How two proteins that bind to RNA contribute to the inflammation of asthma

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A publication in *Frontiers in Cell and Developmental Biology* led by researchers from King's College London has, for the first time, revealed important information on the role of mRNA regulating proteins in

asthma.

Asthma is the most common chronic inflammatory disease of the airways that people experience. It affects over 5 million people in the UK and is estimated to impact approximately 300 million people worldwide.

Asthma is a lung condition which causes breathing problems due to inflammation of the airway tubes that carry air in and out of the lungs. While the inflammatory process that causes asthma is well known among researchers and clinicians, the expression of genes underpinning this inflammation is poorly understood.

Researchers collected a range of RNA genetic data from cells of patients with or without asthma. RNA is a key messenger molecule that allows the transport and interpretation of the genetic code within DNA. RNA can work on its own or translate into proteins. These proteins then form the building blocks of cells and other molecules required in the body.

Understanding what and how RNA molecules work is essential to understand how cells behave and function. This is why investigating proteins that bind RNA tells us about how we interpret and process our DNA genetic code—and how that changes in disease.

Genetic information was obtained from patients with asthmatic symptoms and compared to non-asthmatic people. The results highlighted two proteins known as ZFP36L1 and ZFP36L2, which bind to RNA to regulate their expression, that were significantly dysregulated in people with asthma.

When ZFP36L1 and ZFP36L2 were restored in the cells of patients with severe asthma, there was a change in the expression of genes that control several inflammatory factors behind asthma. This showed that ZFP36L1

and ZFP36L2 acted as regulators of genes that controlled the inflammation underpinning asthma.

The results of further tests showed that those proteins appeared 'mis-localized' in the airways of mice with asthma, suggesting that they contribute to the inflammation that characterizes asthma by performing different functions inside cells.

This publication is the first to demonstrate that RNA binding proteins that contribute to asthma when not properly regulated. This shows that the regulation of mRNA expression is a fundamental process in asthma.

Further research is needed to confirm the role of these RNA proteins in humans and better understand its impact, but the work published provides a better understanding of how important RNA research in asthma is, and it could provide a key to future therapies and biomarkers of disease.

More information: Jennifer Rynne et al, The RNA binding proteins ZFP36L1 and ZFP36L2 are dysregulated in airway epithelium in human and a murine model of asthma, *Frontiers in Cell and Developmental Biology* (2023). DOI: 10.3389/fcell.2023.1241008

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