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Supplementary Appendix

Physicians of the Research Consortium on Genetics of Childhood Idiopathic Nephrotic Syndrome in Japan, who collected blood samples and clinical information for this study

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Supplementary Methods

Case ascertainment

This study included 440 patients with childhood SSNS followed-up in 43 hospitals across Japan. In total, 1,138 healthy adults without current diseases or disease history were recruited from the Tokyo area as controls.

Genotyping in the initial GWAS

In the initial GWAS, 224 patients with SSNS and 419 adult healthy controls were genotyped using the Affymetrix 'Japonica Array', which was specially designed for the Japanese population based on the whole-genome sequencing data of 1,070 healthy Japanese individuals. The genotyping was performed according to the manufacturer's instructions. All genotyped samples passed the recommended sample QC metric for the AXIOM arrays (dish QC >0.82). One control sample with an overall call rate <97% was excluded. We recalled the remaining 642 samples with Genotyping Console software v4.2.0.26 (Affymetrix), and all the samples had an overall call rate ≥97%.

Whole-genome imputation based on the 2KJPN panel

For imputation, the clustering plots were classified by the Ps classification function in the SNPolisher package (version 1.5.2; Affymetrix). SNPs that were assigned 'recommended' by the Ps classification were retained. SNPs with a call rate <99.0%, an HWE test result of P<0.0001 or a MAF <0.5% were excluded. Prephasing was conducted first with the SNPs which passed the filtering step with SHAPEIT (v.2.r644); the options were –burn 10, –prune 10, and –main 25. Genotype imputation was performed on the phased genotypes with IMPUTE2 (ver. 2.3.1) using a phased reference panel of 2,049 healthy Japanese individuals (2KJPN panel). For IMPUTE2, the applied options were –Ne 2000, –k hap 1000,

–k 120, –burnin 15, and –iter 50.

After whole-genome imputation, there were 32,509,374 autosomal SNPs and short INDELs with info score >0.5. QC was conducted using the following threshold: SNP/INDEL call rate ≥97% (980,814 SNPs/INDELs were excluded), MAF ≥5% (27,422,486 SNPs/INDELs were excluded), and HWE *P*-value ≥0.0001 in healthy controls (531 SNPs/INDELs were excluded). After QC, 224 cases and 412 controls with 4,105,543 SNPs/INDELs remained for the further association analyses.

SNP genotyping for validation and replication

For validation and replication, 6 SNPs/INDELs in high LD in the top hit in the *HLA* region, and another 4 SNPs from 2 candidate loci outside the *HLA* region (1 genotyped SNP and 1 imputed SNP with minimum *P*-value in each locus) were selected. Genotyping was performed using the DigiTag2 assay. Genotyping failed for 4 SNPs/INDELs in the *HLA-DR/DQ* region (rs79193269, rs9275103, rs9282090 and rs9275101) and 1 SNP outside the *HLA* region (rs4865828).

HLA imputation and HLA genotyping

In the discovery stage, HLA imputation was performed for 224 cases and 412 controls to clarify the genome-wide associated signals identified in the *HLA* region. We conducted 2-field *HLA* genotype imputation for key *HLA* class I (*HLA-A*, *-C* and *-B*) and class II (*HLA-DRB1*, *-DQB1* and *-DPB1*) loci using the 'HIBAG' R package. After SNP QC (SNP call rate ≥97%, MAF ≥5%, and HWE *P*-value ≥0.0001 in healthy controls), SNP data for each individual were extracted from an extended major histocompatibility complex region, ranging from 25,759,242 to 33,534,827 bp based on the hg19 position. Our in-house Japanese imputation reference was used for *HLA* genotype imputation. We applied post-

imputation QC using CT >0.4. A total of 197 cases and 411 healthy controls in discovery stage passed the post-imputation QC and were included in subsequent analyses. In the replication stage, imputation was performed for the *HLA-DRB1* and *-DQB1* genes using the same approach in 269 healthy controls whose *HLA* genotypes were not available by direct genotyping. Genotyping was performed previously for the 269 controls using the Affymetrix Axiom Genome-Wide ASI 1 Array. SNPs that passed QC using the same criteria were extracted for HLA imputation. A total of 260 of the 269 controls passed the post-imputation QC (CT>0.4) and were included in the replication sample set.

Genotyping of *HLA-DRB1* and *-DQB1* was performed using the PCR-SSO (sequence-specific oligonucleotide probing) method on a Luminex platform with a WAKFlow *HLA* typing kit (Wakunaga, Hiroshima, Japan). Briefly, target DNA was amplified by PCR using biotinylated primers specifically designed for each HLA locus. The PCR product was then denatured and hybridized to complementary oligonucleotide probes immobilized on fluorescently coded microsphere beads. At the same time, biotinylated PCR product was labeled with phycoerythrin-conjugated streptavidin and finally examined using the Luminex system. Genotype determination and data analysis were performed automatically using the WAKFlow typing software. A total of 437 cases (224 cases in the discovery stage and 213 cases in the replication stage) were genotyped successfully. Genotyping for *HLA-DRB1/-DQB1* was conducted previously using the same method for 409 controls in the discovery sample set and 450 controls in the replication sample set, and the genotyped data were used in the current study.

Single-tag SNP for capturing *HLA-DRB1*08:02* and *HLA-DRB1*08:02-DQB1*03:02*

Using the DigTag2 assay, we genotyped rs3129888 in 224 cases in the discovery sample set for validation (concordance rate=100%) and in 216 cases and 719 healthy controls in the replication sample set. To assess the sensitivity and specificity of the tag SNP,

we conducted the analysis using the combined data set for *HLA* allele/haplotype analyses including 437 cases and 1,119 controls. In the dataset, 177 of 184 *HLA-DRB1*08:02* had the G allele of rs3129888 (sensitivity 96.2%), and 2,865 of 2,928 other *HLA-DRB1* sub-alleles had the A allele of rs3129888 (specificity 97.8%). For *HLA-DRB1*08:02-DQB1*03:02*, 110 of 112 *HLA-DRB1*08:02-DQB1*03:02* had the G allele of rs3129888 (sensitivity 98.2%), and 2,870 of 3,000 other *HLA-DRB1-DQB1* haplotypes had the A allele of rs3129888 (specificity 95.7%).

Power calculation for two-stage GWAS

Study power was calculated using the R package 'CATS'. Assuming a disease prevalence of 0.01% in the Japanese population, study power was calculated separately under the additive model for variants with an allele frequency of 5% or 50% using 244 cases in the discovery stage, 412 controls in the discovery stage, 216 cases in the replication stage, and 719 controls in the replication stage, with a significance threshold$\alpha=5\times10^{-8}$.

The power of our two-stage GWAS exceeded 80% to detect common alleles (MAF ≥5%) with a genotypic RR ≥2.95 or variants with an allele frequency ≥50% conferring a RR ≥2.0 at a significant *P*-value threshold of 5×10^{-8}.

Variance explained by *HLA* association

Logistic regression and Nagelkerke's pseudo-R^2 were used to measure the proportion of variance explained by genetic factor(s). Analyses were done by R programming and R package 'rcompanion'. To use informative and independent genetic marker, we included the top SNP in the *HLA* region (rs4642516), which was detected in the discovery stage and replicated in an independent sample set. The results of the conditional analysis in the *HLA* region demonstrated that there was no other SNP showing an

independent effect in the *HLA* region. Logistic regression was performed in replication dataset including 213 cases and 710 controls. Case-control status was used as outcome while the genotype of rs4642516 was used as covariate in logistic regression. 9.7% of disease variance (Nagelkerke's pseudo-R^2) in Japanese childhood SSNS can be explained by rs4642516. We also conducted the logistic regression using the two independent classical *HLA* alleles, *HLA-DRB1*08:02* and *HLA-DQB1*06:04,* in the replication dataset. *HLA-DRB1*08:02* and *HLA-DQB1*06:04* explained 8.1% of the variance in childhood SSNS in the Japanese population (Nagelkerke's pseudo-R^2).

Supplementary Table 1. Definitions of nephrotic syndrome.

Nephrotic syndrome	Urine protein to creatinine ratio ≥2.0 and serum albumin ≤2.5 g/dl
Complete remission	Negative protein on urine dipstick test or urine protein to creatinine ratio 0.2 for 3 consecutive days
Relapse	Protein ≥3+ on urine dipstick test for 3 consecutive days
Steroid-sensitive nephrotic syndrome (SSNS)	Complete remission within 4 weeks after starting 60 mg/m^2 oral prednisolone per day
Steroid-resistant nephrotic syndrome (SRNS)	Persistent proteinuria after 60 mg/m^2 oral prednisolone per day for 4 weeks
Steroid-dependent nephrotic syndrome (SDNS)	Two relapses of nephrotic syndrome during the reduction of steroid treatment or within 2 weeks of discontinuation of steroid treatment
Frequently-relapsing nephrotic syndrome (FRNS)	≥2 relapses of nephrotic syndrome within 6 months after initial remission, or ≥4 relapses within any 12-month period

Supplementary Table 2. Patients in the discovery and replication stages.

Characteristic	Discovery stage	Replication stage	Total
Number of patients	224	216	440
Sex ratio (male:female)	2.3:1 (156:68)	3.1:1 (163:53)	2.6:1
On-set age (median,Range) (years)	3.8 (0.4-16.3)	4.3 (1.3-22.0)	4.0 (0.4-22.0)
Follow-up (median, Range) (years)	5.5 (0-48.2)	6.3 (0-30.3)	5.8 (0-48.2)

Supplementary Table 3A. Candidate SNPs/INDELs identified in the discovery stage using the Cochran-Armitage trend test and the replication of candidate SNPs.

CHR	SNP/INDEL	BP	A1	A2	Annotation	Discovery stage (224 cases vs. 412 controls)			Replication stage (216 cases vs. 719 controls)		
						Freq in cases	Freq in controls	$P_{GC\text{-}corrected}$	Freq in cases	Freq in controls	*P*-value
5	rs4242036	53733306	A	G	Genotyped	0.11	0.04	4.46E-06	0.06	0.05	0.49
5	rs4865828	53733241	A	G	Imputed	0.11	0.04	4.46E-06	/	/	/
5	rs6864175	84134415	T	A	Imputed	0.29	0.18	6.67E-06	0.24	0.21	0.26
5	rs1875277	84127057	C	T	Genotyped	0.29	0.19	1.50E-05	0.25	0.22	0.33
6	rs79193269	32636661	C	CCTT	Imputed	0.08	0.23	1.54E-10	/	/	/
6	rs9275103	32649386	T	C	Imputed	0.11	0.27	2.46E-10	/	/	/
6	rs9282090	32629047	A	AC	Imputed	0.13	0.29	4.60E-10	/	/	/
6	rs9275101	32649355	G	A	Imputed	0.11	0.26	4.69E-10	/	/	/
6	rs4642516	32657543	G	T	Genotyped	0.11	0.26	4.69E-10	0.10	0.28	6.69E-13
6	rs3134996	32636866	A	T	Genotyped	0.09	0.23	7.06E-10	0.12	0.32	9.44E-10

CHR: chromosome; A1: minor allele (test allele); A2: major allele (reference allele).
Freq: Minor allele frequency.
$P_{GC\text{-}corrected}$: *P*-values were calculated using the Cochran-Armitage trend test, corrected by genomic control in the discovery GWAS.
P-value: *P*-values were calculated using the Cochran-Armitage trend test.
/: Genotyping of 5 candidate SNPs/INDELs failed.
Bonferroni correction: a *P*-value required for significance in the replication stage was 0.05/5=0.01.

Supplementary Table 3B. Replication of two candidate SNPs in the *HLA-DR/DQ* region under different genetic models.

CHR	SNP	A1	A2	Genetic model	Cases (n=216)	Controls (n=719)	*P*-Fisher	OR (95% CI)
6	rs4642516	G	T	Genotypic	2/41/173	62/274/381	1.51E-13	/
				Allelic	45/387	398/1036	4.51E-15	0.30 (0.22-0.42)
				Dominant	43/173	336/381	3.43E-13	0.28 (0.20-0.41)
				Recessive	2/214	62/655	9.51E-06	0.10 (0.01-0.41)
6	rs3134996	A	T	Genotypic	15/19/163	138/127/363	3.07E-10	/
				Allelic	49/345	403/853	1.26E-15	0.30 (0.22-0.41)
				Dominant	34/163	265/363	6.24E-11	0.29 (0.19-0.43)
				Recessive	15/182	138/490	1.75E-06	0.29 (0.17-0.51)

CHR: chromosome; A1: minor allele (test allele); A2: major allele (reference allele); *P*-Fisher: *P*-value was calculated using Fisher's exact test.
OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.

Supplementary Table 4. *HLA* allele association analyses of *HLA* class I genes with childhood SSNS in the discovery stage using HLA-imputation data.

HLA alleles[a]	Allele frequency						
	Cases (2n=394)		Controls (2n=822)			Chi-square test	
	No	%	No	%	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
HLA-A							
*A*02:01*	42	10.7	84	10.2	1.05 (0.71-1.55)	NS	-
*A*02:06*	53	13.5	62	7.5	1.91 (1.29-2.81)	9.82E-04	8.84E-03
*A*02:07*	16	4.1	24	2.9	1.41 (0.74-268)	NS	-
*A*11:01*	42	10.7	80	9.7	1.11 (0.75-1.64)	NS	-
*A*24:02*	141	35.8	326	39.7	0.85 (0.66-1.09)	NS	-
*A*26:01*	35	8.9	69	8.4	1.06 (0.70-1.63)	NS	-
*A*26:03*	9	2.3	29	3.5	0.64 (0.30-1.36)	NS	-
*A*31:01*	44	11.2	65	7.9	1.46 (0.98-2.19)	NS	-
*A*33:03*	10	2.5	65	7.9	0.30 (0.15-0.60)	2.70E-04	2.43E-03
HLA-C							
*C*01:02*	64	16.2	140	17.0	0.94 (0.68-1.31)	NS	-
*C*03:03*	57	14.5	113	13.7	1.06 (0.75-1.50)	NS	-
*C*03:04*	58	14.7	102	12.4	1.22 (0.86-1.72)	NS	-
*C*04:01*	24	6.1	42	5.1	1.20 (0.72-2.02)	NS	-
*C*06:02*	2	0.5	7	0.9	0.59 (0.12-2.87)	NS	-
*C*07:02*	45	11.4	119	14.5	0.76 (0.53-1.10)	NS	-
*C*08:01*	41	10.4	48	5.8	1.87 (1.21-2.89)	4.22E-03	5.06E-02
*C*08:03*	4	1.0	12	1.5	0.69 (0.22-2.16)	NS	-
*C*12:02*	44	11.2	81	9.9	1.15 (0.78-1.70)	NS	-
*C*14:02*	37	9.4	49	6.0	1.63 (1.05-2.55)	2.90E-02	3.48E-01
*C*14:03*	4	1.0	60	7.3	0.13 (0.05-0.36)	4.37E-06	5.25E-05
*C*15:02*	9	2.3	31	3.8	0.60 (0.28-1.27)	NS	-
HLA-B							
*B*07:02*	16	4.1	57	6.9	0.57 (0.32-1.00)	4.84E-02	1.06E+00
*B*13:01*	2	0.5	13	1.6	0.32 (0.07-1.41)	NS	-
*B*15:01*	38	9.6	72	8.8	1.11 (0.74-1.68)	NS	-
*B*15:07*	3	0.8	5	0.6	1.25 (0.30-5.27)	NS	-
*B*15:11*	3	0.8	5	0.6	1.25 (0.30-5.27)	NS	-
*B*15:18*	2	0.5	14	1.7	0.29 (0.07-1.30)	NS	-
*B*35:01*	33	8.4	67	8.2	1.03 (0.67-1.59)	NS	-
*B*37:01*	2	0.5	7	0.9	0.59 (0.12-2.87)	NS	-
*B*39:01*	15	3.8	34	4.1	0.92 (0.49-1.70)	NS	-
*B*40:01*	16	4.1	47	5.7	0.70 (0.39-1.25)	NS	-
*B*40:02*	45	11.4	58	7.1	1.70 (1.13-2.56)	1.05E-02	2.31E-01
*B*40:06*	32	8.1	33	4.0	2.11 (1.28-3.49)	2.88E-03	6.34E-02
*B*44:03*	4	1.0	59	7.2	0.13 (0.05-0.37)	5.69E-06	1.25E-04
*B*46:01*	19	4.8	38	4.6	1.05 (0.59-1.84)	NS	-
*B*48:01*	10	2.5	22	2.7	0.95 (0.44-2.02)	NS	-
*B*51:01*	42	10.7	70	8.5	1.28 (0.86-1.92)	NS	-
*B*52:01*	45	11.4	80	9.7	1.20 (0.81-1.76)	NS	-
*B*54:01*	22	5.6	65	7.9	0.69 (0.42-1.13)	NS	-
*B*55:02*	13	3.3	16	1.9	1.72 (0.82-3.61)	NS	-
*B*56:01*	5	1.3	5	0.6	2.10 (0.60-7.30)	NS	-
*B*59:01*	8	2.0	20	2.4	0.83 (0.36-1.90)	NS	-
*B*67:01*	9	2.3	11	1.3	1.72 (0.71-4.19)	NS	-

[a]Alleles: *HLA* alleles with frequencies <0.5% in cases or controls were omitted.

[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for allele frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 5. *HLA* allele association analyses of *HLA* class II genes with childhood SSNS in the discovery stage using HLA-imputation data.

HLA alleles[a]	Allele frequency						
	Cases (2n=394)		Controls (2n=822)		Chi-square test		
	No	%	No	%	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
HLA-DRB1							
*DRB1*01:01*	15	3.8	57	6.9	0.53 (0.30-0.95)	3.06E-02	5.20E-01
*DRB1*04:03*	18	4.6	25	3.0	1.53 (0.82-2.83)	NS	-
*DRB1*04:05*	56	14.2	121	14.7	0.96 (0.68-1.35)	NS	-
*DRB1*04:06*	13	3.3	27	3.3	1.00 (0.51-1.97)	NS	-
*DRB1*08:02*	40	10.2	32	3.9	2.79 (1.72-4.51)	1.50E-05	2.56E-04
*DRB1*08:03*	27	6.9	63	7.7	0.89 (0.56-1.41)	NS	-
*DRB1*09:01*	73	18.5	126	15.3	1.26 (0.91-1.73)	NS	-
*DRB1*11:01*	14	3.6	23	2.8	1.28 (0.65-2.52)	NS	-
*DRB1*12:01*	23	5.8	30	3.6	1.64 (0.94-2.86)	NS	-
*DRB1*12:02*	3	0.8	18	2.2	0.34 (0.10-1.17)	NS	-
*DRB1*13:02*	5	1.3	55	6.7	0.18 (0.07-0.45)	4.40E-05	7.47E-04
*DRB1*14:03*	11	2.8	11	1.3	2.12 (0.91-4.93)	NS	-
*DRB1*14:05*	7	1.8	16	1.9	0.91 (0.37-2.23)	NS	-
*DRB1*14:06*	13	3.3	13	1.6	2.12 (0.97-4.62)	NS	-
*DRB1*14:54*	6	1.5	26	3.2	0.47 (0.19-1.16)	NS	-
*DRB1*15:01*	18	4.6	67	8.2	0.54 (0.32-0.92)	2.19E-02	3.72E-01
*DRB1*15:02*	44	11.2	70	8.5	1.35 (0.91-2.01)	NS	-
HLA-DQB1							
*DQB1*03:01*	62	15.7	99	12.0	1.36 (0.97-1.92)	NS	-
*DQB1*03:02*	68	17.3	75	9.1	2.08 (1.46-2.96)	3.77E-05	4.14E-04
*DQB1*03:03*	79	20.1	133	16.2	1.30 (0.95-1.77)	NS	-
*DQB1*04:01*	53	13.5	121	14.7	0.90 (0.64-1.27)	NS	-
*DQB1*04:02*	8	2.0	26	3.2	0.63 (0.28-1.41)	NS	-
*DQB1*05:01*	16	4.1	63	7.7	0.51 (0.29-0.89)	1.70E-02	1.87E-01
*DQB1*05:02*	6	1.5	17	2.1	0.73 (0.29-1.87)	NS	-
*DQB1*05:03*	11	2.8	29	3.5	0.79 (0.39-1.59)	NS	-
*DQB1*06:01*	71	18.0	133	16.2	1.14 (0.83-1.56)	NS	-
*DQB1*06:02*	14	3.6	65	7.9	0.43 (0.24-0.77)	3.94E-03	4.33E-02
*DQB1*06:04*	2	0.5	53	6.4	0.07 (0.02-0.31)	3.09E-06	3.40E-05
HLA-DPB1							
*DPB1*02:01*	102	25.9	210	25.5	1.02 (0.77-1.34)	NS	-
*DPB1*02:02*	10	2.5	35	4.3	0.59 (0.29-1.19)	NS	-
*DPB1*03:01*	8	2.0	36	4.4	0.45 (0.21-0.98)	4.01E-02	4.01E-01
*DPB1*04:01*	8	2.0	43	5.2	0.38 (0.17-0.81)	9.17E-03	9.17E-02
*DPB1*04:02*	30	7.6	83	10.1	0.73 (0.47-1.13)	NS	-
*DPB1*05:01*	188	47.7	316	38.4	1.46 (1.15-1.86)	2.13E-03	2.13E-02
*DPB1*06:01*	2	0.5	5	0.6	0.83 (0.16-4.32)	NS	-
*DPB1*09:01*	40	10.2	65	7.9	1.32 (0.87-1.99)	NS	-
*DPB1*13:01*	4	1.0	12	1.5	0.69 (0.22-2.16)	NS	-
*DPB1*14:01*	2	0.5	10	1.2	0.41 (0.09-1.90)	NS	-

[a]Alleles: *HLA* alleles with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for allele frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for the multiplicity of testing by the number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 6. Association analysis of *HLA-A-C-B* haplotypes with childhood SSNS in the discovery stage using HLA-imputation data.

HLA-A-C-B haplotypes[a]	Haplotype frequency						
	Cases (2n=394)		Controls (2n=822)		Chi-square test		
	No	%	No	%	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*A*02:01-C*01:02-B*54:01*	4	1.0	7	0.9	1.19 (0.35-4.10)	NS	-
*A*02:01-C*03:03-B*15:01*	3	0.8	8	1.0	0.78 (0.21-2.96)	NS	-
*A*02:01-C*03:04-B*40:01*	2	0.5	5	0.6	0.83 (0.16-4.32)	NS	-
*A*02:06-C*03:03-B*35:01*	4	1.0	11	1.3	0.76 (0.24-2.39)	NS	-
*A*02:06-C*07:02-B*39:01*	5	1.3	14	1.7	0.74 (0.27-2.07)	NS	-
*A*02:06-C*08:01-B*40:06*	16	4.1	9	1.1	3.82 (1.67-8.73)	6.47E-04	1.94E-02
*A*02:06-C*14:02-B*51:01*	2	0.5	7	0.9	0.59 (0.12-2.87)	NS	-
*A*02:07-C*01:02-B*46:01*	11	2.8	19	2.3	1.21 (0.57-2.58)	NS	-
*A*11:01-C*01:02-B*54:01*	2	0.5	17	2.1	0.24 (0.06-1.05)	4.00E-02	1.20E+00
*A*11:01-C*03:03-B*35:01*	2	0.5	5	0.6	0.83 (0.16-4.32)	NS	-
*A*11:01-C*04:01-B*15:01*	11	2.8	19	2.3	1.21 (0.57-2.58)	NS	-
*A*11:01-C*07:02-B*67:01*	3	0.8	6	0.7	1.04 (0.26-4.19)	NS	-
*A*24:02-C*01:02-B*54:01*	8	2.0	32	3.9	0.51 (0.23-1.12)	NS	-
*A*24:02-C*01:02-B*55:02*	3	0.8	7	0.9	0.89 (0.23-3.47)	NS	-
*A*24:02-C*01:02-B*59:01*	5	1.3	15	1.8	0.69 (0.25-1.92)	NS	-
*A*24:02-C*03:03-B*15:01*	7	1.8	5	0.6	2.96 (0.93-9.37)	NS	-
*A*24:02-C*03:03-B*35:01*	10	2.5	14	1.7	1.50 (0.66-3.41)	NS	-
*A*24:02-C*03:04-B*40:01*	3	0.8	11	1.3	0.57 (0.16-2.04)	NS	-
*A*24:02-C*03:04-B*40:02*	9	2.3	19	2.3	0.99 (0.44-2.20)	NS	-
*A*24:02-C*07:02-B*07:02*	10	2.5	45	5.5	0.45 (0.22-0.90)	2.11E-02	6.33E-01
*A*24:02-C*08:01-B*40:06*	4	1.0	6	0.7	1.39 (0.39-4.97)	NS	-
*A*24:02-C*12:02-B*52:01*	39	9.9	77	9.4	1.06 (0.71-1.59)	NS	-
*A*24:02-C*14:02-B*51:01*	8	2.0	14	1.7	1.20 (0.50-2.88)	NS	-
*A*26:01-C*03:03-B*15:01*	7	1.8	5	0.6	2.96 (0.93-9.37)	NS	-
*A*26:01-C*03:03-B*35:01*	5	1.3	11	1.3	0.95 (0.33-2.75)	NS	-
*A*26:01-C*03:04-B*40:02*	8	2.0	15	1.8	1.12 (0.47-2.65)	NS	-
*A*26:01-C*08:01-B*40:06*	4	1.0	6	0.7	1.39 (0.39-4.97)	NS	-
*A*31:01-C*03:04-B*40:02*	8	2.0	5	0.6	3.39 (1.10-10.42)	3.45E-02	1.04E+00
*A*31:01-C*14:02-B*51:01*	19	4.8	16	1.9	2.55 (1.30-5.02)	5.00E-03	1.50E-01
*A*33:03-C*14:03-B*44:03*	4	1.0	54	6.6	0.15 (0.05-0.41)	2.11E-05	6.33E-04

[a]Haplotypes: *HLA-A-C-B* haplotypes with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for *HLA* haplotype frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the

number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 7. Association analysis of *HLA-DRB1-DQB1* haplotypes with childhood SSNS in the discovery stage using HLA-imputation data.

HLA-DRB1-DQB1 haplotypes[a]	Haplotype frequency						
	Cases (2n=394)		Controls (2n=822)		Chi-square test		
	No	%	No	%	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*DRB1*01:01-DQB1*05:01*	15	3.8	57	6.9	0.53 (0.30-0.95)	3.06E-02	6.12E-01
*DRB1*04:03-DQB1*03:02*	18	4.6	24	2.9	1.59 (0.85-2.97)	NS	-
*DRB1*04:05-DQB1*04:01*	53	13.5	120	14.6	0.91 (0.64-1.29)	NS	-
*DRB1*04:06-DQB1*03:02*	13	3.3	27	3.3	1.00 (0.51-1.97)	NS	-
*DRB1*08:02-DQB1*03:02*	33	8.4	17	2.1	4.33 (2.38-7.87)	2.17E-07	4.34E-06
*DRB1*08:02-DQB1*04:02*	7	1.8	15	1.8	0.97 (0.39-2.41)	NS	-
*DRB1*08:03-DQB1*06:01*	27	6.9	63	7.7	0.89 (0.56-1.41)	NS	-
*DRB1*09:01-DQB1*03:03*	72	18.3	123	15.0	1.27 (0.92-1.75)	NS	-
*DRB1*11:01-DQB1*03:01*	14	3.6	22	2.7	1.34 (0.68-2.65)	NS	-
*DRB1*12:01-DQB1*03:01*	16	4.1	22	2.7	1.54 (0.80-2.96)	NS	-
*DRB1*12:01-DQB1*03:03*	6	1.5	8	1.0	1.57 (0.54-4.57)	NS	-
*DRB1*12:02-DQB1*03:01*	3	0.8	18	2.2	0.34 (0.10-1.17)	NS	-
*DRB1*13:02-DQB1*06:04*	2	0.5	53	6.4	0.07 (0.02-0.31)	3.09E-06	6.17E-05
*DRB1*14:03-DQB1*03:01*	11	2.8	11	1.3	2.12 (0.91-4.93)	NS	-
*DRB1*14:05-DQB1*05:03*	7	1.8	15	1.8	0.97 (0.39-2.41)	NS	-
*DRB1*14:06-DQB1*03:01*	13	3.3	13	1.6	2.12 (0.97-4.62)	NS	-
*DRB1*14:54-DQB1*05:02*	2	0.5	13	1.6	0.32 (0.07-1.41)	NS	-
*DRB1*14:54-DQB1*05:03*	4	1.0	13	1.6	0.64 (0.21-1.97)	NS	-
*DRB1*15:01-DQB1*06:02*	14	3.6	65	7.9	0.43 (0.24-0.77)	3.94E-03	7.87E-02
*DRB1*15:02-DQB1*06:01*	44	11.2	70	8.5	1.35 (0.91-2.01)	NS	-

[a]Haplotypes: *HLA-DRB1-DQB1* haplotypes with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for *HLA* haplotype frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 8. Association analysis of *HLA-DRB1-DQB1-DPB1* haplotypes with childhood SSNS in the discovery stage using HLA-imputation data.

HLA-DRB1-DQB1-DPB1 haplotypes[a]	Haplotype frequency						
	Cases (2n=394)		Controls (2n=822)		Chi-square test		
	No	%	No	%	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*DRB1*01:01-DQB1*05:01-DPB1*04:02*	11	2.8	49	6.0	0.45 (0.23-0.88)	1.69E-02	4.40E-01
*DRB1*04:03-DQB1*03:02-DPB1*02:01*	9	2.3	10	1.2	1.90 (0.77-4.71)	NS	-
*DRB1*04:03-DQB1*03:02-DPB1*05:01*	9	2.3	9	1.1	2.11 (0.83-5.36)	NS	-
*DRB1*04:05-DQB1*04:01-DPB1*02:01*	10	2.5	12	1.5	1.76 (0.75-4.10)	NS	-
*DRB1*04:05-DQB1*04:01-DPB1*05:01*	38	9.6	69	8.4	1.16 (0.77-1.76)	NS	-
*DRB1*04:06-DQB1*03:02-DPB1*02:01*	4	1.0	19	2.3	0.43 (0.15-1.28)	NS	-
*DRB1*08:02-DQB1*03:02-DPB1*05:01*	20	5.1	15	1.8	2.88 (1.46-5.68)	1.51E-03	3.91E-02
*DRB1*08:02-DQB1*04:02-DPB1*05:01*	4	1.0	7	0.9	1.19 (0.35-4.10)	NS	-
*DRB1*08:03-DQB1*06:01-DPB1*02:01*	6	1.5	16	1.9	0.78 (0.30-2.01)	NS	-
*DRB1*08:03-DQB1*06:01-DPB1*02:02*	3	0.8	16	1.9	0.39 (0.11-1.33)	NS	-
*DRB1*08:03-DQB1*06:01-DPB1*05:01*	16	4.1	22	2.7	1.54 (0.80-2.96)	NS	-
*DRB1*09:01-DQB1*03:03-DPB1*02:01*	40	10.2	32	3.9	2.79 (1.72-4.51)	1.50E-05	3.91E-04
*DRB1*09:01-DQB1*03:03-DPB1*05:01*	24	6.1	77	9.4	0.63 (0.39-1.01)	NS	-
*DRB1*11:01-DQB1*03:01-DPB1*02:01*	2	0.5	9	1.1	0.46 (0.10-2.14)	NS	-
*DRB1*11:01-DQB1*03:01-DPB1*05:01*	7	1.8	11	1.3	1.33 (0.51-3.47)	NS	-
*DRB1*12:01-DQB1*03:01-DPB1*05:01*	9	2.3	10	1.2	1.90 (0.77-4.71)	NS	-
*DRB1*12:01-DQB1*03:03-DPB1*05:01*	4	1.0	7	0.9	1.19 (0.35-4.10)	NS	-
*DRB1*12:02-DQB1*03:01-DPB1*05:01*	2	0.5	10	1.2	0.41 (0.09-1.90)	NS	-
*DRB1*13:02-DQB1*06:04-DPB1*04:01*	2	0.5	35	4.3	0.11 (0.03-0.48)	3.66E-04	9.52E-03
*DRB1*14:05-DQB1*05:03-DPB1*05:01*	4	1.0	11	1.3	0.76 (0.24-2.39)	NS	-
*DRB1*14:54-DQB1*05:03-DPB1*05:01*	4	1.0	7	0.9	1.19 (0.35-4.10)	NS	-
*DRB1*15:01-DQB1*06:02-DPB1*02:01*	3	0.8	39	4.7	0.15 (0.05-0.50)	3.71E-04	9.65E-03
*DRB1*15:01-DQB1*06:02-DPB1*04:02*	3	0.8	5	0.6	1.25 (0.30-5.27)	NS	-
*DRB1*15:01-DQB1*06:02-DPB1*05:01*	4	1.0	13	1.6	0.64 (0.21-1.97)	NS	-
*DRB1*15:02-DQB1*06:01-DPB1*05:01*	9	2.3	10	1.2	1.90 (0.77-4.71)	NS	-
*DRB1*15:02-DQB1*06:01-DPB1*09:01*	34	8.6	48	5.8	1.52 (0.96-2.40)	NS	-

[a]Haplotypes: *HLA-DRB1-DQB1-DPB1* haplotypes with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for *HLA* haplotype frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 9. Association analysis of *HLA-A-C-B-DRB1-DQB1* haplotypes with childhood SSNS in the discovery stage using HLA-imputation data.

HLA-A-C-B-DRB1-DQB1 haplotypes[a]	Haplotype frequency						
	Cases (2n=394)		Controls (2n=822)		Chi-square test		
	No	%	No	%	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*A*02:06-C*08:01-B*40:06-DRB1*09:01-DQB1*03:03*	12	3.0	5	0.6	5.13 (1.80-14.67)	7.04E-04	6.34E-03
*A*02:07-C*01:02-B*46:01-DRB1*08:03-DQB1*06:01*	9	2.3	16	1.9	1.18 (0.52-2.69)	NS	-
*A*11:01-C*04:01-B*15:01-DRB1*04:06-DQB1*03:02*	9	2.3	18	2.2	1.04 (0.46-2.35)	NS	-
*A*24:02-C*01:02-B*54:01-DRB1*04:05-DQB1*04:01*	5	1.3	24	2.9	0.43 (0.16-1.13)	NS	-
*A*24:02-C*01:02-B*59:01-DRB1*04:05-DQB1*04:01*	5	1.3	13	1.6	0.80 (0.28-2.26)	NS	-
*A*24:02-C*07:02-B*07:02-DRB1*01:01-DQB1*05:01*	9	2.3	39	4.7	0.47 (0.23-0.98)	3.92E-02	3.53E-01
*A*24:02-C*08:01-B*40:06-DRB1*09:01-DQB1*03:03*	2	0.5	5	0.6	0.83 (0.16-4.32)	NS	-
*A*24:02-C*12:02-B*52:01-DRB1*15:02-DQB1*06:01*	38	9.6	62	7.5	1.31 (0.86-2.00)	NS	-
*A*26:01-C*08:01-B*40:06-DRB1*09:01-DQB1*03:03*	2	0.5	6	0.7	0.69 (0.14-3.45)	NS	-

[a]Haplotypes: *HLA-A-C-B-DRB1-DQB1* haplotypes with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for *HLA* haplotype frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 10. Replication and combined analysis of *HLA-DRB1* alleles with childhood SSNS.

HLA-DRB1 alleles[a]	Replication stage					Combined analysis				
	Cases (2n=426)	Controls (2n=1420)	Chi-square test			Cases (2n=874)	Controls (2n=2238)	Chi-square test		
	No (%)	No (%)	OR (95% CI)[b]	*P*-value	*P*-corrected[c]	No (%)	No (%)	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*DRB1*01:01*	11 (2.6%)	86 (6.1%)	0.41 (0.22-0.78)	4.82E-03	9.16E-02	26 (3.0%)	143 (6.4%)	0.45 (0.29-0.69)	1.58E-04	3.17E-03
*DRB1*04:01*	5 (1.2%)	11 (0.8%)	1.52 (0.53-4.40)	NS	-	6 (0.7%)	21 (0.9%)	0.73 (0.29-1.81)	NS	-
*DRB1*04:03*	10 (2.3%)	39 (2.7%)	0.85 (0.42-1.72)	NS	-	28 (3.2%)	63 (2.8%)	1.14 (0.73-1.80)	NS	-
*DRB1*04:05*	71 (16.7%)	158 (11.1%)	1.60 (1.18-2.16)	2.35E-03	4.46E-02	128 (14.6%)	279 (12.5%)	1.20 (0.96-1.51)	NS	-
*DRB1*04:06*	4 (0.9%)	56 (3.9%)	0.23 (0.08-0.64)	2.16E-03	4.10E-02	20 (2.3%)	84 (3.8%)	0.60 (0.37-0.98)	4.10E-02	8.20E-01
*DRB1*04:10*	4 (0.9%)	19 (1.3%)	0.70 (0.24-2.07)	NS	-	12 (1.4%)	31 (1.4%)	0.99 (0.51-1.94)	NS	-
*DRB1*08:02*	44 (10.3%)	62 (4.4%)	2.52 (1.69-3.77)	3.49E-06	6.64E-05	90 (10.3%)	94 (4.2%)	2.62 (1.94-3.54)	9.11E-11	1.82E-09
*DRB1*08:03*	35 (8.2%)	110 (7.7%)	1.07 (0.72-1.59)	NS	-	68 (7.8%)	173 (7.7%)	1.01 (0.75-1.35)	NS	-
*DRB1*09:01*	83 (19.5%)	196 (13.8%)	1.51 (1.14-2.01)	4.09E-03	7.77E-02	162 (18.5%)	319 (14.3%)	1.37 (1.11-1.68)	2.98E-03	5.97E-02
*DRB1*11:01*	11 (2.6%)	44 (3.1%)	0.83 (0.42-1.62)	NS	-	27 (3.1%)	67 (3.0%)	1.03 (0.66-1.63)	NS	-
*DRB1*12:01*	23 (5.4%)	43 (3.0%)	1.83 (1.09-3.07)	2.08E-02	3.95E-01	51 (5.8%)	73 (3.3%)	1.84 (1.27-2.65)	9.72E-04	1.94E-02
*DRB1*12:02*	5 (1.2%)	19 (1.3%)	0.88 (0.33-2.36)	NS	-	8 (0.9%)	37 (1.7%)	0.55 (0.25-1.18)	NS	-
*DRB1*13:02*	7 (1.6%)	125 (8.8%)	0.17 (0.08-0.37)	4.91E-07	9.32E-06	12 (1.4%)	180 (8.0%)	0.16 (0.09-0.29)	3.65E-12	7.31E-11
*DRB1*14:03*	11 (2.6%)	22 (1.5%)	1.68 (0.81-3.50)	NS	-	22 (2.5%)	33 (1.5%)	1.73 (1.00-2.98)	4.73E-02	9.45E-01
*DRB1*14:05*	7 (1.6%)	32 (2.3%)	0.72 (0.32-1.65)	NS	-	18 (2.1%)	47 (2.1%)	0.98 (0.57-1.70)	NS	-
*DRB1*14:06*	7 (1.6%)	19 (1.3%)	1.23 (0.51-2.95)	NS	-	22 (2.5%)	32 (1.4%)	1.78 (1.03-3.08)	3.68E-02	7.37E-01
*DRB1*14:54*	2 (0.4%)	26 (1.8%)	/	/	/	9 (1.0%)	52 (2.3%)	0.44 (0.21-0.89)	1.93E-02	3.86E-01
*DRB1*15:01*	19 (4.5%)	113 (8.0%)	0.54 (0.33-0.89)	1.40E-02	2.66E-01	40 (4.6%)	180 (8.0%)	0.55 (0.39-0.78)	6.98E-04	1.40E-02
*DRB1*15:02*	52 (12.2%)	178 (12.5%)	0.97 (0.70-1.35)	NS	-	97 (11.1%)	248 (11.1%)	1.00 (0.78-1.28)	NS	-
*DRB1*16:02*	5 (1.2%)	12 (0.8%)	1.39 (0.49-3.98)	NS	-	9 (1.0%)	14 (0.6%)	1.65 (0.71-3.83)	NS	-

[a]Alleles: *HLA* alleles with frequencies < 0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for allele frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
/:The *HLA-DRB1* allele was excluded from association analysis because of low frequency (<0.5%) in the replication stage.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant (*P*>=0.05); *P*-corrected was omitted.

Supplementary Table 11. Replication and combined analysis of *HLA-DQB1* alleles with childhood SSNS.

HLA-DQB1 alleles[a]	Replication stage					Combined analysis				
	Cases (2n=426)	Controls (2n=1420)	chi-square test			Cases (2n=874)	Controls (2n=2238)	Chi-square test		
	No (%)	No (%)	OR (95% CI)[b]	*P*-value	*P*-corrected[c]	No (%)	No (%)	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*DQB1*03:01*	69 (16.2%)	151 (10.6%)	1.62 (1.19-2.21)	1.88E-03	2.07E-02	140 (16.0%)	250 (11.2%)	1.52 (1.21-1.90)	2.42E-04	2.66E-03
*DQB1*03:02*	48 (11.3%)	136 (9.6%)	1.20 (0.85-1.70)	NS	-	128 (14.6%)	213 (9.5%)	1.63 (1.29-2.06)	3.86E-05	4.25E-04
*DQB1*03:03*	82 (19.2%)	211 (14.9%)	1.37 (1.03-1.81)	2.97E-02	3.26E-01	173 (19.8%)	340 (15.2%)	1.38 (1.13-1.69)	1.87E-03	2.06E-02
*DQB1*04:01*	70 (16.4%)	158 (11.1%)	1.57 (1.16-2.13)	3.51E-03	3.86E-02	123 (14.1%)	279 (12.5%)	1.15 (0.92-1.44)	NS	-
*DQB1*04:02*	19 (4.5%)	50 (3.5%)	1.28 (0.75-2.19)	NS	-	36 (4.1%)	76 (3.4%)	1.22 (0.82-1.83)	NS	-
*DQB1*05:01*	12 (2.8%)	91 (6.4%)	0.42 (0.23-0.78)	4.62E-03	5.08E-02	28 (3.2%)	154 (6.9%)	0.45 (0.30-0.68)	8.53E-05	9.38E-04
*DQB1*05:02*	6 (1.4%)	32 (2.3%)	0.62 (0.26-1.49)	NS	-	12 (1.4%)	49 (2.2%)	0.62 (0.33-1.17)	NS	-
*DQB1*05:03*	8 (1.9%)	62 (4.4%)	0.42 (0.20-0.88)	1.84E-02	2.02E-01	22 (2.5%)	90 (4.0%)	0.62 (0.38-0.99)	4.29E-02	4.72E-01
*DQB1*06:01*	87 (20.4%)	284 (20.0%)	1.03 (0.78-1.34)	NS	-	163 (18.6%)	417 (18.6%)	1.00 (0.82-1.22)	NS	-
*DQB1*06:02*	14 (3.3%)	108 (7.6%)	0.41 (0.23-0.73)	1.65E-03	1.81E-02	29 (3.3%)	173 (7.7%)	0.41 (0.27-0.61)	7.13E-06	7.84E-05
*DQB1*06:04*	5 (1.2%)	117 (8.2%)	0.13 (0.05-0.33)	2.63E-07	2.89E-06	7 (0.8%)	170 (7.6%)	0.10 (0.05-0.21)	1.90E-13	2.09E-12

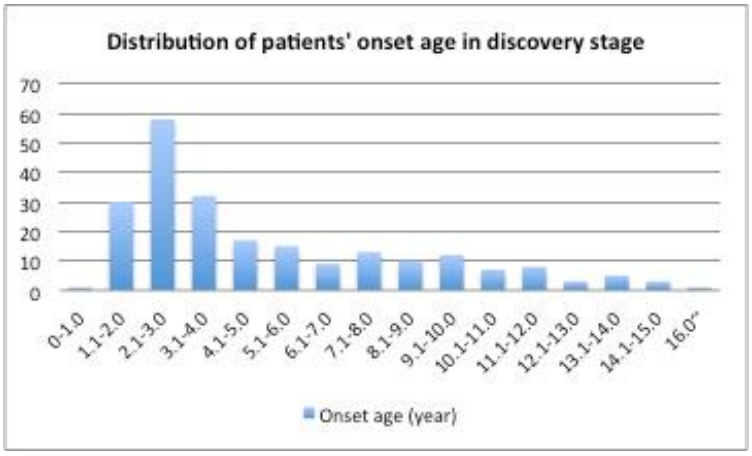
[a]Alleles: *HLA* alleles with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for allele frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Table 12. Replication and combined analysis of *HLA-DRB1-DQB1* haplotypes with childhood SSNS.

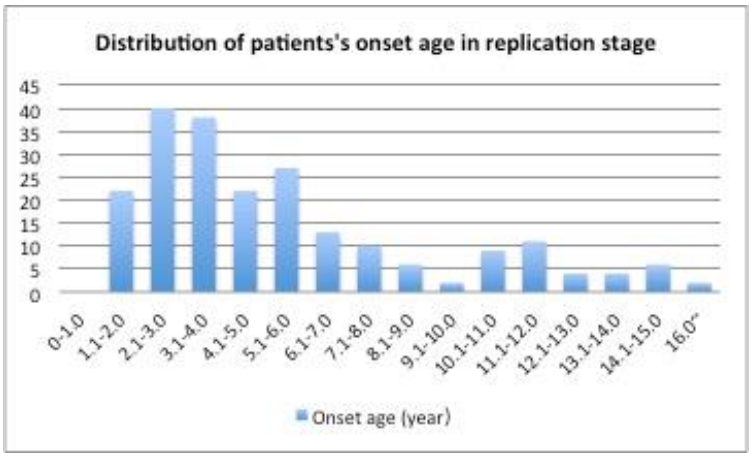
HLA-DRB1-DQB1 haplotypes[a]	Replication stage					Combined analysis				
	Cases (2n=426)	Controls (2n=1420)	Chi-square test			Cases (2n=874)	Controls (2n=2238)	Chi-square test		
	No (%)	No (%)	OR (95% CI)[b]	*P*-value	*P*-corrected[c]	No (%)	No (%)	OR (95% CI)[b]	*P*-value	*P*-corrected[c]
*DRB1*01:01-DQB1*05:01*	11 (2.6%)	85 (6.0%)	0.42 (0.22-0.79)	5.52E-03	1.10E-01	26 (3.0%)	142 (6.3%)	0.45 (0.30-0.69)	1.85E-04	4.07E-03
*DRB1*04:01-DQB1*03:01*	5 (1.2%)	11 (0.8%)	1.52 (0.53-4.40)	NS	-	6 (0.7%)	21 (0.9%)	0.73 (0.29-1.81)	NS	-
*DRB1*04:03-DQB1*03:02*	10 (2.3%)	38 (2.7%)	0.87 (0.43-1.77)	NS	-	28 (3.2%)	61 (2.7%)	1.18 (0.75-1.86)	NS	-
*DRB1*04:05-DQB1*04:01*	70 (16.4%)	155 (10.9%)	1.60 (1.18-2.18)	2.27E-03	4.54E-02	123 (14.1%)	275 (12.3%)	1.17 (0.93-1.47)	NS	-
*DRB1*04:06-DQB1*03:02*	4 (0.9%)	56 (3.9%)	0.23 (0.08-0.64)	2.16E-03	4.32E-02	20 (2.3%)	84 (3.8%)	0.60 (0.37-0.98)	4.10E-02	9.02E-01
*DRB1*04:10-DQB1*04:02*	4 (0.9%)	17 (1.2%)	0.78 (0.26-2.34)	NS	-	12 (1.4%)	28 (1.3%)	1.10 (0.56-2.17)	NS	-
*DRB1*08:02-DQB1*03:02*	28 (6.6%)	31 (2.2%)	3.15 (1.87-5.32)	6.25E-06	1.25E-04	64 (7.3%)	48 (2.1%)	3.60 (2.46-5.29)	3.19E-12	7.01E-11
*DRB1*08:02-DQB1*04:02*	15 (3.5%)	30 (2.1%)	1.69 (0.90-3.17)	NS	-	24 (2.7%)	45 (2.0%)	1.38 (0.83-2.27)	NS	-
*DRB1*08:03-DQB1*06:01*	35 (8.2%)	106 (7.5%)	1.11 (0.74-1.65)	NS	-	66 (7.6%)	169 (7.6%)	1.00 (0.74-1.34)	NS	-
*DRB1*09:01-DQB1*03:03*	80 (18.8%)	193 (13.6%)	1.47 (1.10-1.96)	8.16E-03	1.63E-01	158 (18.1%)	312 (13.9%)	1.36 (1.10-1.68)	3.78E-03	8.31E-02
*DRB1*11:01-DQB1*03:01*	11 (2.6%)	43 (3.0%)	0.85 (0.43-1.66)	NS	-	25 (2.9%)	64 (2.9%)	1.00 (0.63-1.60)	NS	-
*DRB1*12:01-DQB1*03:01*	20 (4.7%)	26 (1.8%)	2.64 (1.46-4.78)	8.82E-04	1.76E-02	38 (4.3%)	48 (2.1%)	2.07 (1.35-3.20)	7.53E-04	1.66E-02
*DRB1*12:01-DQB1*03:03*	2 (0.4%)	17 (1.1%)	/	/	/	8 (0.9%)	23 (1.0%)	0.89 (0.40-2.00)	NS	-
*DRB1*12:02-DQB1*03:01*	5 (1.2%)	19 (1.3%)	0.88 (0.33-2.36)	NS	-	8 (0.9%)	37 (1.7%)	0.55 (0.25-1.18)	NS	-
*DRB1*13:02-DQB1*06:04*	5 (1.2%)	117 (8.2%)	0.13 (0.05-0.33)	2.63E-07	5.25E-06	7 (0.8%)	170 (7.6%)	0.10 (0.05-0.21)	1.90E-13	4.18E-12
*DRB1*14:03-DQB1*03:01*	11 (2.6%)	22 (1.5%)	1.68 (0.81-3.50)	NS	-	22 (2.5%)	33 (1.5%)	1.73 (1.00-2.98)	4.73E-02	1.04E+00
*DRB1*14:05-DQB1*05:03*	7 (1.6%)	29 (2.0%)	0.80 (0.35-1.84)	NS	-	16 (1.8%)	43 (1.9%)	0.95 (0.53-1.70)	NS	-
*DRB1*14:06-DQB1*03:01*	7 (1.6%)	19 (1.3%)	1.23 (0.51-2.95)	NS	-	22 (2.5%)	32 (1.4%)	1.78 (1.03-3.08)	3.68E-02	8.10E-01
*DRB1*14:54-DQB1*05:03*	1 (0.2%)	17 (1.2%)	/	/	/	6 (0.7%)	30 (1.3%)	0.51 (0.21-1.23)	NS	-
*DRB1*15:01-DQB1*06:02*	14 (3.3%)	107 (7.5%)	0.42 (0.24-0.74)	1.89E-03	3.77E-02	29 (3.3%)	172 (7.7%)	0.41 (0.28-0.62)	8.41E-06	1.85E-04
*DRB1*15:02-DQB1*06:01*	52 (12.2%)	177 (12.5%)	0.98 (0.70-1.36)	NS	-	97 (11.1%)	247 (11.0%)	1.01 (0.78-1.29)	NS	-
*DRB1*16:02-DQB1*05:02*	5 (1.2%)	12 (0.8%)	1.39 (0.49-3.98)	NS	-	9 (1.0%)	14 (0.6%)	1.65 (0.71-3.83)	NS	-

[a]Haplotypes: *HLA-DRB1-DQB1* haplotypes with frequencies <0.5% in cases or controls were omitted.
[b]OR: odds ratio; 95% CI: lower and upper limits of confidence interval at 95%.
[c]*P*-corrected: *P*-values for *HLA* haplotype frequency comparisons between cases and controls using the Pearson's chi-square test or Fisher's exact test and then corrected for multiplicity of testing based on the number of comparisons.
/: The *HLA-DRB1-DQB1* haplotype was excluded from association analysis because of low frequency (<0.5%) in the replication stage.
NS: not significant ($P \geq 0.05$).
-: The *P*-value before multiple correction was not significant ($P \geq 0.05$); *P*-corrected was omitted.

Supplementary Figures



A.

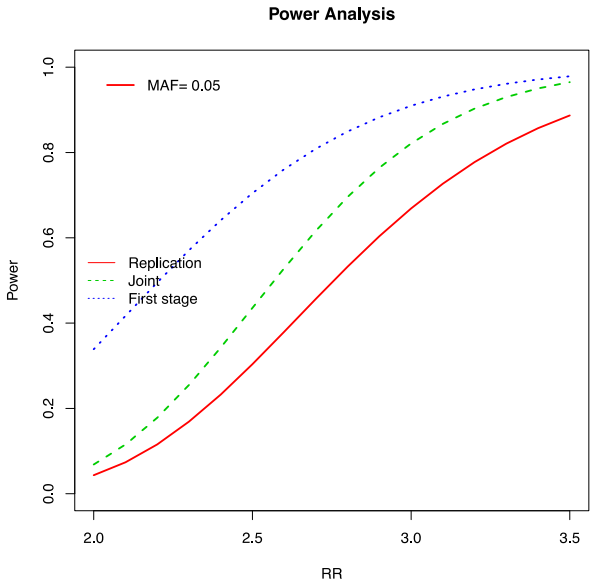


B.

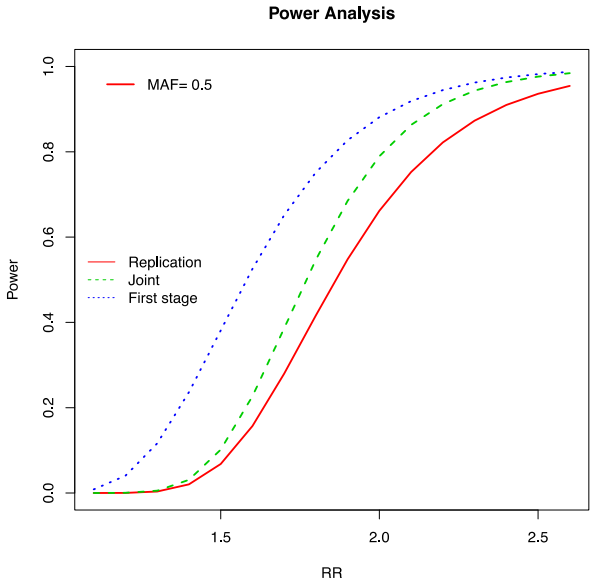
Supplementary Figure 1. Distribution of patients' onset age: No onset-age bias between the discovery case samples and the replication case samples (*P*=0.12).

(A) Distribution of patients' onset age in the discovery stage.

(B) Distribution of patients' onset age in the replication stage.

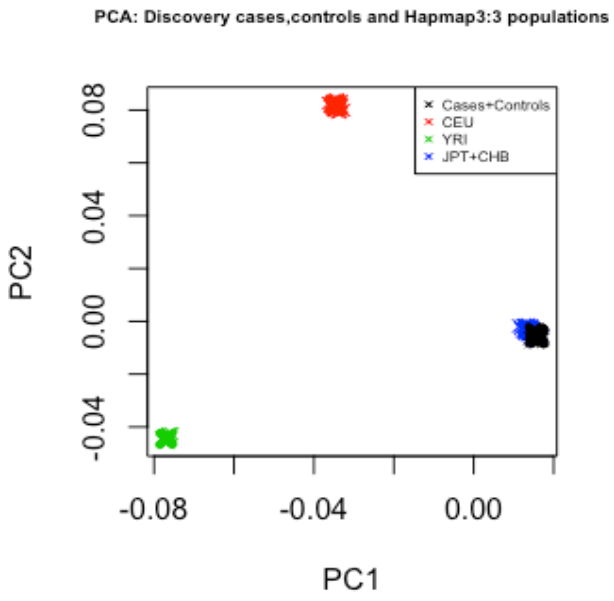


A

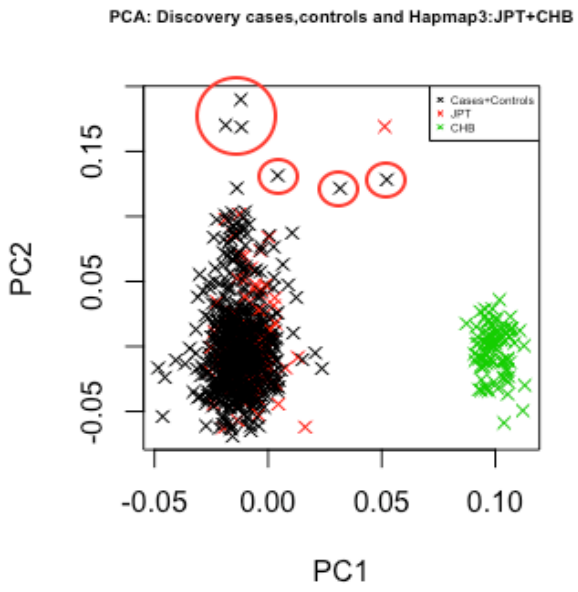


B

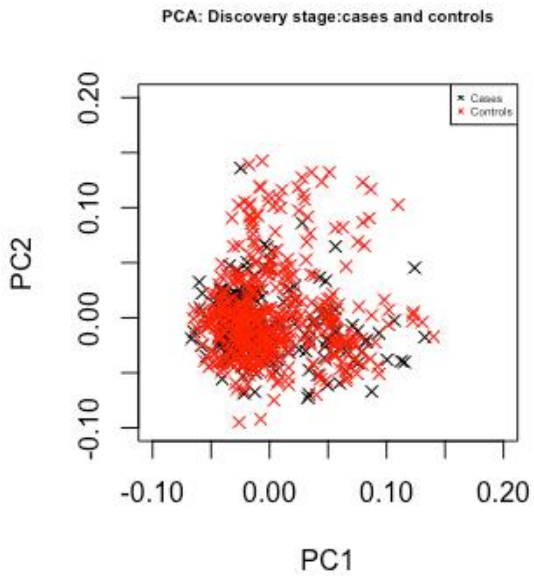
Supplementary Figure 2. The power of the current GWAS. The power of our two-stage GWAS exceeded 80% to detect common alleles (minor allele frequency [MAF] ≥5%) with a genotypic relative risk (RR) >2.95 (**A**), or variants with an allele frequency >50% conferring a RR >2.0 (**B**) at a significant *P*-value threshold of 5 $\times 10^{-8}$ under the additive model.



A



B



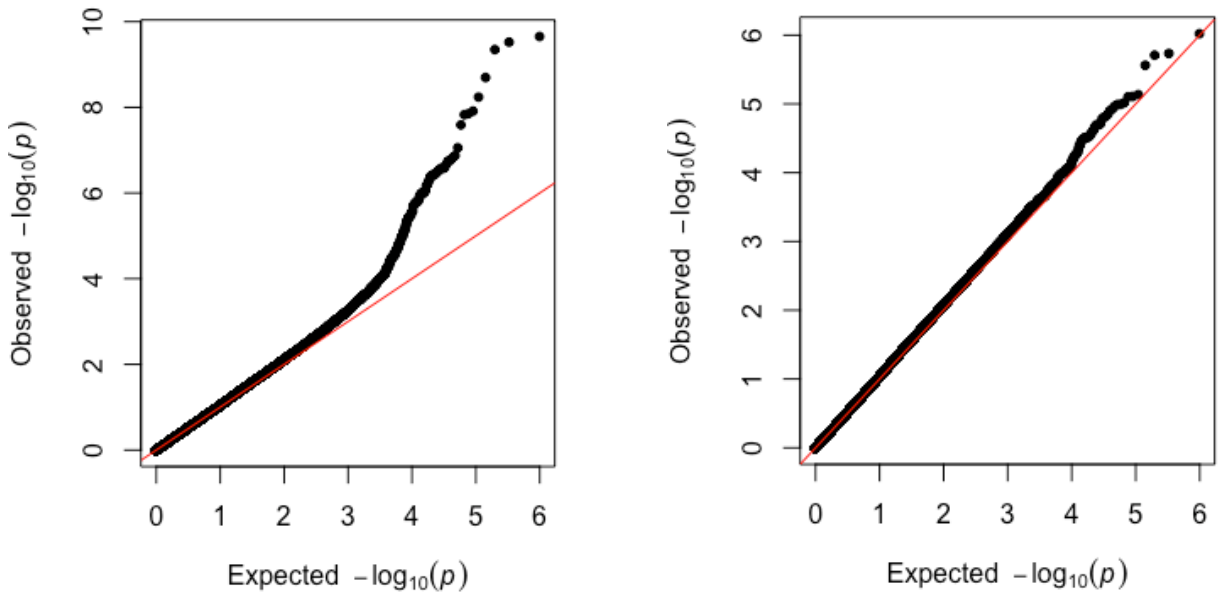
C

Supplementary Figure 3. Principal component analysis (PCA) of 642 samples (224 cases and 418 healthy controls) from the GWAS stage and HapMap Phase III samples (113 Utah residents with ancestry from northern and western Europe [CEU], 113 Yoruba in Ibadan [YRI], 84 Han Chinese in Beijing [CHB], and 86 Japanese in Tokyo [JPT]).

(**A**) All groups, no outliners were detected.

(**B**) Focused on Asian samples (JPT and CHB): 6 controls around the JPT cluster were identified as outliers (highlighted by red circles) and then excluded.

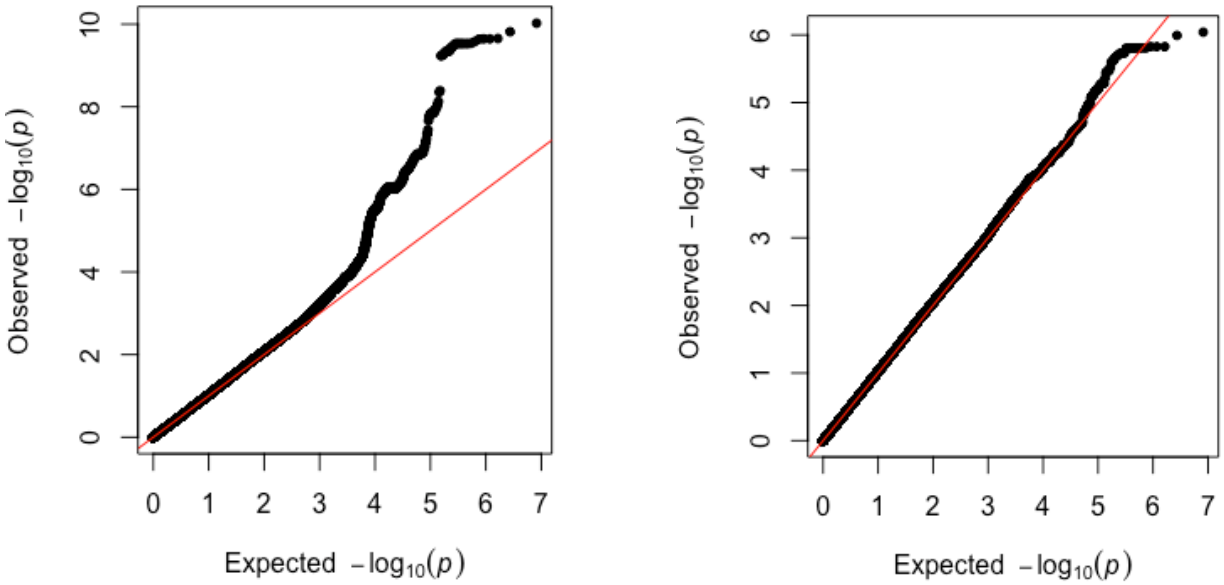
(**C**) A total of 224 cases and 412 controls for association analyses after the removal of outliers based on the PCA results.



A **B**

Supplementary Figure 4. Quantile-quantile plots of P-values for each SNP calculated using the Cochran-Armitage trend test in the initial GWAS (224 cases with childhood SSNS and 412 healthy controls).

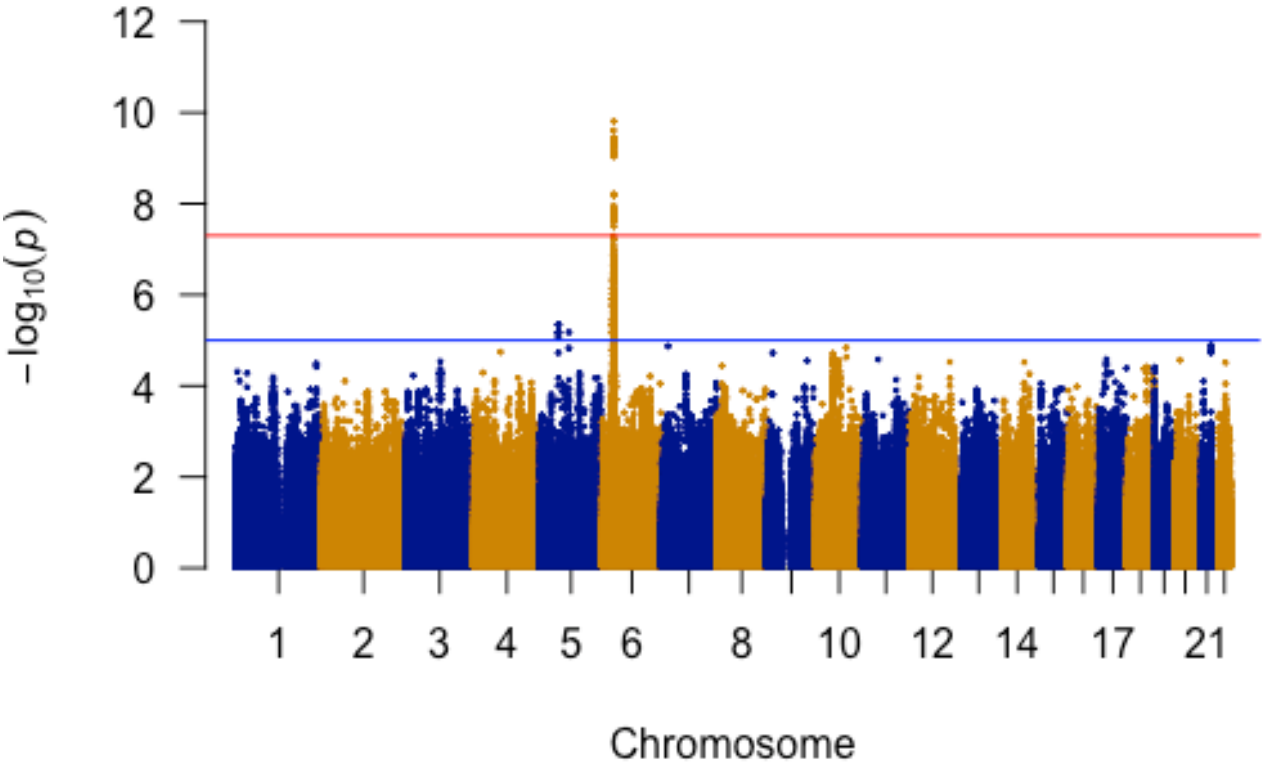
The inflation factor, λ, was estimated as (**A**) 1.045 for all tested SNPs, including those in the *HLA* region, and (**B**) 1.040 when SNPs in the *HLA* region (Hg19: chr6: 29,691,116–33,054,976) were excluded.



A **B**

Supplementary Figure 5. Quantile-quantile plots of *P*-values for each SNP calculated using the Cochran-Armitage trend test after whole-genome imputation (224 cases with childhood SSNS and 412 healthy controls).

The inflation factor, λ, was estimated as (**A**) 1.023 for all tested variations, including those in the *HLA* region, and (**B**) 1.019 when SNPs or INDELs in the *HLA* region (Hg19: chr6: 29,691,116–33,054,976) were excluded.



Supplementary Figure 6. Whole-genome imputation was performed using the 2KJPN panel. The associations were assessed using the Cochran-Armitage trend test; *P*-values were corrected based on genomic control.