Comprehensive analysis of the association between IL10 gene variants and Vogt-Koyanagi-Harada disease in a Japanese population

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Background:

- Interleukin-10 (IL-10) is a potent suppressor of inflammatory cytokines, and *IL10* gene variants are reportedly associated with several immune-mediated diseases.
- IL-10 may play an important role in controlling Vogt-Koyanagi-Harada (VKH) disease. Here we investigated whether *IL10* gene variants were associated with VKH disease and its clinical symptoms among Japanese patients.

Materials & Methods:

- A total of 380 Japanese patients with VKH disease and 1,066 Japanese healthy controls were recruited.
- We genotyped 10 single-nucleotide polymorphisms (SNPs) in the *IL10* gene region.
- We also performed an imputation analysis to evaluate potential associations of un-genotyped *IL10* SNPs using the data of 10 genotyped SNPs, and the 33 SNPs were imputed.

Results:

- None of the genotyped and imputed SNPs were significantly associated with VKH disease itself (Figure 1).
- On the other hand, five SNPs in the 3'-untranslated region (UTR) or 5'-UTR of the *IL10* gene were significantly associated with the symptom of nausea (*P* = 0.0016, corrected *P* (*P*c) = 0.016, odds ratio (OR) = 4.21) and showed suggestive association with hypersensitivity to touch of hair and skin (*P* = 0.016, *P*c = 0.16, OR = 2.61) (Table 1).
- Additionally, other three SNPs in the intron or 5'-UTR were significantly associated with poliosis (*P* = 0.0043, *P*c = 0.043, OR = 2.11). Moreover, another intronic SNP showed suggestive association with the symptom of vitiligo (*P* = 0.017, *P*c = 0.17, OR = 2.11) (Table 1).
- Expression analysis revealed that the risk alleles of these SNPs showed significant association with decreased *IL10* gene expression (*P* < 0.00001) (Figure 2).

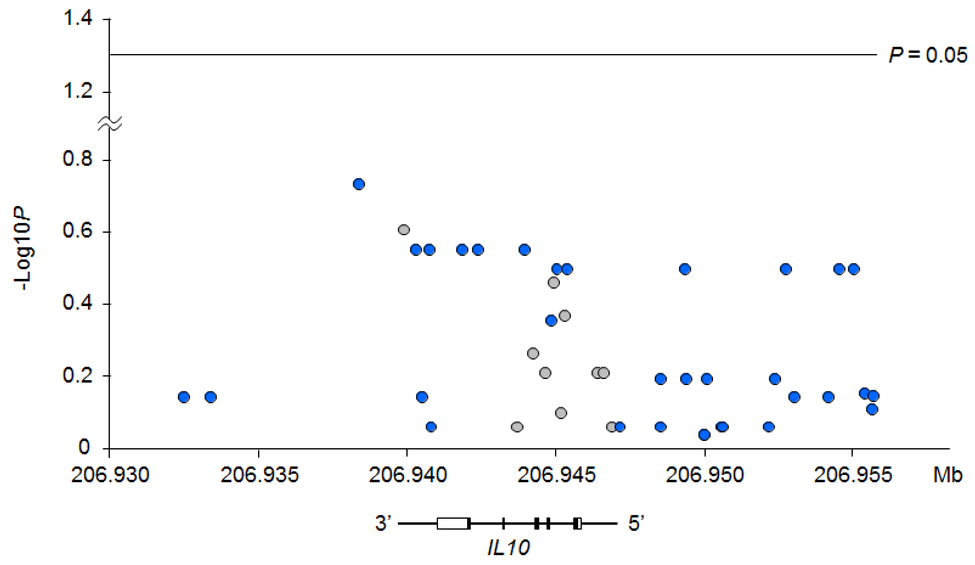

Figure 1. Distribution of the allelic association results for SNPs across the *IL10* gene region

Genotyped SNPs are indicated by a grey circle, and imputed SNPs are indicated by a blue circle.

Table 1. Allelic association between *IL10* SNPs and clinical symptoms of VKH

Clinical symptoms	SNP	Position on Chr.1	Gene location	Alleles (1>2)	MAF, % Cases	MAF, % Controls	*P*	*P*c*	OR (95% CI)
Nausea (n=20)	rs13376708	206,932,503	3'-UTR	G>A					
	rs117652932	206,933,410	3'-UTR	G>A					
	rs12047368	206,940,523	3'-UTR	G>A	12.5	3.3	0.0016	0.016	4.21 (1.60-11.07)
	rs12029597	206,953,042	5'-UTR	C>T					
	rs12027844	206,954,175	5'-UTR	G>C					
Hypersensitivity to touch of hair and skin (n=43)	rs13376708	206,932,503	3'-UTR	G>A					
	rs117652932	206,933,410	3'-UTR	G>A					
	rs12047368	206,940,523	3'-UTR	G>A	8.1	3.3	0.016	0.16	2.61 (1.16-5.86)
	rs12029597	206,953,042	5'-UTR	C>T					
	rs12027844	206,954,175	5'-UTR	G>C					
Poliosis (n=29)	rs1518111	206,944,645	Intron	T>C					
	rs1800872	206,946,407	5'-UTR	T>G	50.0	32.2	0.0043	0.043	2.11 (1.25-3.56)
	rs1800871	206,946,634	5'-UTR	A>G					
Vitiligo (n=20)	rs3024490	206,945,311	Intron	A>C	52.5	34.3	0.017	0.17	2.11 (1.13-3.96)

1, major allele; 2, minor allele; MAF, minor allele frequency; CI, confidence interval.

**P* values were corrected for multiple testing by Bonferroni correction. In this correction, *P* values were multiplied by the number of genotyped SNPs (10).

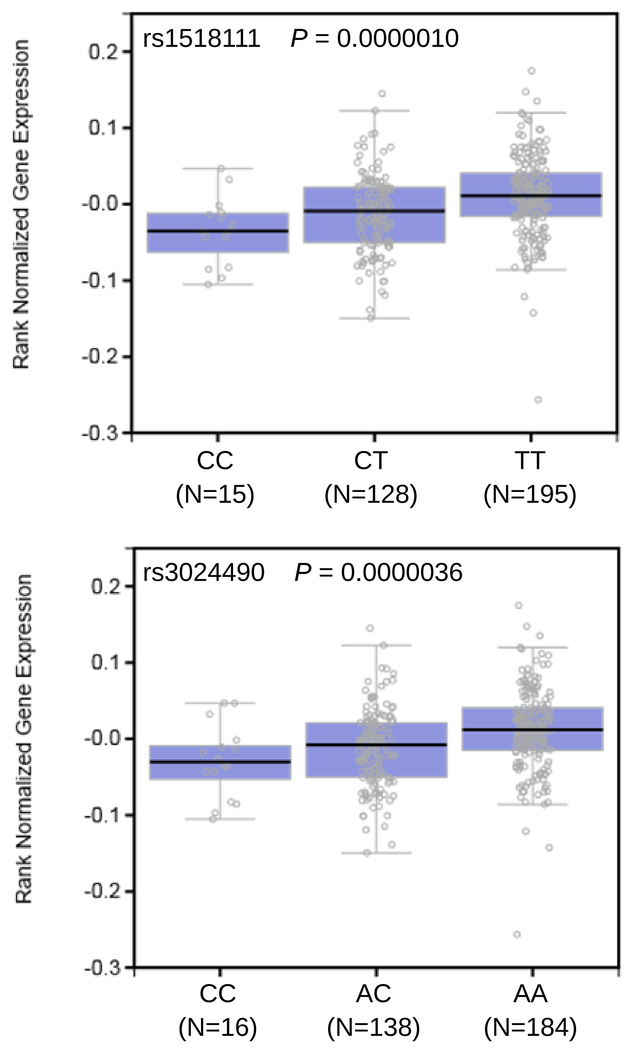

Figure 2. eQTL results of the *IL10* gene extracted from GTEx Portal online databse

Conclusions:

- Our results suggest that the *IL10* variants contribute to the development of particular clinical symptoms of VKH disease.
- To confirm our findings, future validation studies with other independent populations are needed.