

06.04 - Genes and environment

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## **Interaction with air pollution exposure for genetic loci associated with lung function**

Air pollution, Genetics, Spirometry

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Air pollution has been found to be associated with reduced lung function; also 279 genetic signals of association with lung function have been identified that implicate multiple genes and pathways. In this study, we examined if any of these signals interact with air pollution measures NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub>.

In 259,389 unrelated European individuals from UK Biobank, we tested for a gene-environment interaction effect on lung function with NO<sub>2</sub>, PM<sub>2.5</sub> and PM<sub>10</sub> for each of the 279 signals. Lung function measures (FEV<sub>1</sub>, FEV<sub>1</sub>/FVC and FVC) were adjusted for sex, age, age<sup>2</sup>, height, and smoking, income and educational status, with adjustment for 15 principal components for fine-scale population structure. A significance threshold of  $P < 1.8 \times 10^{-4}$  ( $P < 0.05$  adjusted for 279 tests) was set.

We found statistically significant evidence for an interaction with PM<sub>2.5</sub> on FEV<sub>1</sub>/FVC for rs10841302 on chromosome 12 (minor allele frequency=45.2%, interaction  $P = 1.55 \times 10^{-5}$ ). The SNP was also nominally significant for an interaction with PM<sub>10</sub> and NO<sub>2</sub> ( $P = 5.2 \times 10^{-4}$  and  $2.3 \times 10^{-3}$ , respectively). This SNP did not show an interaction with tobacco smoke in a previous analysis. A further 16 SNPs had a nominally significant ( $P < 0.05$ ) interaction effect on lung function with air pollution but did not meet  $P < 1.8 \times 10^{-4}$ .

The gene underlying the association of rs10841302 with lung function has not been determined but the SNP lies close to the AEBP2 gene which encodes AE Binding Protein 2, a transcriptional repressor which may have a role in histone methylation. Identification and characterisation of genes whose effect is influenced by air pollution exposure will enable us to understand how the environment influences respiratory health.