia Esser-von Bieren have now discovered. "Although drugs already exist that target leukotrienes, we still know too little about the exact disease mechanisms," said the group leader at the Center for Allergy and Environment (ZAUM), a joint research center of Helmholtz Zentrum München and Technical University Munich.

In the current study, the researchers were particularly interested in whether there were age-dependent differences in the expression of an allergy to dust mites. In collaboration with Professor Benjamin Marsland of the University Hospital CHUV in Lausanne, they studied a corresponding experimental model. It was found that an extract from house dust mites elicited different responses, depending on the time window in which it came in contact with the immune system.

"It is striking that leukotrienes appear to play an important role, especially when adults acquire an allergy," said Katharina Dietz, lead author of the study. "They are part of a whole cascade of signals ultimately leading to a response to the house dust mite extract." According to the study, in particular the signaling protein Wnt5a, the enzymes transglutaminase2 and phospholipase A2 as well as the leukotrienes themselves are involved. The scientists were able to confirm these results in human cells and in tissue from nasal polyps of patients.

### **Cortisone cannot halt progression**

It was also interesting for the researchers to find out where these molecules come from. They showed that especially the epithelial cells of the bronchi are the drivers of the cascade. "Previously it was assumed that the leukotrienes are mainly produced by certain white blood cells, the eosinophil granulocytes," said study leader Esser-von Bieren, analyzing the results.

However, the results are not only relevant for understanding the disease, but also for the therapy. "This cascade cannot be stopped through treatment with cortisone, the standard treatment for allergy," said Esser-von Bieren. She therefore considers it possible that the results could also impact allergy therapy: "The strong presence of the leukotriene cascade in the inflamed airway epithelium refutes the common assumption that structural cells can be neglected as leukotriene producers. On the contrary: In a chronic, cortisone-resistant inflammation in the form of asthma or nasal polyps, the use of drugs targeting the leukotriene cascade should be considered, depending on the age and allergy status of the patients."

## Further Information

### Background:

This collaborative study involved experts from different subareas: The ZAUM researchers from Munich are very familiar with responses of the airway epithelium. In a recent study, they showed how allergies influence the [surface of the airways](#). The Swiss researchers from Lausanne are focused on elucidating the temporal sequence of allergy processes. Among other research objectives, they are studying the pathogenesis of asthma in the early stage of development and [which role microbes play](#) in this regard.

\*This includes e.g. the increased deposition of connective tissue in the wall of the bronchi, an increase of mucus-producing gland cells in the bronchial epithelium or increased growth of muscle cells in the airway walls. An important trigger for this misdirected remodeling is the apparent ongoing inflammation in the airways.

### Original Publication:

Dietz, K. et al. (2016): [Age dictates a steroid resistant cascade of Wnt5a, transglutaminase-2 and leukotrienes in inflamed airways](#). Journal of Allergy and Clinical Immunology, doi: 10.1016/j.jaci.2016.07.014

The [Helmholtz Zentrum München](#), the German Research Center for Environmental Health, pursues the goal of developing personalized medical approaches for the prevention and therapy of major common diseases such as diabetes and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. The Helmholtz Zentrum München is headquartered in Neuherberg in the north of Munich and has about 2,300 staff members. It is a member of the Helmholtz Association, a community of 18 scientific-technical and medical-biological research centers with a total of about 37,000 staff members. [www.helmholtz-muenchen.de/en](http://www.helmholtz-muenchen.de/en)

The [Center of Allergy & Environment](#) (ZAUM) in Munich is a joint undertaking by the Helmholtz Zentrum München and the Technical University of Munich (TUM). This cooperation, which is the only one of its kind in the German research landscape, is dedicated to interdisciplinary basic research and forms a link between clinicians at the hospital and clinical research staff at the university. Thanks to this approach, findings about the mechanisms that lie behind allergies are translated into preventive and therapeutic measures. The development of effective, individually tailored treatments enables better care to be provided for allergy-sufferers. [www.zaum-online.de](http://www.zaum-online.de)

[Technical University of Munich](#) (TUM) is one of Europe's leading research universities, with more than 500 professors, around 10,000 academic and non-academic staff, and 39,000 students. Its focus areas are the engineering sciences, natural sciences, life sciences and medicine, reinforced by schools of management and education. TUM acts as an entrepreneurial university that promotes talents and creates value for society. In that it profits from having strong partners in science and industry. It is represented worldwide with a campus in Singapore as well as offices in Beijing, Brussels, Cairo, Mumbai, San Francisco, and São Paulo. Nobel Prize winners and inventors such as Rudolf Diesel, Carl von Linde, and Rudolf Mößbauer have done research at TUM. In 2006 and 2012 it won recognition as a German "Excellence University." In international rankings, TUM regularly places among the best universities in Germany. [www.tum.de/en/homepage](http://www.tum.de/en/homepage)

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