IL18 Polymorphism Is Associated with Behçet’s Disease But Not Lupus in Patients from Turkey

JASMINE HTOON, AJAY NADIG, TRAVIS HUGHES, SULE YAVUZ, HANER DIRESKENELI, GÜHER SARUHAN-DIRESKENELI and AMR H. SAWALHA

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To the Editor:

Sánchez, et al have recently reported an association between a putative functional genetic variant in the promoter region of IL18 (rs360719) and systemic lupus erythematosus in Spanish patients. They found an increase in the relative expression of IL18 mRNA in individuals with the rs360719 lupus-risk allele. Interleukin 18 (IL-18) is a pleiotropic cytokine that can induce Th1 and Th2 responses in the presence and absence, respectively, of IL-12. Studies have described overproduction of IL-18 in several autoimmune and inflammatory diseases including Behçet’s disease (BD) and lupus. Indeed, serum IL-18 levels in patients with lupus and BD correlate with disease activity.1-2

We attempted to replicate the results of Sánchez, et al in a set of Turkish patients with lupus. We examined the same putative functional IL18 polymorphism is associated with BD in Turkish patients. We genotyped 2 additional potentially functional single-nucleotide polymorphisms (SNP) in the IL18 promoter region (rs1946518, –607 C/A, and rs187238, –137 G/C). Our sample set consisted of 189 patients with lupus, 156 with BD, and 253 ethnically matched healthy controls.

All lupus patients and all BD patients fulfilled the 1997 American College of Rheumatology classification criteria for lupus and the 1990 International Study Group classification criteria for BD, respectively.

Genotyping was performed using TaqMan allelic discrimination assays (Applied Biosystems, Foster City, CA, USA). The genotyping success rate was ≥ 97.5%. Only individuals successfully genotyped in at least 2 out of the 3 SNP were included in the analysis. There was no departure from Hardy-Weinberg equilibrium in controls. Data analysis was performed using PLINK and Haploview 4.2.

We found no genetic association between IL18 and lupus in Turkish patients (Table 1). The frequency of the minor allele in rs360719 was 19.3% in cases and 19.5% in controls (OR 0.99, 95% CI 0.70–1.40, p = 0.80). This is in contrast to the findings of Sánchez, et al, who reported that allele “A” is the lupus-risk allele in the study. Interleukin-18 and tumour necrosis factor-alpha levels are increased through an association study in systemic lupus erythematosus. Hum Mol Genet 2009;18:3739-48.

We found a genetic association between allele “A” in rs1946518 (–607 C/A) and BD (OR 1.48, 95% CI 1.10–1.97, p = 0.0088). Our study had 85% power to detect a genetic association in these 2 SNP given the minor allele frequencies and odds ratios detected. However, our study was underpowered to detect an association in these 2 SNP given the minor allele frequencies and odds ratios detected.

We found a genetic association between IL18 and BD but not lupus in Turkish patients. Palomino-Morales, et al have reported a similar association between allele “A” in rs1946518 and giant cell arteritis.3 In addition, the association between rs187238 and Henoch-Schönlein purpura has been reported.4 This suggests that IL18 might be a common susceptibility locus for at least 3 vasculitic diseases. Whether IL18 is a susceptibility gene in other vasculitides remains to be investigated.

**REFERENCES**


**Table 2. Genetic association analysis of single-nucleotide polymorphisms located in the promoter region of IL18 in Behçet’s disease cases and controls.**

<table>
<thead>
<tr>
<th>Marker Position</th>
<th>Minor Allele</th>
<th>Cases, n (%)</th>
<th>Controls, n (%)</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs187238 –137</td>
<td>C</td>
<td>68 (22.2)</td>
<td>98 (20.2)</td>
<td>1.13 (0.80–1.60)</td>
<td>0.49</td>
</tr>
<tr>
<td>rs1946518 –607</td>
<td>A</td>
<td>140 (45.2)</td>
<td>172 (35.8)</td>
<td>1.48 (1.10–1.97)</td>
<td>0.0088</td>
</tr>
<tr>
<td>rs360719 –1297</td>
<td>C</td>
<td>66 (22.0)</td>
<td>93 (19.5)</td>
<td>1.17 (0.82–1.67)</td>
<td>0.39</td>
</tr>
</tbody>
</table>