Meta-analysis of exome array data identifies six novel genetic loci for lung function

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4484983
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Year 2018

Title Meta-analysis of exome array data identifies six novel genetic loci for lung function

Journal Wellcome Open Research

Volume 3

Pages / **Article-Number** 4

Background: Over 90 regions of the genome have been associated with lung function to date, many of which have also been implicated in chronic obstructive pulmonary disease. Methods: We carried out meta-analyses of exome array data and three lung function measures: forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and the ratio of FEV1 to FVC (FEV1/FVC). These analyses by the SpiroMeta and CHARGE consortia included 60,749 individuals of European ancestry from 23 studies, and 7,721 individuals of African Ancestry from 5 studies in the discovery stage, with follow-up in up to 111,556 independent individuals. Results: We identified significant (P<2ů8x10-7) associations with six SNPs: a nonsynonymous variant in RPAP1, which is predicted to be damaging, three intronic SNPs (SEC24C, CASC17 and UQCC1) and two intergenic SNPs near to LY86 and FGF10. Expression quantitative trait loci analyses found evidence for regulation of gene expression at three signals and implicated several genes, including TYRO3 and PLAU. Conclusions: Further interrogation of these loci could provide greater understanding of the determinants of lung function and pulmonary disease.

Publisher F1000Research

ISSN/ISBN 2398-502X

edoc-URL https://edoc.unibas.ch/65424/
Full Text on edoc Available;
Digital Object Identifier DOI 10.12688/wellcomeopenres.12583.3
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/30175238
ISI-Number MEDLINE:30175238
Document type (ISI) Journal Article