Body's cellular 'recycling system' implicated in chronic asthma

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Current asthma treatments are quite effective in reducing patient symptoms in the short term however the structural changes in an asthmatic's airways, caused by persistent and chronic inflammation, is difficult to reverse.

A new study has discovered that when one of the body's crucial regulatory systems, known as autophagy, is activated in asthmatic lungs, changes take place that progress the severity of the disease. The changes are believed to "remodel" the lungs with excessive muscle mass and greater amounts of extracellular proteins such as collagen contributing to persistent breathlessness, acute asthma attacks and loss of lung function.

The authors of the study, published in the *American Journal of Respiratory and Cell Molecular Biology*, say that autophagy is selectively enhanced in asthma patients and that this insight means treatments that target the autophagy pathway could alleviate airway remodelling in asthma.

Dr. Pawan Sharma, the lead investigator of the research says that the process of autophagy is often referred to as "nature's inner-recycling mechanism that is vital to maintain normal tissue homeostasis."

Dr. Sharma, a researcher at the University of Technology Sydney (UTS), says that while autophagy has been linked to various diseases the association with asthma is only just emerging.

This unique study utilised a variety of in vitro and in vivo approaches ranging from murine models to human lung specimens that also involved collaboration with some of the leading researchers from the Woolcock Institute, Thomas Jefferson University (USA), University of Manitoba (Canada) and University of Tasmania and is the first to suggest that autophagy is closely associated with airway remodelling in asthma—potentially opening doors for a new therapeutic target in asthma.

Lead author Kielan McAlinden, a Ph.D. candidate in the UTS Graduate School of Health, says that certain airway changes, such as a thickening of the basement membrane in the lungs, are key indicators for the development of asthma later in life and have been seen in children as young as three or four.

"This led us to think about various signalling pathways such as autophagy that can be irregular and contribute to disease later in life," he says.

"Our data from adult human lungs clearly demonstrates a link between an increase in airway smooth muscle mass and an increase in autophagy biomarkers in the asthmatic lung, a feature not observed in the non-asthmatic human lung," he says.

The researchers say that if the results can be replicated in a larger group of asthma patients future research can focus on selective chemical

targeting of lung cells, ultimately leading to the development of treatments that will protect asthma sufferers from a variety of triggers such as allergens and pollens.

"Asthma affects an estimated 2.5 million Australians and more than 330 million people globally and causes enormous human and economic costs," Dr. Sharma says.

"This research not only extends the knowledge of how autophagy can modulate airway dysfunction in asthma, but also provides a research direction for new therapies for difficult-to-treat chronic asthma cases as well as a broader application in other pulmonary diseases where fibrosis plays a key role," he says.

More information: Kielan D McAlinden et al. Autophagy Activation in Asthma Airways Remodeling, *American Journal of Respiratory Cell and Molecular Biology* (2018). DOI: 10.1165/rcmb.2018-0169OC

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