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Study unveils potential genetic links to lung disease risk

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A new study involving data from more than 20,000 individuals has uncovered several DNA sequences linked to impaired pulmonary function. The research, an analysis that combined the results of several smaller studies, provides insight into the mechanisms involved in reaching full lung capacity. The findings may ultimately lead to better understanding of lung function and diseases like asthma and chronic obstructive pulmonary disease (COPD), the fourth leading cause of death in the United States.

"We have known for a while that genetic factors put some people at risk for lower lung function — a factor in COPD and a risk for early mortality. But, we did not know which specific genetic regions were involved," said Stephanie London, M.D., Dr.P.H., senior investigator at the National Institute of Environmental Health Sciences (NIEHS), part of National Institutes of Health (NIH), and a senior author on the paper. "These findings point to specific gene regions."

Impaired lung function is a hallmark of COPD and other lung diseases. But it is also linked to mortality from a wide range of other diseases, including cardiovascular disease and cancer. So knowing some of the genes involved is a first step toward understanding the relationship between lung function and mortality, as well as developing new interventions to manage lung diseases.

"Leveraging our investment in collecting these samples has led to new findings and will help focus future research efforts," said James P.

Kiley, Ph.D., director of the Division of Lung Diseases at the National Heart, Lung, and Blood Institute (NHLBI).

To conduct the analysis that is published online in the Dec. 13, 2009 issue of Nature Genetics, the researchers used data from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium. CHARGE is an ongoing study — a group of groups — that combines genome-wide association study (GWAS) results from several population-based studies. Pooling data from many studies gives much greater power to find the specific genes involved than looking at any one study alone.

The GWAS approach involves measuring hundreds of thousands of genetic variants, in thousands of individuals, in hopes of finding novel genetic variations associated with specific diseases or conditions.

This meta-analysis provided data from more than 20,000 participants. The individual studies included three US-based population studies supported by the NHLBI — the Artherosclerosis Risk in Communities, the Cardiovascular Health Study, and the Framingham Heart Study — and the Rotterdam Study in the Netherlands.

The researchers focused on finding genetic commonalities in DNA that lead to some people having lower lung function than others of the same age, gender, race, size and smoking history.

One way researchers determine airflow obstruction is by using a machine called a spirometer to measure how much air a person breathes in and out, as well as how fast it is blown out, or expired. Spirometry is an important tool used to diagnose asthma, pulmonary fibrosis, cystic fibrosis, COPD, as well as the impact of environmental exposure on lung health. In disease, the ratio between forced expiratory volume (FEV1) and forced vital capacity (FVC) — an indicator of airflow obstruction —

is abnormally low.

"This is a beautiful example of how modern genomic approaches can unearth valuable new insights from previous research," said NIEHS Director Linda Birnbaum, Ph.D. "It sets us on a course for learning much more about how lung diseases develop and how environmental triggers like smoking and air pollution work in combination with genes."

More information: Hancock DB, Eijgelsheim M, Wilk JB, Gharib SA, Loehr LR, Marciante KD, Franceschini N, van Durme YMTA, Chen T, Barr RG, Schabath MB, Couper DJ, Brusselle GG, Psaty BM, van Duijn CM, Rotter JI, Uitterlinden AG, Hofman A, Punjabi NM, Rivadeneira F, Morrison AC, Enright PL, North KE, Heckbert SR, Lumley T, Stricker BHC, O'Connor GT, London SJ. 2009. Meta-analyses of genome-wide association studies identify multiple loci associated with pulmonary function. *Nature Genetics*. Online Dec. 13.

Source: NIH/National Institute of Environmental Health Sciences