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Differential association of two *PTPN22* coding variants with Crohn's disease and ulcerative colitis

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Introduction

The *PTPN22* gene is an important risk factor for human autoimmunity. Two *PTPN22* missense-SNPs, both with functional influence, the R620W (1858C>T, rs2476601) in exon 14 and the R263Q (788G>A, rs33996649) in exon 10 have been associated with autoimmune diseases [1-4].

Aim

The aim of this study was to evaluate for the first time the role of the R263Q *PTPN22* polymorphism in ulcerative colitis (UC) and Crohn's disease (CD), and re-evaluated the association of the R620W *PTPN22* polymorphism with both diseases.

Patients and methods

A total of 1,677 UC patients, 1,903 CD patients and 3,107 healthy controls, from an initial case-control set of Spanish Caucasian ancestry and two independent sample sets of European ancestry (Dutch and New Zealand), were included in the study. Genotyping was performed using TaqMan SNP assays for the R263Q and R620W *PTPN22* polymorphisms. Meta-analysis was performed on 6977 CD, 5695 UC and 9254 controls to test the overall effect of the minor allele of R620W variant, and on the three Caucasian cohorts for the R263Q polymorphism.

Results

The *PTPN22* 263Q loss-of-function variant showed an initial evidence of a significant association with UC in the Spanish cohort (p=0.026,OR=0.61,95%CI=0.39-0.95), which was confirmed in the meta-analysis (p=0.013pooled, OR=0.69,95%CI=0.51-0.93). In contrast, the 263Q allele showed no association to CD, (p=0.22pooled,OR=1.16,95% CI=0.91-1.47). We found in the pooled analysis that the PTPN22 620W gain-of-function variant was associated with reduced risk of CD (p=7.4E-06pooled, OR=0.81,95% CI=0.75-0.89) but not of UC (p=0.88pooled, OR=0.98,95% CI=0.85-1.15).

Conclusion

Our data suggest that two autoimmunity-associated polymorphisms of the *PTPN22* gene are differentially associated with CD and UC. The R263Q polymorphism only associated with UC meanwhile the R620W was significantly related with CD. Our findings support the idea that the two major IBD phenotypes differ in some genetic components, and also in specific variants within a single gene, thus suggesting the involvement of different immunological mechanisms with a related nature.

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