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Epigenetic study highlights drug targets for allergies and asthma

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Scientists have discovered over 30 new genes that predispose people to allergies and asthma, some of which could be targets for new drugs.

Asthma affects one child in 10 in the UK, and allergies may affect one third of the population. The new findings could lead to new treatments for allergic diseases, and will help to predict who will best respond to currently available treatments.

This new study, published in *Nature* and led by scientists at Imperial College London, has taken 10 years involving researchers in the UK, US, Canada and Sweden, who have used new ways to study the genes in the immune system.

The team looked at epigenetic changes, which do not affect the genetic code itself but which influence the activity of genes.

Using this approach, the researchers were able to pinpoint genes that regulate a particular antibody that is involved in triggering allergic responses. This antibody, called immunoglobin E (IgE), was known to researchers already but before today's study scientists had been unable to identify which genes regulate its activities.

The new study turned to epigenetics to look for new therapeutic targets. Genes can be rendered inactive by attaching methyl molecules to the DNA, a process called methylation. The researchers analysed white blood cells from families with asthma in the UK to see whether

methylation levels in certain parts of the genome were correlated with the level of IgE in the blood. To be sure of their results, the researchers tested whether they held true in additional volunteers with high and low levels of IgE from Wales and further asthmatic families from Quebec.

They found strong associations between IgE and low methylation at 36 places in 34 genes. In people with asthma, these genes are overactive, making them produce more IgE which contributes to asthma symptoms.

Some of the IgE-related genes were known to encode proteins produced by eosinophils, a type of white blood cell that promotes inflammation in asthma sufferers' airways. The researchers believe these genes may activate the eosinophils, priming them to cause the most damage. To test this idea, they isolated eosinophils from the blood of 24 subjects and showed that all 34 genes are most active in asthmatics with high IgE levels.

Therapies that neutralise eosinophils already exist, but they are very expensive and only effective in some asthmatics. The newly found activation signals provide a possible means of identifying which patients will respond before starting therapy.

The study was led by Professor William Cookson and Professor Miriam Moffatt from the National Heart & Lung Institute at Imperial College London.

Professor Moffatt said: "The genes we identified represent new potential drug targets for allergic diseases as well as biomarkers that may predict which patients will respond to existing expensive therapies."

Professor Cookson said: "Our pioneering approach, using epigenetics, allowed us to obtain insights that we weren't able to get from traditional genetics. It isn't just the genetic code that can influence disease and

DNA sequencing can only take you so far. Our study shows that modifications on top of the DNA that control how genes are read may be even more important."

More information: L. Liang et al. 'An epigenome-wide association study of total serum immunoglobulin E concentration.' *Nature*, 2015. DOI: 10.1038/nature14125