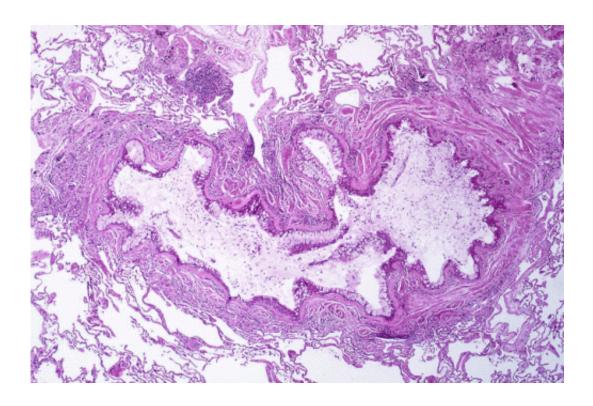


Study reveals new insights into how asthma 'pathways' could be blocked

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Obstruction of the lumen of a bronchiole by mucoid exudate, goblet cell metaplasia, and epithelial basement membrane thickening in a person with asthma. Credit: Yale Rosen/Wikipedia/CC BY-SA 2.0

Researchers from the University of Leicester and University Hospitals of Leicester NHS Trust, working with the National Institute of Allergy and Infectious Diseases (NIAID) and Genentech, have discovered new insights into how asthma may be caused, by identifying three distinct



groups of asthma patients characterised by the activity of different genes in an individual's airways.

Asthma affects about five million people in the UK. Not all patients respond the same way to current treatments, suggesting that asthma is more than a single disease. Drugs that target specific molecules in the lungs suggest that the typical symptoms of asthma can be caused by different processes.

In the study, titled 'Th2 and Th17 inflammatory pathways are reciprocally regulated in asthma' which is published in the journal *Science Translational Medicine*, University of Leicester researchers led by Professor Peter Bradding from the Department of Infection, Immunity and Inflammation, in collaboration with Genentech, looked prospectively at lung samples from 51 <u>asthma patients</u> who had a range of disease severity and identified three different clusters in the airways called Th2-high, Th17-high, and Th2/17-low.

Patients exhibited either high Th2 or high Th17 activity, or low activity of both pathways. Interestingly, no patients had simultaneously high Th2 and Th17 activity, indicating that these pathways are somehow mutually exclusive.

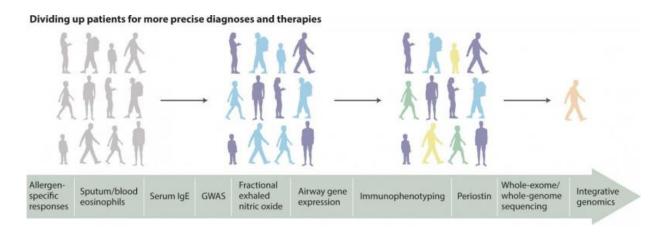
The research team at NIAID in the USA found in a <u>mouse model</u> of asthma that when Th2-activity was inhibited this promoted Th17 activity. When Th2 and Th17 were simultaneously blocked in the mouse model of asthma, the researchers observed greater benefit than blocking one pathway alone, suggesting that new therapies targeting both pathways may demonstrate better efficacy than targeting either pathway alone.

Professor Peter Bradding from the University of Leicester's Department of Infection, Immunity and Inflammation said: "This research gives new



insight into the molecular mechanisms that drive asthma. Because new treatments that block Th2 pathways may promote Th17 pathways, it may be more effective to block both at the same time, rather than either alone. This can be tested in future research trials in patients."

Overall, gaining a better understanding of how these immune pathways cross-regulate in people will advance therapeutic research for <u>asthma</u> and other inflammatory diseases.



As researchers developed new technologies and defined new biomarkers, a population of asthma patients (gray) has been subdivided, first into Th2-high (purple) and Th2-low (blue) groups. The Th2-low group was then further divided into a Th17-high group (green) + an interferon γ (IFN- γ)—high group + a yet-to-be-subdivided group (sage green). In the future, additional groups will be defined, with the ultimate goal of precision medicine in an individual asthma patient (gold). Credit: V. Altounian / Science Translational Medicine

More information: "TH2 and TH17 inflammatory pathways are reciprocally regulated in asthma," by D.F. Choy; stm.sciencemag.org/lookup/doi/...scitranslmed.aab3142



Provided by University of Leicester

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