Scientists discover three genes associated with fatal lung disease

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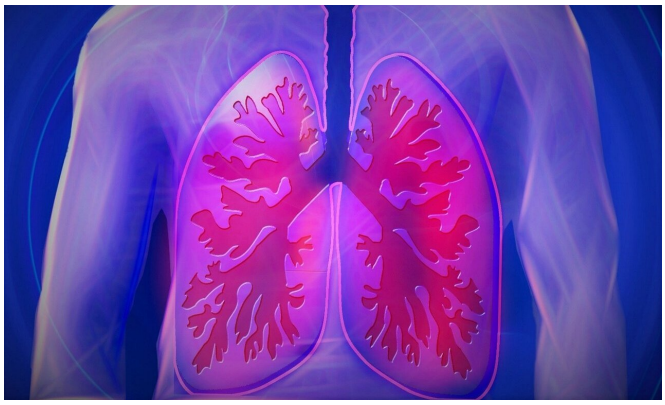

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Researchers at the Universities of Leicester and Nottingham have discovered parts of the DNA that put some people at higher risk of an incurable lung disease called idiopathic pulmonary fibrosis (IPF). The findings are published in the *American Journal of Respiratory and Critical Care Medicine* today, after an earlier version was posted online in November 2019 prior to final review.

IPF is a devastating lung disease where scar tissue builds up in the lungs. This scarring makes it difficult to breathe and half of all patients die within three years of diagnosis. About 6,000 people are diagnosed every year in the UK, though this number appears to be rising. There are no cures for IPF and current treatments can only slow the progression of the disease. This means an improved understanding of what causes IPF is vital in the development of more effective treatments.

Professor Louise Wain and Dr. Richard Allen from the University of Leicester, and Professor Gisli Jenkins from the University of Nottingham, led the study that included collaborators from over 30 institutions across six countries. The leadership of this collaboration unites the NIHR Biomedical Research Centres (BRCs) of Leicester and Nottingham—partnerships between their respective universities, Nottingham University Hospitals NHS Trust and the University Hospitals of Leicester NHS Trust. The purpose of the NIHR BRCs is to take scientific discoveries and translate them into treatments and care pathways for the direct benefit of patients.

The research teams compared the DNA of 4,000 people with IPF to 20,000 people without IPF. In total they investigated over 10 million changes in the DNA and found that people with IPF were more likely to have changes in three genes that have not previously been known to be involved with the disease. These genes suggest biological pathways which crucially could be potential targets for new drugs.

One of these genes lies in a pathway that has recently been shown to promote fibrosis in the lungs. There are currently drugs under development that can target this pathway and might benefit patients. The other two genes highlight pathways not previously investigated for IPF but which might drive development of new treatments in the future.

Dr. Richard Allen, Action for Pulmonary Fibrosis Research Fellow at the University of Leicester, said: "These are really exciting discoveries and improve our understanding of the disease. Hopefully this research will help in the development of treatments which are desperately needed for this devastating disease."

Professor Louise Wain, British Lung Foundation Chair in Respiratory Research at the University of Leicester, said: "Genetic studies hold real promise in helping us find new treatments for IPF. This study was undertaken by a large international team of scientists and doctors and wouldn't have been possible were it not for patients with IPF contributing their genetic data for research. The

next step is to find out how these findings can enable us to find new and better treatments for IPF."

Ian Jarrold, Head of Research at the British Lung Foundation, said: "IPF kills more people than leukaemia every year in the UK, but it has been a major challenge to identify the biological factors that are responsible for this insidious lung condition.

"Genomics has helped us to take big steps forward in finding new treatments for this condition. By teasing out the complex relationships between different genes, we have a huge opportunity to turn the tide against IPF.

"We urgently need treatments that can stop lung scarring in its tracks. The exciting prospect of three newly identified genes, which could lead us to these new treatments, brings hope to the many thousands of people whose lives have been devastated by IPF."

Steve Jones, Chair of Action for Pulmonary Fibrosis said: "Idiopathic Pulmonary Fibrosis (IPF) is a devastating disease, which accounts for one percent of all deaths in the UK. To find a cure, it is vital that we understand the genetic changes associated with the process of lung fibrosis. This path-breaking research has identified three genes, which could lead to new treatments bringing hope to the large number of people around the world living with the disease."

More information: Richard J. Allen et al, Genome-Wide Association Study of Susceptibility to Idiopathic Pulmonary Fibrosis, *American Journal of Respiratory and Critical Care Medicine* (2019). DOI: 10.1164/rccm.201905-1017OC

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