# New clues about why non-smokers, as well as smokers, develop chronic lung disease revealed

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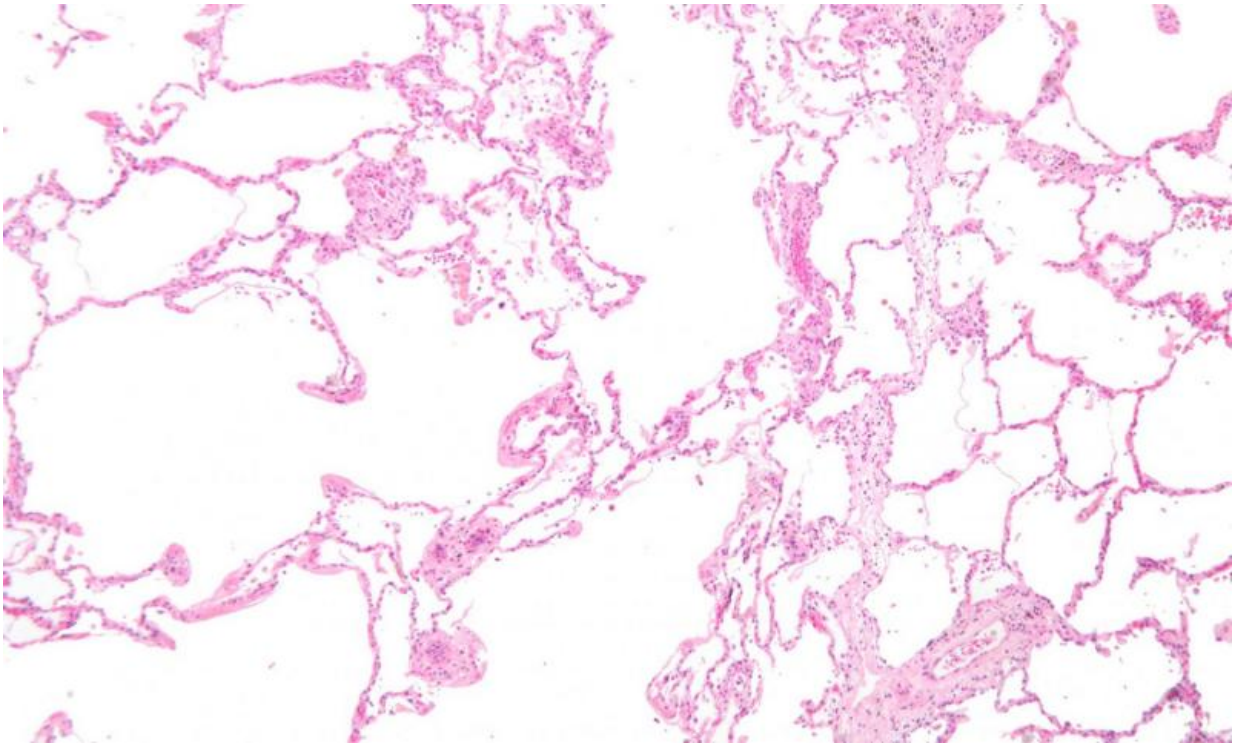

Micrograph showing emphysema (left – large empty spaces) and lung tissue with relative preservation of the alveoli (right). Credit: Wikipedia, CC-BY-SA 3.0

The new study, published in *Nature Genetics*, shows that genetic differences help explain why some people who have never smoked

develop chronic obstructive pulmonary disease (COPD), and why some smokers are at higher risk of getting the disease than other smokers.

During the two-year study, researchers measured 20 million differences in the DNA in each of the 400,000 people who took part and compared them to measurements of lung function taken from breath tests. The results found 139 new genetic differences that influence lung health and COPD. These differences increase someone's risk of developing COPD, in addition to smoking.

COPD is a life-limiting lung condition which causes increasing breathlessness due to damage to the airways. Although smoking greatly increases a person's risk of developing COPD, 1 in 5 people who have the disease have never smoked.

Professor Louise Wain, British Lung Foundation Professor of Respiratory Research at the University of Leicester and lead author of the study, said: "It is well established that smoking is a major risk factor for COPD, yet the mechanisms which cause smokers and non-smokers alike to develop COPD are poorly understood. Our study provides vital clues as to why some people develop COPD and others don't, and new knowledge that will help to develop new treatments to halt the decline in lung function observed in patients with COPD."

The researchers divided people into 10 different genetic risk groups, depending on the number of DNA differences shown to affect lung health. 8 out of 10 smokers in the highest genetic risk group develop COPD. People who have never smoked were overall at very much lower risk, but around 2 in 10 non-smokers in the highest genetic risk group still develop COPD. In all, 279 differences in the DNA were found to affect lung health and the risk of COPD.

Professor Martin Tobin, Chair of the Leicester Precision Medicine

Institute, a partnership between the University of Leicester and Leicester's Hospitals, and co-lead author of the study, added: "We are closer to understanding the genetic causes of this condition in people who have never smoked. People who smoke also appear to have a similar pattern of genetic risk factors, alongside the added risk of tobacco smoking. Our findings can help in developing new treatments that will benefit both groups.

"These advances would not have been possible without the generosity of the participants in UK Biobank and in the international research projects that also contributed to this research."

The team were able to show that the genetic differences they identified were also important contributors to COPD risk in other ethnic groups, including African American and Chinese populations. COPD affects 250 million people and is responsible for 5 per cent (or approximately 3.1 million deaths) worldwide every year. If the genetic differences identified in this study can be used to develop new treatments, these could impact on global health.

The research was supported by the Wellcome Trust, the Medical Research Council, the British Lung Foundation and the National Institute for Health Research (NIHR).

Professor Ian Hall, Director of the Nottingham Biomedical Research Centre, said: "We have shown how close working between the NIHR Biomedical Research Centres in Leicester and Nottingham, together with our international collaborations, enables powerful research to improve future healthcare.

"The most important measure to prevent COPD in the UK is to avoid smoking. All smokers can reduce their risk of developing COPD by quitting smoking. Reducing exposure to high levels of air pollution is

also likely to be beneficial. Patients who already have COPD need new treatments. We are delighted that our research has brought this a step closer."

**More information:** New genetic signals for lung function highlight pathways and chronic obstructive pulmonary disease associations across multiple ancestries, *Nature Genetics* (2019). DOI: 10.1038/s41588-018-0321-7 , www.nature.com/articles/s41588-018-0321-7

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