First UK Biobank genetic study reveals new associations with lung disease and smoking behavior

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New research published in *The Lancet Respiratory Medicine* and presented at this year's European Respiratory Society (ERS) meeting in Amsterdam presents the first analyses of genetic data from the UK Biobank that reveal new associations with lung disease and smoking behaviour. The study is by Prof Ian Hall, Queen's Medical Centre, University of Nottingham, UK, and Prof Martin Tobin, University of Leicester, UK, and colleagues.

Chronic obstructive pulmonary disease (COPD) is a global public health concern and is currently the third leading cause of death worldwide. Understanding the genetic basis of airflow obstruction and smoking behaviour is key to determining the mechanisms which cause COPD. In this study, the UK Biobank Lung Exome Variant Evaluation (UK BiLEVE), the authors generated extensive new genetic data in the UK Biobank to investigate the genetic causes of smoking behaviour and lung health.

The study sampled individuals from the UK Biobank with the best, average or the poorest lung function among heavy smokers and never smokers. Using a new genotyping array, which measures over 800,000 genetic variants in each UK Biobank participant, and new methods of analysis of genetic data, they were able to compare lung health and smoking behaviour with both common and rare genetic variations across the whole human genome.

The team discovered six independent genetic variants associated with lung health and COPD. They also found genetic variants associated with COPD in people who have never smoked. One of these new signals is the first example of structural variation of the human genome affecting lung health. The team found that the numbers of copies of duplicated sequence of the genome on Chromosome 17 was associated with lung health in heavy smokers and also in never smokers. This, and other findings in the study, point to possible widespread effects on gene regulation and, in turn, protein production. Importantly for the prevention of COPD and other smoking-related diseases, five independent genetic variants were discovered which were associated with heavy smoking.

The authors say, "These findings, taken together with previous findings, will help define pathways underlying predisposition to development of COPD and smoking behaviours. A full understanding of the biological mechanisms underlying these genetic associations will improve our understanding of the pathophysiology of COPD and smoking behaviour, and potentially give rise to novel therapeutic strategies for the management of airway disease and prevention of nicotine addiction."

They add, "We especially wish to thank all the UK Biobank participants, whose willingness to contribute to the study has made these scientific discoveries possible. The research was also made possible by many years of preparatory work by the UK Biobank team and by the support of the Medical Research Council. We now look forward to hearing the findings from new studies underway that utilise the genetic data generated by the UK BiLEVE study. Ultimately, we would like to see improved prevention and treatment of lung disease and these discoveries are important steps towards this ambitious goal."

In a linked Comment, Professor Guy Brusselle, Ghent University Hospital, Ghent, Belgium, and Erasmus Medical Center, Rotterdam, the

Netherlands, and Dr Ken Bracke, Ghent University Hospital, Ghent , Belgium, say: "We are looking forward to new genetic studies in the UK Biobank investigating other lung function measurements, and other hallmarks of COPD such as chronic bronchitis and emphysema. Thanks to the vast number of participants, the optimal genotyping arrays, and the smart study designs in the UK Biobank, the future looks bright for unravelling the genetic cause of COPD."

More information: *The Lancet Respiratory Medicine*, www.thelancet.com/journals/lan … (15)00283-0/abstract

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