

Publication

Adult onset asthma and interaction between genes and active tobacco smoking : The GABRIEL consortium

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Genome-wide association studies have identified novel genetic associations for asthma, but without taking into account the role of active tobacco smoking. This study aimed to identify novel genes that interact with ever active tobacco smoking in adult onset asthma.; We performed a genome-wide interaction analysis in six studies participating in the GABRIEL consortium following two meta-analyses approaches based on 1) the overall interaction effect and 2) the genetic effect in subjects with and without smoking exposure. We performed a discovery meta-analysis including 4,057 subjects of European descent and replicated our findings in an independent cohort (LifeLines Cohort Study), including 12,475 subjects.; First approach: 50 SNPs were selected based on an overall interaction effect at $p < 10^{-4}$. The most pronounced interaction effect was observed for rs9969775 on chromosome 9 (discovery meta-analysis: $OR_{int} = 0.50$, $p = 7.63 \times 10^{-5}$, replication: $OR_{int} = 0.65$, $p = 0.02$). Second approach: 35 SNPs were selected based on the overall genetic effect in exposed subjects ($p < 10^{-4}$). The most pronounced genetic effect was observed for rs5011804 on chromosome 12 (discovery meta-analysis $OR_{int} = 1.50$, $p = 1.21 \times 10^{-4}$; replication: $OR_{int} = 1.40$, $p = 0.03$).; Using two genome-wide interaction approaches, we identified novel polymorphisms in non-annotated intergenic regions on chromosomes 9 and 12, that showed suggestive evidence for interaction with active tobacco smoking in the onset of adult asthma.

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