Genome-wide assessment of genetic risk loci for childhood acute lymphoblastic leukemia in Japanese patients

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Supplementary Information

Genome-wide assessment of genetic risk loci for childhood acute lymphoblastic leukemia in Japanese

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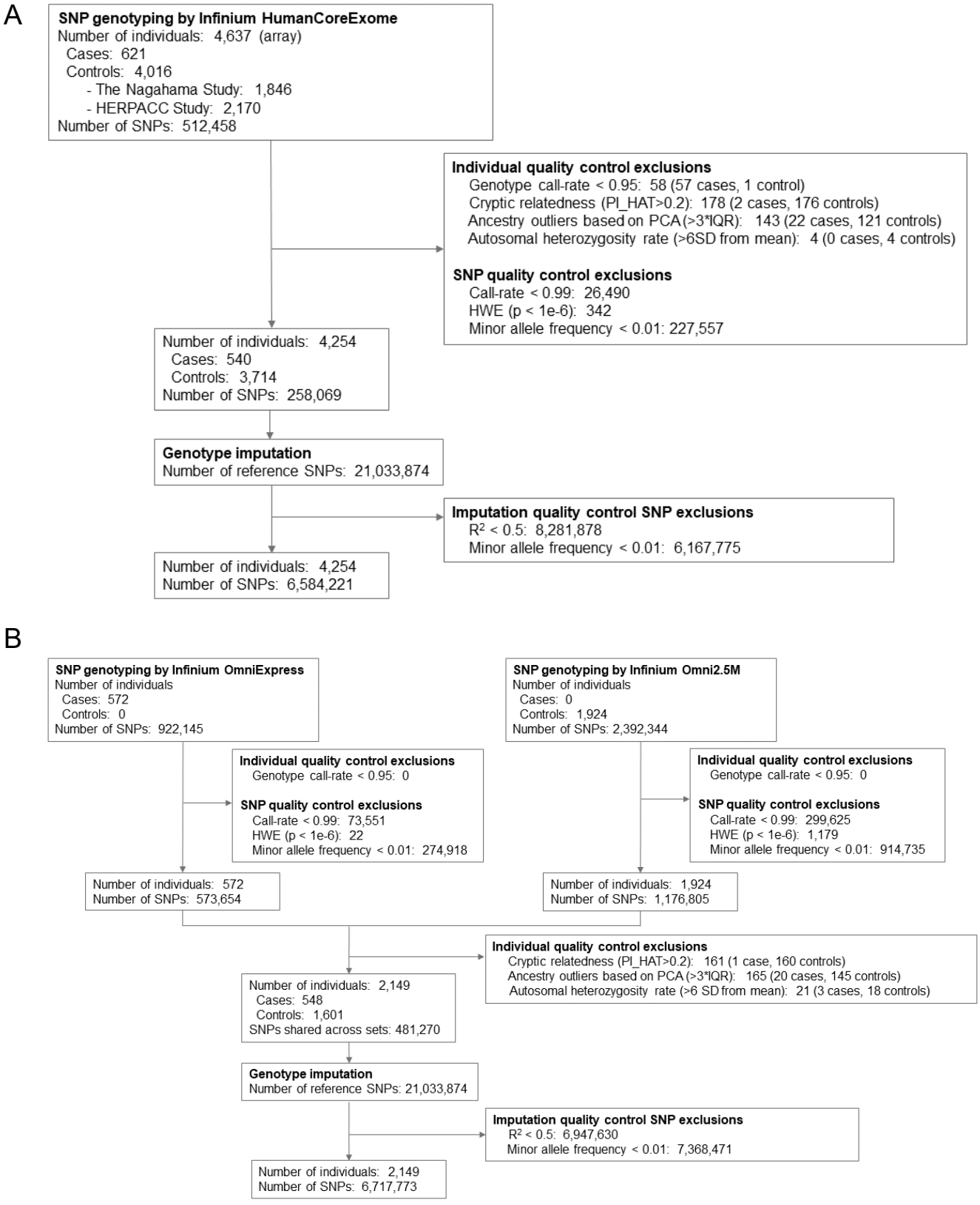
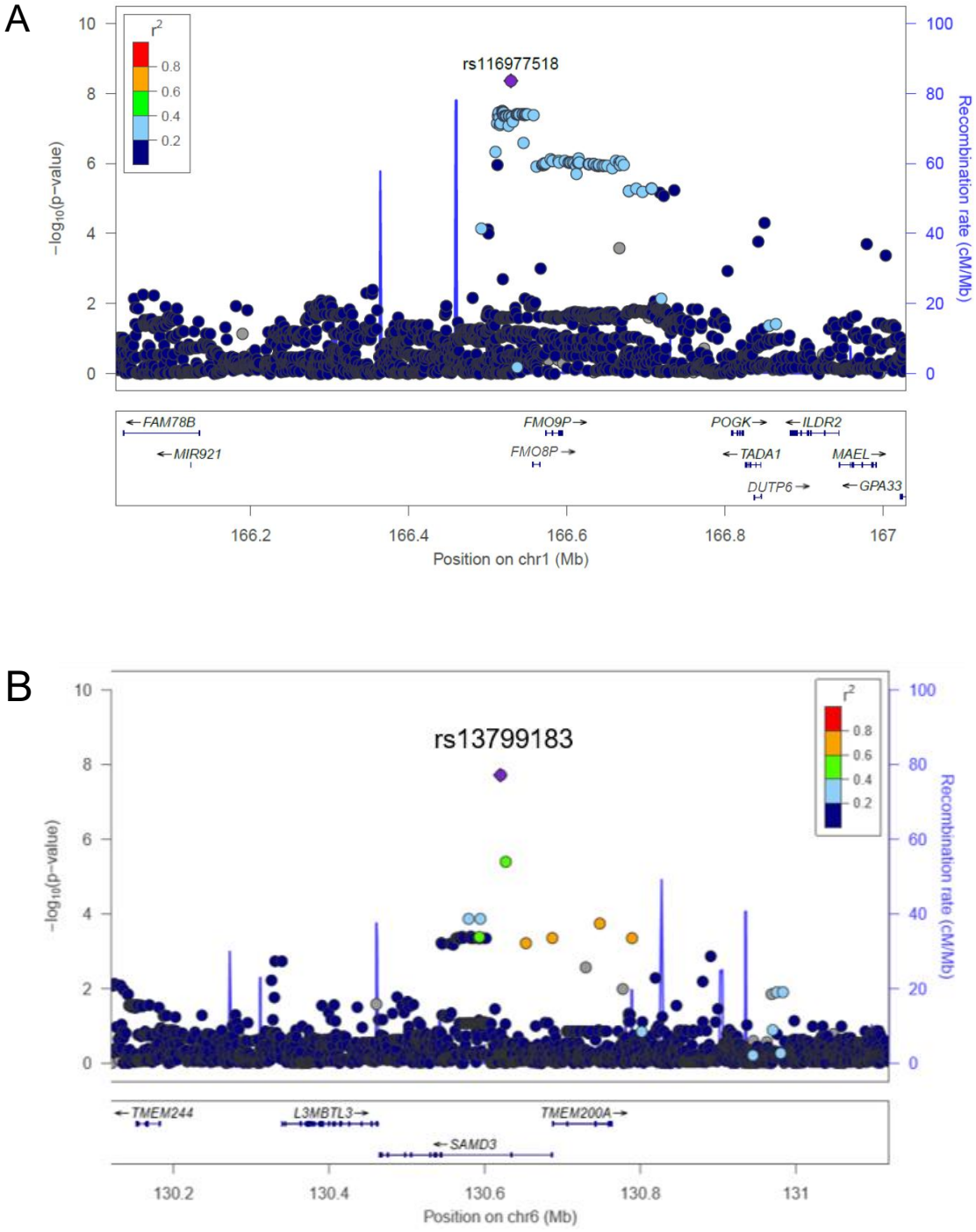


Supplementary Figure 1. Flow of individual and genotype quality control. (A) TCCSG GWAS cases and controls were genotyped using the Illumina HumanCoreExome microarray Infinium assay. (B) JPLSG GWAS cases and controls were genotyped using the Illumina Omni family of microarrays Infinium assay.



Supplementary Figure 2. Results of the putative novel ALL risk loci identified in the TCCSG and JPLSG genome-wide association analyses. (A) Regional plot of the TCCSG GWAS results around the genome-wide significant region identified at chromosome 1q24.1. The leading SNP is represented as a purple diamond and the colors of the surrounding SNPs show the degree of correlation (r^2) to the leading SNP. (B) Regional plot of JPLSG GWAS results around the genome-wide significant region identified in *SAMD3* at chromosome 6q23.1.

Supplementary Table 1. Results of previous GWAS-identified SNPs and targeted examination of the candidate loci in Japanese

				Allele frequency[c]	Previous report		TCCG+JPLSG GWAS (Japanese)	
Study, year	SNP	Chr:position[a]	Allele[b]	CEU/AMR/AFR/JPT	OR (95% CI) [d]	*P*	OR (95% CI) [d]	P_{meta}
ARID5B (r^2: JPT=1.00, EUR=1.00)[e]								
Trevino, 2009[1]	rs10821936	10:63723577	C / T	0.32/0.48/0.20/0.34	1.91 (1.6–2.2)	1.4×10^{-15}	1.83 (1.63–2.04)	2.4×10^{-25}
Current (leading SNP)	rs7896246	10:63724390	A / G	0.32/0.46/0.04/0.34	-	-	1.83 (1.63–2.05)	1.4×10^{-25}
IKZF1 (r^2: JPT<0.01, EUR<0.01)								
Papaemmanuil, 2009[2]	rs4132601	7:50470604	G / T	0.28/0.23/0.18/0.09	1.69 (1.58–1.81)	1.2×10^{-19}	1.38 (1.14–1.67)	1.0×10^{-3}
Current (leading SNP)	rs77563422	7:50454209	G / C	0.00/0.19/0.09/0.16	-	-	1.55 (1.35–1.78)	5.9×10^{-10}
DDC (r^2: JPT=1.00, EUR=0.46)								
Papaemmanuil, 2009[2]	rs7809758	7:50573333	G / A	0.39/0.45/0.34/0.25	1.44 (1.32–1.54)	2.4×10^{-10}	1.27 (1.13–1.44)	1.1×10^{-4}
Current (leading SNP)	rs7808025	7:50576903	A / G	0.26/0.35/0.36/0.24	-	-	1.28 (1.13–1.45)	9.0×10^{-5}
CEBPE (r^2: JPT=0.38, EUR=0.73)								
Papaemmanuil, 2009[2]	rs2239633	14:23589057	G / A	0.55/0.55/0.83/0.47	1.34 (1.22–1.45)	2.9×10^{-7}	1.15 (1.03–1.29)	0.013
Current (leading SNP)	rs2239630	14:23589349	A / G	0.49/0.52/0.94/0.48	-	-	1.19 (1.06–1.33)	2.7×10^{-3}
CDKN2A (1) (r^2: JPT=0.07, EUR=NA)								
Sherborne, 2010[3]	rs3731217	9:21984661	A/ C	0.86/0.91/0.90/0.82	1.41 (1.28–1.56)	3.0×10^{-11}	0.90 (0.78–1.04)	0.16
Current (leading SNP)	rs149570278	9:21993686	A / G	0.00/0.00/0.00/0.01	-	-	1.84 (1.20–2.80)	5.0×10^{-3}
CDKN2A (2) (r^2: JPT=NA, EUR=NA)								
Xu, 2015[4]	rs3731249	9:21970916	T / C	0.03/0.01/0.00/0.00*	2.23 (1.90-2.61)	9.4×10^{-23}	NA	NA
Current (leading SNP)	rs3731235	9:21977450	C / A	1.00/1.00/1.00/0.96	-	-	1.34 (1.01–1.79)	0.045
CDKN2B (r^2: JPT=NA, EUR=NA)								
Hungate, 2016[5]	rs77728904	9:22057530	C / A	0.07/0.04/0.10/0.00*	1.71 (1.42–2.05)	1.0×10^{-8}	NA	NA
Current (leading SNP)	rs144964843	9:22016243	C / T	1.00/1.00/1.00/0.97	-	-	1.44 (1.01–2.05)	0.041
PIP4K2A (r^2: JPT=1.00, EUR=0.96)								
Xu, 2013[6]	rs7088318	10:22852948	A / C	0.53/0.75/0.34/0.61	1.40 (1.28–1.53)	1.1×10^{-11}	1.17 (1.04–1.31)	7.5×10^{-3}
Current (leading SNP)	rs10159730	10:22854947	A/ G	0.53/0.76/0.43/0.62	-	-	1.22 (1.08–1.37)	9.9×10^{-4}
GATA3 (r^2: JPT=0.88, EUR=0.36)								
Perez_Andreu, 2013[7]	rs3824662	10:8104208	A / C	0.13/0.37/0.08/0.31	3.85 (2.71–5.47)	1.1×10^{-8}	1.13 (1.01–1.27)	0.040
Current (leading SNP)	rs374641	10:8103980	C / T	0.36/0.49/0.31/0.34	-	-	1.14 (1.02–1.28)	0.026
WWOX (r^2: JPT=0.55, EUR=0.56)								
Shi, 2016[8]	rs1121404	16:79089869	C / CT	0.60/0.59/0.53/0.38	1.38 (1.25–1.54)	5.3×10^{-10}	1.05 (0.94–1.18)	0.38
Current (leading SNP)	rs9972822	16:79094856	G / C	0.56/0.38/0.12/0.22	-	-	1.12 (0.98–1.27)	0.095
LHPP (r^2: JPT=0.23, EUR=0.23)								
Vijayakrishnan, 2017	rs35837782	10:126293309	G / A	0.66/0.53/0.63/0.61	1.21 (1.15–1.28)	1.4×10^{-11}	1.10 (0.98–1.23)	0.11

Current (leading SNP)	rs71487970	10:126293897	T / G	0.30/0.27/0.05/0.25	-	-	1.15 (1.01–1.30)	0.030
ELK3 (r^2: JPT=0.02, EUR=NA)								
Vijayakrishnan, 2017[9]	rs4762284	12:96612762	T / A	0.31/0.49/0.45/0.56	1.19 (1.12–1.26)	8.4×10^{-9}	1.01 (0.91–1.14)	0.81
Current (leading SNP)	rs143908265	12:96605017	A / G	0.00/0.00/0.00/0.03	-	-	1.42 (1.02–1.96)	0.035
IKZF3 (r^2: JPT=0.03, EUR=0.81)								
Wiemels, 2018[10]	rs2290400	17:38066240	T / C	0.51/0.60/0.51/0.73	1.18 (1.11–1.25)	2.1×10^{-8}	1.17 (1.03–1.33)	0.017
Current (leading SNP)	rs12942330	17:37939839	C / T	0.53/0.65/0.82/0.67	-	-	1.16 (1.03–1.31)	0.014
SP4 (r^2: JPT=0.04, EUR=0.26)								
Wiemels, 2018[10]	rs2390536	7:21485397	A / G	0.39/0.19/0.04/0.04	1.20 (1.13–1.29)	3.6×10^{-8}	0.97 (0.73–1.28)	0.81
Current (leading SNP)	rs9639379	7:21484410	T / G	0.30/0.59/0.37/0.42	-	-	1.15 (1.03–1.28)	0.014
BMI1 (r^2: JPT=0.43, EUR=0.73)								
de Smith, 2018[11]	rs12769953	10:22407656	T / C	0.78/0.73/0.81/0.85	1.28 (1.21-1.35)	6.1×10^{-11}	1.00 (0.85–1.18)	0.983
Current (leading SNP)	rs2986335	10:22377233	A/ G	0.28/0.32/0.74/0.08	-	-	1.24 (0.99–1.55)	0.062
8q24.21 (r^2: JPT=1.00, EUR=0.99)								
Vijayakrishnan, 2018[12]	rs28665337	8:130194104	A / C	0.11/0.08/0.07/0.02	1.34 (1.21–1.47)	3.9×10^{-9}	1.70 (1.16–2.50)	6.6×10^{-3}
Current (leading SNP)	rs5003704	8:130222435	A / G	0.11/0.08/ 0.07/0.02	-	-	1.77 (1.20–2.60)	4.0×10^{-3}
ERG (r^2: JPT=0.01, EUR=0.01)								
Qian, 2019[13]	rs2836371	21:39773528	C / T	0.30/0.35/0.05/0.17	1.64 (1.40-1.93)	1.4×10^{-9}	1.05 (0.90–1.21)	0.511
Current (leading SNP)	rs2410021	21:39815267	T / C	0.95/0.91/0.85/0.86	-	-	1.24 (1.05–1.46)	0.012
9q21.31 (TLE1) (r^2: JPT=NA, EUR=NA)								
Vijayakrishnan, 2019[14]	rs76925697	9:83747371	A / T	0.96/0.97/0.97/0.00	1.52 (1.31-1.76)	2.1×10^{-8}	NA	NA
Current (leading SNP)	rs148407651	9:83753262	G / A	1.00/1.00/1.00/0.99	-	-	1.65 (0.92–2.96)	0.093

Abbreviations: Chr, chromosome; CI, confidence interval; EUR, European ancestry; NA, not available; OR, odds ratio; SNP, single nucleotide polymorphism

[a] Chromosome and genomic positions are based on GRCh37/hg19

[b] Tested allele / other allele.

[c] Tested allele frequencies for CEU (Northern and Western European Ancestry), AMR (Admixed American), and AFR (African) from 1000 Genomes Project data (phase 3); JPT are allele frequencies from the TCCSG control group.

[d] Odds ratio and 95% confidence intervals associated with the tested allele of the leading SNP extracted from the previous genome-wide association study; association results of the tested allele from the current Japanese study are also shown, if available.

[e] Measure of pairwise linkage disequilibrium (r^2) between the SNP previously reported and the leading SNP in the current analysis; estimates are based on 1000 Genomes Project data (phase 3)

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