World lung health study allows scientists to predict your chance of developing COPD

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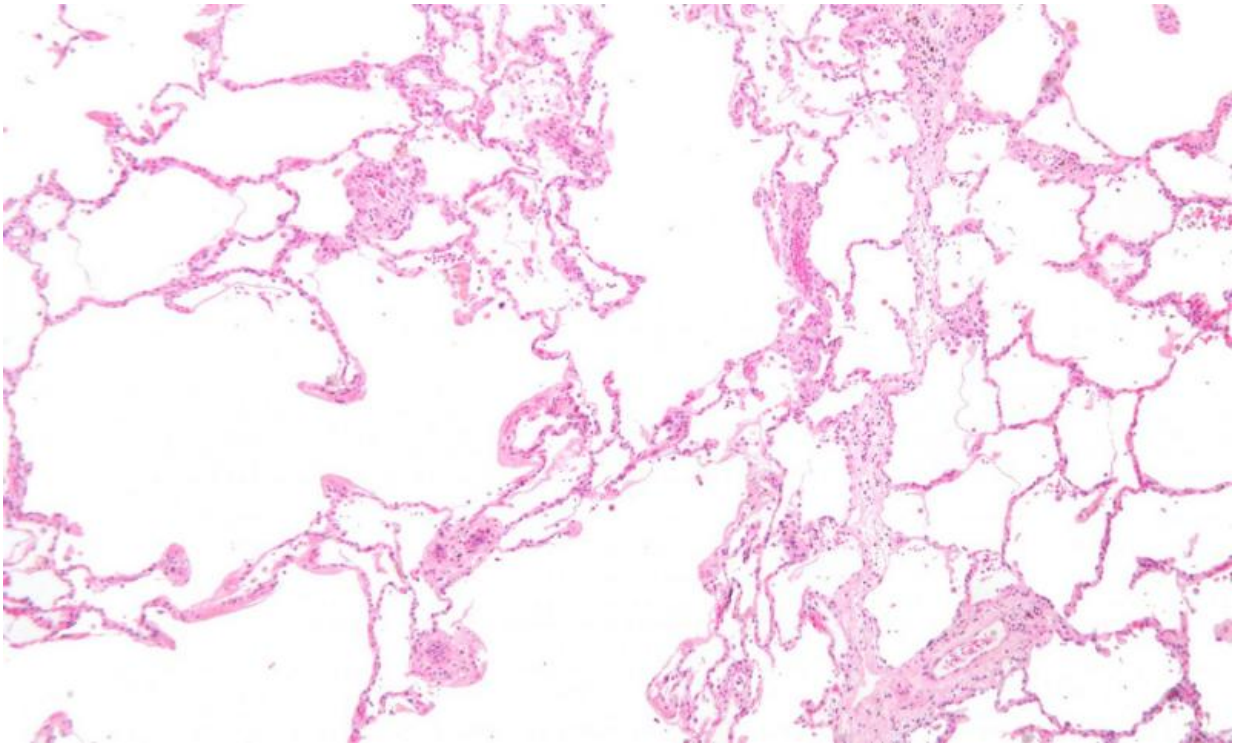

Micrograph showing emphysema (left – large empty spaces) and lung tissue with relative preservation of the alveoli (right). Credit: Wikipedia, CC-BY-SA 3.0

The world's biggest study into an individual's genetic make-up and the risk of developing lung disease could allow scientists to more accurately 'predict' - based on genes and smoking - your chance of developing COPD, a deadly disease which is the third commonest cause of death in

the world.

By comparing 24 million genetic variants - genetic differences between people - in each participant with measures of lung health, the scientists from 14 countries, led by a team from the University of Leicester and University of Nottingham, were able to group people based on genetic variants to show their risk of developing COPD.

They discovered that those in the highest risk group were at 3.7 times the risk of developing COPD than those in the lowest risk group. Because smokers are already at higher risk of developing COPD, this could mean that 72 of 100 smokers in the genetically high-risk group will develop COPD in later life.

Through this study, the researchers almost doubled the number of genetic variants known to be associated with lung health and COPD. These advances could help to explain why and how COPD develops and one day could help personalise treatments based on an individual's genetic make-up.

The breakthrough advance could help defuse a 'ticking timebomb' for serious lung disease, with over 1 billion smokers worldwide at risk.

Chronic obstructive pulmonary disease (COPD) is a lung disease which makes it difficult to breathe and is the third commonest cause of death worldwide. In the UK there are around 900,000 people living with COPD, costing the NHS over £800m annually and costing the economy £3.8 billion in lost productivity.

Smoking is a strong risk factor for COPD, but not all people affected by COPD are smokers and not all smokers develop the disease. In large part, this is due to one's genetic make-up. The new research aimed to discover genetic variation in the DNA content of cells between

individuals that is associated with the risk of developing lung disease.

At present there are no drug treatments for COPD that alter the course of the disease. But this study led by the scientists at the University of Leicester and University of Nottingham has identified many new genetic variants which are associated with enhanced or worsened lung function in both smokers and non-smokers. It paves the way for the development of new treatments.

The study, published by *Nature Genetics*, was funded by the Medical Research Council (MRC) using detailed genetic data provided by UK Biobank and data provided by other countries, and supported by the Wellcome Trust. Led by the Universities of Leicester and Nottingham, the four-year study involved over 100 scientists and 350,000 people from 13 countries. It is spurring new collaborations with pharmaceutical company partners aimed at developing new medicines for COPD.

Professor Martin Tobin from the University of Leicester who co-led the study said: "Our findings point to proteins that will help guide the development of new drugs and to proteins that are targets for drugs already tested for different diseases. This indicates that repurposing drugs already tested for different diseases could be one way to improve treatments for COPD.

"As a result of this work, we can now better predict who will develop COPD - opening up the possibility of using this information in prevention (such as for targeting smoking cessation services).

"This genetic information guides future treatments including the development of new drugs as well as the repurposing of drugs already tested for different diseases."

Professor Ian Hall from the University of Nottingham who co-led the

study said: "Given how common COPD is, we know surprisingly little about the reasons why one individual develops the condition whilst another does not. The study of genetic variation between individuals provides a powerful way to understand these mechanisms which underlie disease risk, which in turn will provide a stimulus for drug development."

Dr Louise Wain, Associate Professor in Genetic Epidemiology who led the team of analysts at the University of Leicester added: "The research shows the value of the UK Biobank study and of 'big data' for making discoveries that will improve health. The discoveries were the result of bringing together these very large datasets, highly skilled analysts and the outstanding high performance computing facilities at the University of Leicester."

Apart from help in developing new drug treatments for COPD, the study is important for understanding whether there may be distinct subtypes of COPD in which patients respond differently to treatment. This means some patients may benefit from particular treatments whereas in others these treatments may be ineffective or harmful (precision medicine).

The research is also important for understanding risk of COPD in smokers and in non-smokers, giving the potential to offer better advice and preventive strategies.

Professor Tobin added: "I'd like to thank the UK Biobank participants who have contributed to these studies and the junior scientists who have shown sustained dedication throughout the project. I'm very proud of the 10 Leicester researchers who have undertaken analyses and contributed to the paper and delighted that this has transformed our knowledge of the genetics of lung health and disease."

Professor Hall added: "The research represents the culmination of

almost a decade of strategic collaboration between the Universities of Nottingham and Leicester. We are delighted that East Midlands-led genomic studies have made such an impact on our knowledge of lung health and COPD, paving the way for improving treatment for COPD in the future."

Ian Jarrold, Head of Research at the British Lung Foundation, said: "COPD has a devastating effect on the lives of people who live with it, and on their loved ones and carers. Understanding how COPD develops and progresses is key to the discovery of new effective treatments and for using existing treatments more effectively. This work represents an important step towards this, and may also lead to better prevention, earlier diagnosis and earlier treatment of COPD."

The same group of researchers also co-authored another paper published in the same issue of *Nature Genetics*. The research described in the parallel paper was led by Harvard University and the University of Groningen. It corroborates that many genetic variants that affect lung health in general populations also affect the risk of COPD. It also shows some overlap between the genetic causes of COPD and those of the less common but severe disease, idiopathic pulmonary fibrosis. This study was part-funded by the National Heart, Lung, and Blood Institute

More information: Genome-wide association analyses for lung function and chronic obstructive pulmonary disease identify new loci and potential druggable targets, *Nature Genetics*, nature.com/articles/doi:10.1038/ng.3787

Provided by University of Leicester