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.

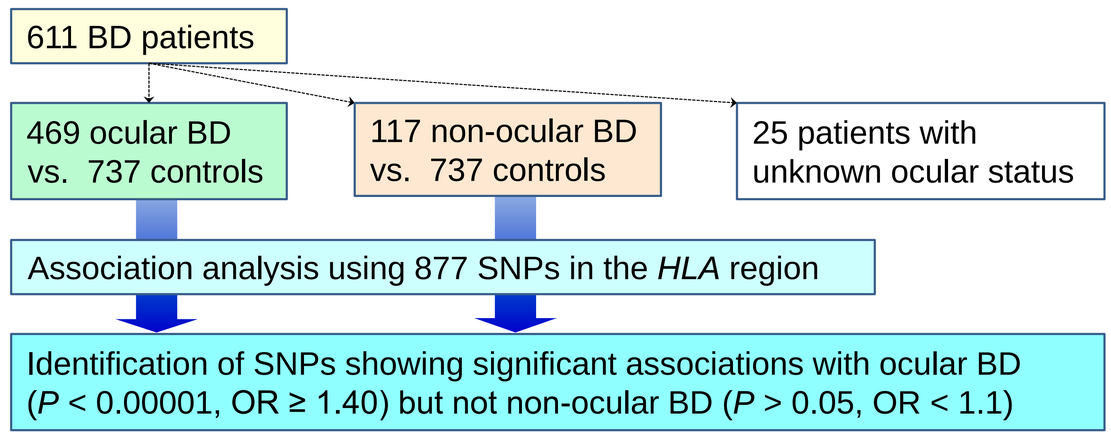

Figure 1. Screening of susceptibility *HLA* loci/genes for ocular BD

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 ($r^2 < 0.10$) and were independently associated with ocular BD.

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)

					Risk alelle freq.				Risk alelle freq.			
Locus	SNP	Position on Chr. 6 (GRCh37)	Nearest gene	Risk allele	Ocular cases	Ctrls	P	OR	Non-ocular cases	Ctrls	P	OR
1	rs1736913	29,704,400	*HLA-F*	C	0.871	0.757	7.4E-12	2.17	0.769	0.757	0.68	1.07
2	rs6923832	30,062,058	*TRIM31*	A	0.222	0.104	5.7E-15	2.44	0.098	0.104	0.78	0.94
3	rs3131621	31,425,499	*MICB*	T	0.920	0.860	7.9E-06	1.87	0.868	0.860	0.75	1.07

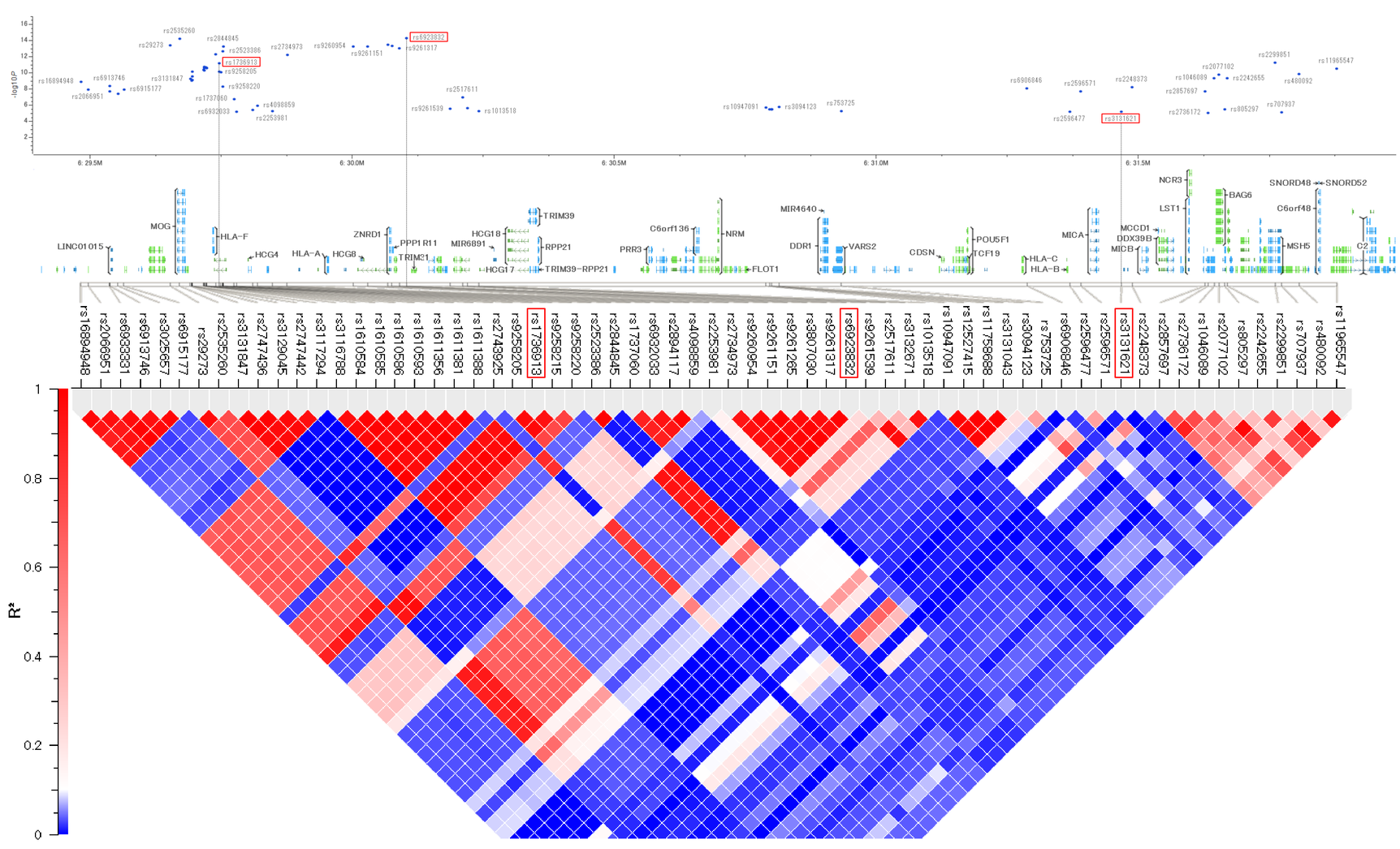

Figure 2. Distribution of the allelic association results and linkage disequilibrium of the 65 *HLA* SNPs identified in this study

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.