A comprehensive evaluation of potential lung function associated genes in the SpiroMeta general population sample

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RATIONALE: Lung function measures are heritable traits that predict population morbidity and mortality and are essential for the diagnosis of chronic obstructive pulmonary disease (COPD). Variations in many genes have been reported to affect these traits, but attempts at replication have provided conflicting results. Recently, we undertook a meta-analysis of Genome Wide Association Study (GWAS) results for lung function measures in 20,288 individuals from the general population (the SpiroMeta consortium). OBJECTIVES: To comprehensively analyse previously reported genetic associations with lung function measures, and to investigate whether single nucleotide polymorphisms (SNPs) in these genomic regions are associated with lung function in a large population sample. METHODS: We analysed association for SNPs tagging 130 genes and 48 intergenic regions (+/-10 kb), after conducting a systematic review of the literature in the PubMed database for genetic association studies reporting lung function associations. RESULTS: The analysis included 16,936 genotyped and imputed SNPs. No loci showed overall significant association for FEV(1) or FEV(1)/FVC traits using a carefully defined significance threshold of 1.3x10(-5). The most significant loci associated with FEV(1) include SNPs tagging MACROD2 (P = 6.81x10(-5)), CNTN5 (P = 4.37x10(-4)), and TRPV4 (P = 1.58x10(-3)). Among ever-smokers, SERPINA1 showed the most significant association with FEV(1) (P = 8.41x10(-5)), followed by PDE4D (P = 1.22x10(-4)). The strongest association with FEV(1)/FVC ratio was observed with ABCC1 (P = 4.38x10(-4)), and ESR1 (P = 5.42x10(-4)) among ever-smokers. CONCLUSIONS: Polymorphisms spanning previously associated lung function genes did not show strong evidence for association with lung function measures in the SpiroMeta consortium population. Common SERPINA1 polymorphisms may affect FEV(1) among smokers in the general population
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