INTERACTIONS BETWEEN CANDIDATE GENE POLYMORPHISMS AND ENVIRONMENTAL POLLUTANTS ON ASTHMA SEVERITY IN ADULTS

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Introduction

Asthma is a complex chronic disease, which involves the interplay of multiple genetic, environmental and lifestyle factors, and includes clinical conditions that differ in etiopathogenesis, biological basis, clinical manifestations, course over time and response to therapy [1].

Aim

To identify single nucleotide polymorphisms (SNPs) in candidate genes that modify the relationship between environmental pollutants and asthma severity in adult patients from the general Italian population.

Methods

We analyzed phenotypic and genetic data from 198 adult subjects with current asthma (mean age 42.3 years; female 46.0%), who had been identified in Verona as part of the Gene Environment Interactions in Respiratory Diseases (GEIRD; 2008-2010) survey [2]. These subjects provided information on 166 polymorphisms tagging 50 candidate genes or gene regions (genotyped by a custom GoldenGate Genotyping Assay) [3].
We carried out a genetic association analysis using the Symptom frequency and anti-asthmatic Treatment intensity Score (STS) as the outcome. STS is a continuous measure of the frequency of respiratory symptoms and the intensity of anti-asthmatic treatment reported by patients [4]. The interaction between each SNP (classified according to the additive genetic model) and each environmental pollutant (nitrogen dioxide, ozone, PM2.5, PM10) on zero-skewness Box-Cox transformed STS score was assessed using a reparametrized linear regression model [5], with age and sex as adjusting variables. The difference in slope was tested for each of the three pairs of genotypes and the lowest p-value was corrected to control the false discovery rate (FDR) using Simes' multiple testing procedure [6].

Results

We identified an interaction between SNP rs1553318 (genotype GG: 58 subjects; CG: 99 subjects; CC: 38 subjects) in Hepatitis A Virus Cellular Receptor 1 (*HAVCR1*) gene and nitrogen dioxide on asthma severity (uncorrected p-value = 0. 0002; FDR-corrected p-value = 0.030).

Conclusion

HAVCR1 gene encodes a membrane receptor that acts as a regulator of T-cell proliferation and Th1/Th2 differentiation, which are crucial processes in the development of inflammatory responses. Variants in *HAVCR1* gene may be involved in the moderation of asthma and allergic diseases [7].

Bibliography

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