STUDYING THE INFLUENCE OF PTPN22 GENE IN SYSTEMIC SCLERODERMA

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Background:

Two single nucleotide polymorphisms in the PTPN22 gene (R620W; rs24746601 and R263Q; rs33996649) with functional implications, have been previously associated to autoimmune diseases. The first one, a gain-of-function R620W polymorphism is a confirmed risk factor for some autoimmune disorders. In contrast the second one, a loss-of-function R263Q polymorphism is associated with reduced risk of systemic lupus erythematosus. The aim of the present study was to investigate the possible role of the rs33996649 single nucleotide polymorphism (SNP) and to re-evaluate the role of rs24746601 PTPN22 polymorphism in the genetic predisposition to systemic sclerosis (SSc) susceptibility or clinical phenotype.

Methods:

A total of 3426 SSc patients (1999 with limited cutaneous SSc (lCSSc) and 1018 with diffuse cutaneous SSc (dCSSc)) and 3661 healthy controls, from an initial case-control set of Spanish Caucasian ancestry and six independent cohorts of European ancestry (The Netherlands, Belgium, England, Germany, Italy, USA and Sweden), were included in the study. Genotyping was performed using a polymerase chain reaction system with a pre-developed TaqMan allelic discrimination assay for the rs33996649 and rs2476601 polymorphisms in the PTPN22 gene. A Meta-analysis including the seven study cohorts was performed to test the overall effect of the minor allele of each polymorphism in the PTPN22 gene in SSc susceptibility or its clinical phenotypes using the Mantel-Haenszel test.

Results:

We observed that the rs2476601 T allele is associated with SSc susceptibility, according with the meta-analysis results (p=0.023 pooled, OR= 1.14, 95% CI=1.01-1.28). Moreover, the rs2476601 T allele is significantly associated with anti-centromere (ACA) positive status (p=0.01 pooled, OR= 1.27, 95% CI=11-1.5). Although we found that the rs33996649 A allele was significantly associated with SSc in Spanish population (p=0.02, OR=0.6, 95% CI=0.4-0.9), this association was not confirmed in the meta-analysis that included the six replication cohorts (p=0.26 pooled, OR=0.87, 95% CI= 0.7-1.1).

Conclusion:

Our study shows that the PTPN22 R620W polymorphism influences SSc genetic susceptibility. Moreover, our data increase the evidence of the R620W polymorphism as a common risk factor in autoimmunity.