

Publication

A large scale gene-centric association study of lung function in newly-hired female cotton textile workers with endotoxin exposure

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Occupational exposure to endotoxin is associated with decrements in pulmonary function, but how much variation in this association is explained by genetic variants is not well understood.; We aimed to identify single nucleotide polymorphisms (SNPs) that are associated with the rate of forced expiratory volume in one second (FEV1) decline by a large scale genetic association study in newly-hired healthy young female cotton textile workers.; DNA samples were genotyped using the Illumina Human CVD BeadChip. Change rate in FEV1 was modeled as a function of each SNP genotype in linear regression model with covariate adjustment. We controlled the type 1 error in study-wide level by permutation method. The false discovery rate (FDR) and the family-wise error rate (FWER) were set to be 0.10 and 0.15 respectively.; Two SNPs were found to be significant ($P > 6.29 \times 10^{-5}$), including rs1910047 ($P = 3.07 \times 10^{-5}$, FDR = 0.0778) and rs9469089 ($P = 6.19 \times 10^{-5}$, FDR = 0.0967), as well as other eight suggestive ($P > 5 \times 10^{-4}$) associated SNPs. Gene-gene and gene-environment interactions were also observed, such as rs1910047 and rs1049970 ($P = 0.0418$, FDR = 0.0895); rs9469089 and age ($P = 0.0161$, FDR = 0.0264). Genetic risk score analysis showed that the more risk loci the subjects carried, the larger the rate of FEV1 decline occurred ($P \text{ trend} = 3.01 \times 10^{-18}$). However, the association was different among age subgroups ($P = 7.11 \times 10^{-6}$) and endotoxin subgroups ($P = 1.08 \times 10^{-2}$). Functional network analysis illustrates potential biological connections of all interacted genes.; Genetic variants together with environmental factors interact to affect the rate of FEV1 decline in cotton textile workers.

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