Ion channel regulates molecule that contributes to COPD

14 January 2022

Chronic obstructive pulmonary disease—COPD for short—is one of the most common diseases of the lung. It affects almost 300 million people worldwide, of which about three million die every year. A collective term for chronic obstructive bronchitis and pulmonary emphysema, COPD develops primarily as a response to environmental toxins—particularly cigarette smoke—or due to genetic defects. LMU pharmacologist Prof. Christian Grimm from the Walther Straub Institute of Pharmacology and Toxicology has now been able to demonstrate, in collaboration with Prof. Martin Biel (Department of Pharmacy) and Dr. Ali Önder Yildirim (Helmholtz Zentrum München), that specific ion channels in immune cells play a decisive role in the inflammation process. According to the scientists, these ion channels could potentially be targets for new therapies.

Using various methods, the researchers subsequently investigated the expression and function of TRPML3 in the lung in order to clarify how the MMP12 concentration is regulated. "To our surprise, we found that it is not the secretion of MMP12 that is impaired in COPD, but the endocytosis. As such, it is not that the inflammation causes more MMP12 to be released, but that the reabsorption of excess MMP12 by TRPML3 does not work well enough," says Grimm. "This is further supported by our demonstrating, with the aid of endolysosomal patch clamp technology, that the channel is expressed above all in the so-called early endosomes, whose job it is to absorb particles."

A comparison of specimens from human patients with and without COPD showed that TRPML3 is very strongly upregulated in COPD patients—i.e. much more of it is produced. The scientists assume that the body tries in this way to counteract harmful influences by breaking down as much of the damaging MMP12 as possible. Overall, therefore, the results indicated that TRPML3 is an important regulator of MMP-12 absorption through alveolar macrophages and could serve as a therapeutic target for COPD.

More information: Barbara Spix et al, Lung emphysema and impaired macrophage elastase...

Provided by Ludwig Maximilian University of Munich


This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.