Association between HLA region and ocular involvement in Behçet’s disease in a Japanese population: preliminary report

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Background:
• Behçet’s disease (BD) is a chronic systemic inflammatory disorder characterized by recurrent ocular symptoms, oral and genital ulcers, and skin lesions.
• The etiology of BD is still uncertain, but currently some external environmental factors are thought to trigger BD in individuals with a particular genetic background. It is well established that BD is strongly associated with the human leukocyte antigen (HLA) class I allele, HLA-B*51, in many different ethnic groups.
• In this study, we performed a comprehensive association analysis between the HLA region and ocular involvement in BD.

Materials & Methods:
• We used a total of 877 single nucleotide polymorphisms (SNPs) in the HLA region genotyped in the genome-wide association study [Nat Genet 2010; 42(8): 703-6.] which enrolled 611 Japanese BD patients (including 469 patients with ocular involvement) and 737 Japanese healthy controls.
• Screening of susceptibility HLA loci/genes for ocular BD was performed by the method shown in Figure 1.

Results:
• We identified 65 SNPs, ascribed to three loci, showing significant associations with ocular BD (P < 0.00001, OR ≥ 1.40) but not non-ocular BD (P > 0.05, OR < 1.1) (Table 1, Figure 2).
• These three loci are located in the HLA class I region, but they were in weak linkage disequilibrium with each other (r² < 0.10) and were independently associated with ocular BD.

Conclusions:
• Preliminary results of the ongoing study point out to risk loci for ocular BD in the HLA region.
• To confirm the findings, future validation studies with other independent populations are needed.

Table 1. Lead SNPs in three HLA loci showing significant associations with ocular BD (P < 0.00001, OR ≥ 1.40) but not non-ocular BD (P > 0.05, OR < 1.1)

<table>
<thead>
<tr>
<th>Locus</th>
<th>SNP</th>
<th>Position on Chr 6 (GRCh37)</th>
<th>Nearest gene</th>
<th>Risk allele freq.</th>
<th>Risk allele freq.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ocular cases</td>
<td>Non-ocular cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ctrls P OR</td>
<td>Ctrls P OR</td>
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<tr>
<td>1</td>
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<td>29,794,400</td>
<td>HLA-F</td>
<td>C</td>
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<td>A</td>
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<tr>
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<td>31,425,499</td>
<td>MICB</td>
<td>T</td>
<td>0.920</td>
</tr>
</tbody>
</table>

Figure 2. Distribution of the allelic association results and linkage disequilibrium of the 65 HLA SNPs identified in this study