Lack of association of the GSDMB gene at locus 17q12 with predisposition to rheumatoid arthritis

Sirs.

Rheumatoid arthritis (RA) is a chronic inflammatory disease, in which pathogenesis many genetic, environmental and hormonal factors have been implicated. To date, the known genetic factors account for 60% of the genetic basis of the disease (1) implicated 37 candidate molecular pathways (2) and therefore more genetic association studies are needed to explore the additional polymorphisms in RA predisposition with probably lower penetrance. In a recent multietnic approach for the identification of RA susceptibility loci, two chromosome loci, the 1p36 and the 17q12, were revealed as most likely associated with RA manifestation (3). Subsequently, bioinformatic analyses identified TNFRSF14-MME1L at the 1p36 locus and IKZF3-ORMDL3-GSDMB at the 17q12 locus as the most probably related genes with RA liability (3). Since the genetic association of locus TNFRSF14-MME1L with RA has been reported previously (4), our interest has focused on genes IKZF3-ORMDL3-GSDMB at locus 17q12.

At locus 17q12 the most associated polymorphism with RA, in this multi-ethnic approach, was the rs2872507. This intergenic variant was found to be in linkage disequilibrium (LD) with the missense polymorphism rs2305479 which alters a glycine to arginine at codon 299 in the GSDMB (gadermin B) gene and predicted to be damaging (5). Therefore, in the present study, we investigated, for the first time, the plausible probably association of the GSDMB gene with RA predisposition by genotyping polymorphism rs2305479.

One hundred and eighty-five unrelated RA patients, who satisfied the American College of Rheumatology criteria, and 174 ethnically-matching healthy volunteers were enrolled in the study. Genomic DNA was extracted from peripheral blood lymphocytes according to the standard salt extraction procedure. GSDMB polymorphism rs2305479 was amplified using the following primer pair: rs2305479F: 5'- CTA AGA AAG CCT TGC GGC AGA -3', rs2305479R: 5'- TCC AGA ATG GCT TTT GCA CG -3'. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) assay was conducted using the restriction endonuclease Msp I. The SPSS statistical package was used to test differences in polymorphism distribution between RA patients and controls (Pearson’s chi-square). Furthermore, the odds ratio (OR) with a confidence interval (CI) of 95% was calculated. A difference at p<0.05 was considered as statistically significant.

The studied polymorphism was found in Hardy-Weinberg equilibrium in both RA patients (p=0.268) and controls (p=0.159). No statistical significant difference was observed in genotypes' and alleles' rs2305479 distribution between RA patients and controls as shown in Table I.

Table I. Genotypes’ and alleles’ distribution of GSDMB gene polymorphism rs2305479 in rheumatoid arthritis (RA) patients and controls.

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>RA n=185 (%)</th>
<th>Controls n=174 (%)</th>
<th>p-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GG</td>
<td>41 (22.2)</td>
<td>82 (55.8)</td>
<td>0.889</td>
<td>0.992 (0.730–1.374)</td>
</tr>
<tr>
<td>GA</td>
<td>31 (21.1)</td>
<td>82 (55.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>10 (5.4)</td>
<td>30 (20.7)</td>
<td></td>
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OR = 0.992 (p<0.05).

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References