

Allergic response to house dust mites is agedependent

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Immunohistochemical staining of nasal polyp tissue: components of the leukotriene cascade (green and red) are active in epithelial cells and infiltrating inflammatory cells (cell nuclei in blue). Credit: Helmholtz Zentrum München



In adults with a house dust mite allergy, a cascade of inflammatory signals on the surface of the airways leads to airway remodeling. This process cannot be influenced by standard cortisone therapy. Researchers at Helmholtz Zentrum München and the Technical University of 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 that target the leukotriene cascade exist, 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 the Technical University of Munich.

In the current study, the researchers were particularly interested in whether there were age-dependent differences in the expression of an <u>allergy</u> 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 <u>house dust</u> mite extract." According to the study, in particular the signaling protein Wnt5a, the



enzymes transglutaminase 2 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 in allergies, leukotrienes are mainly produced by certain white blood cells, the eosinophil granulocytes," said study leader Esser-von Bieren.

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 Esservon 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 epithelial leukotriene cascade should be considered, depending on the age and allergy status of the patients."

More information: Katharina Dietz et al. Age dictates a steroid resistant cascade of Wnt5a, transglutaminase-2 and leukotrienes in inflamed airways, *Journal of Allergy and Clinical Immunology* (2016). DOI: 10.1016/j.jaci.2016.07.014

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