Genes and pathways underlying susceptibility to impaired lung function in the context of environmental tobacco smoke exposure

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Studies aiming to assess genetic susceptibility for impaired lung function levels upon exposure to environmental tobacco smoke (ETS) have thus far focused on candidate-genes selected based on a-priori knowledge of potentially relevant biological pathways, such as glutathione S-transferases and ADAM33. By using a hypothesis-free approach, we aimed to identify novel susceptibility loci, and additionally explored biological pathways potentially underlying this susceptibility to impaired lung function in the context of ETS exposure.; Genome-wide interactions of single nucleotide polymorphism (SNP) by ETS exposure (0 versus ≥1ăh/day) in relation to the level of forced expiratory volume in one second (FEV1) were investigated in 10,817 subjects from the Dutch LifeLines cohort study, and verified in subjects from the Swiss SAPALDIA study (nă=ă1276) and the Dutch Rotterdam Study (nă=ă1156). SNP-by-ETS exposure p-values obtained from the identification analysis were used to perform a pathway analysis.; Fourty Five SNP-by-ETS exposure interactions with p-values <10(-4) were identified in the LifeLines study, two being replicated with nominally significant p-values (<0.05) in at least one of the replication cohorts. Three pathways were enriched in the pathway-level analysis performed in the identification cohort LifeLines, i.E. the apoptosis, p38 MAPK and TNF pathways.; This unique, first genome-wide gene-by-ETS interaction study on the level of FEV1 showed that pathways previously implicated in chronic obstructive pulmonary disease (COPD), a disease characterized by airflow obstruction, may also underlie susceptibility to impaired lung function in the context of ETS exposure.
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