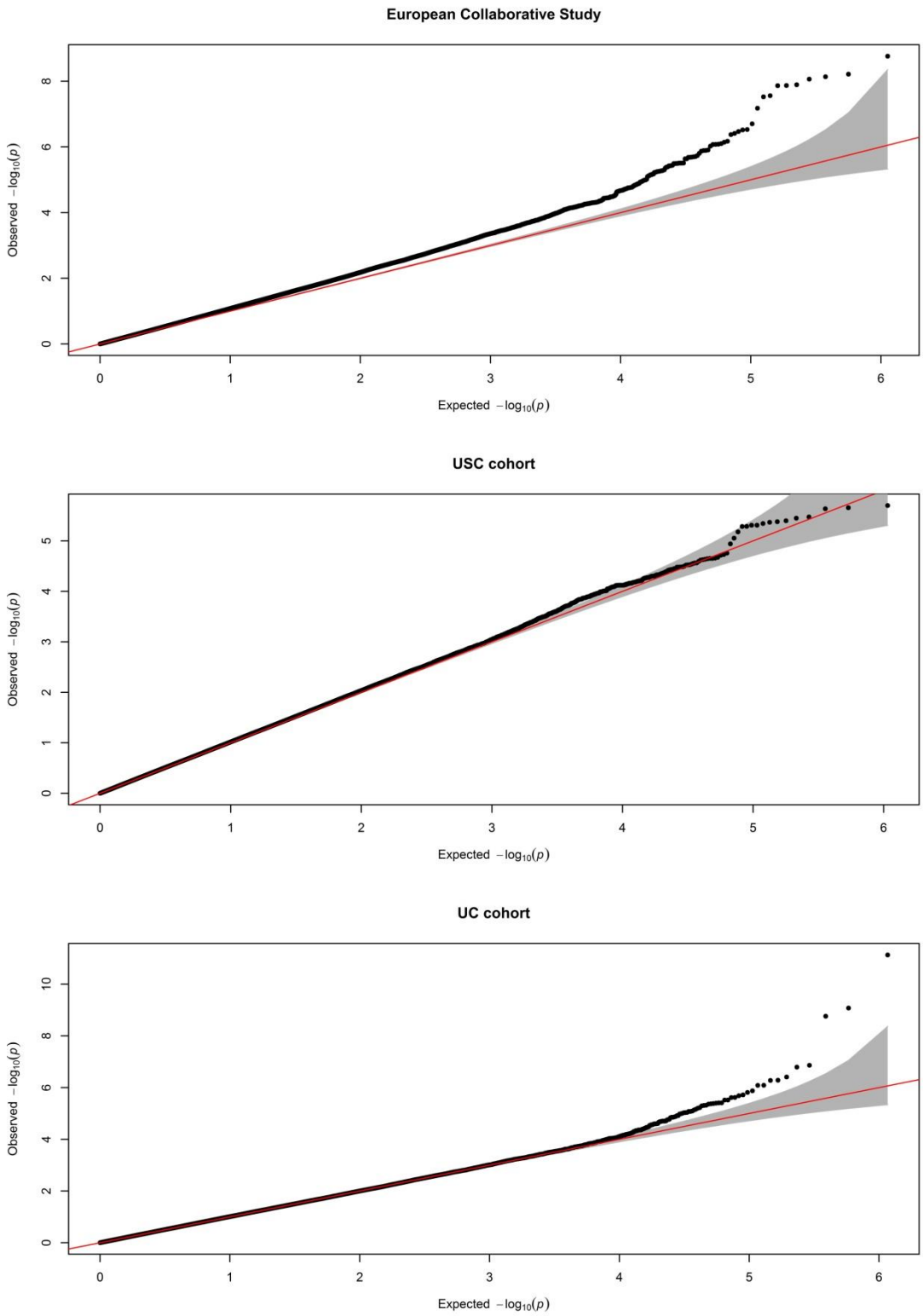
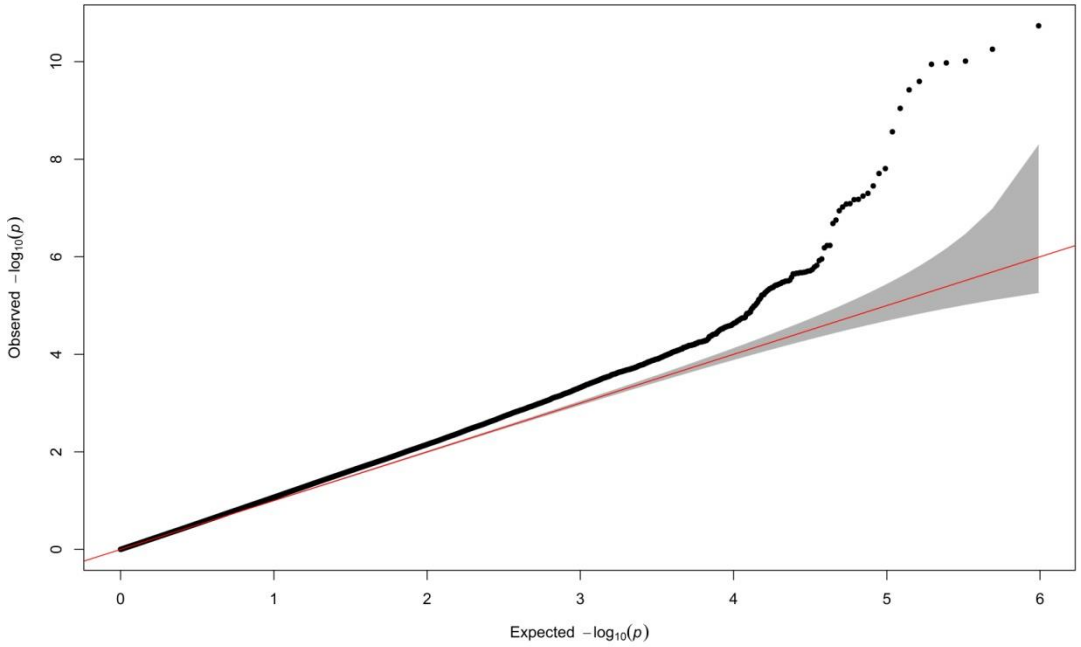


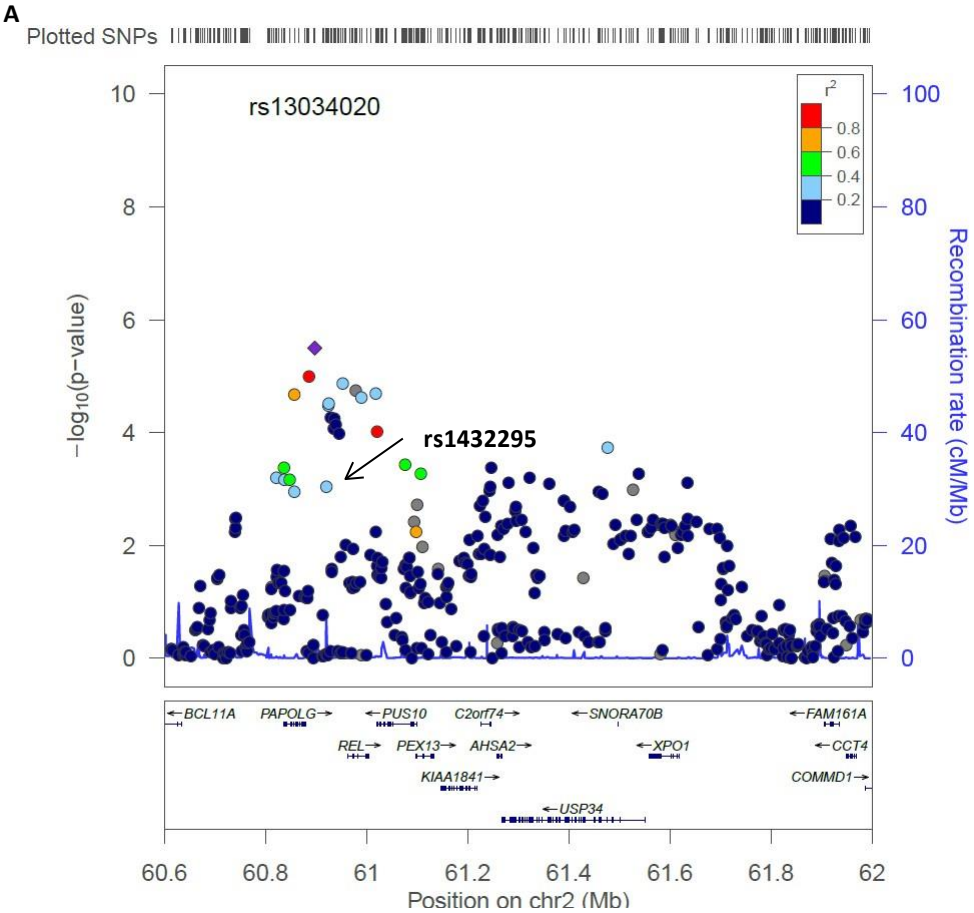
Supplementary Figure 1. Quantile-quantile (Q-Q) plots in $-\log_{10}$ scale for the three centers.

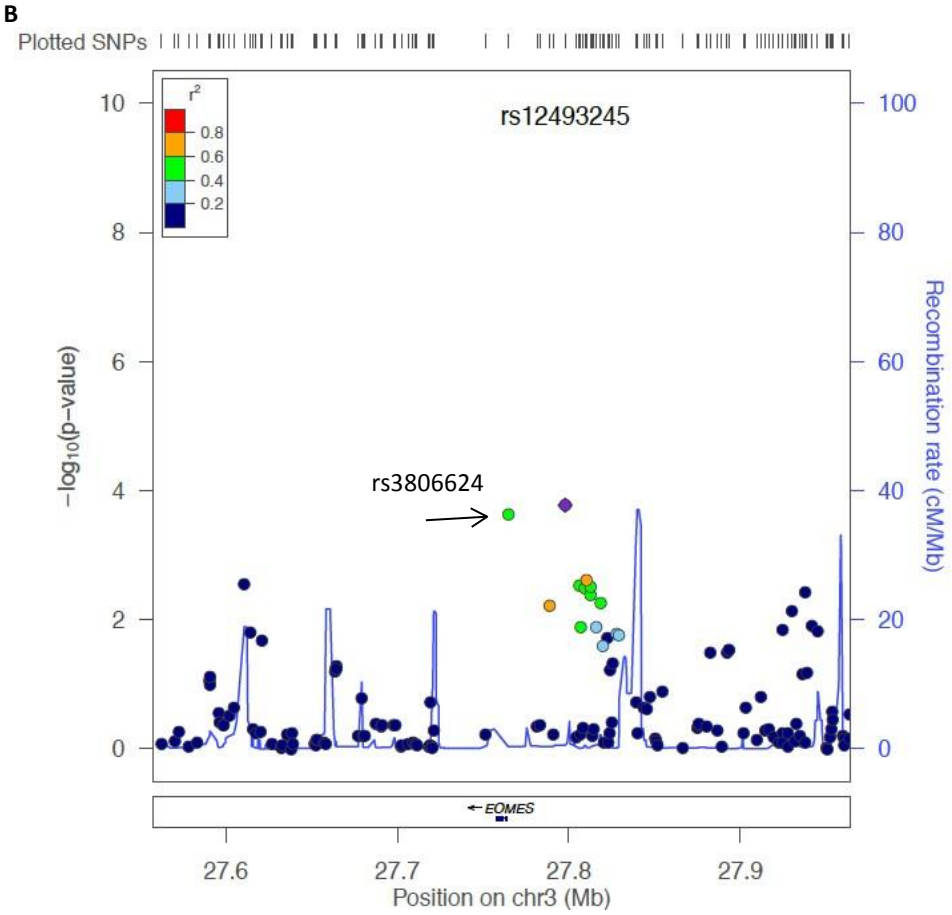
The red line represents concordance of observed and expected values. The shaded area indicates 99% concentration band. HLA region (chr6, 25,000,000 – 35,000,000) was excluded when calculating the inflation factor (λ) and creating the Q-Q plot. (A) The European Collaborative Study GWAS (cases = 1241 and controls = 5726). Inflation factor

(λ) excluding the HLA susceptibility region on chromosome 6 = 1.10; (B) USC GWAS (cases = 366 and controls = 1137), λ excluding the HLA susceptibility region on chromosome 6 = 1.02; (C) UC GWAS (cases = 209 and controls = 1014), λ excluding the HLA susceptibility region on chromosome 6 = 1.01. λ was calculated as a ratio of the median of the observed chi-square statistics for association from the Wald tests over the median (= 0.455) of the chi-square distribution with 1 df[54].

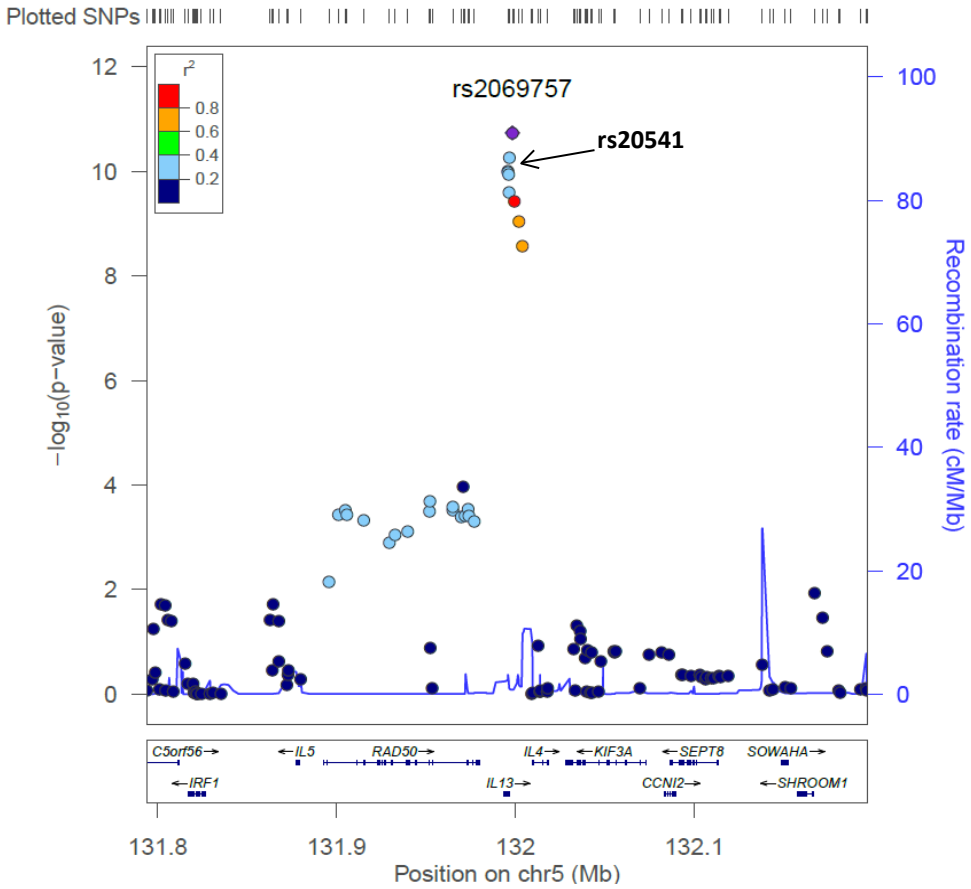


Supplementary Figure 2. The Quantile-quantile (Q-Q) plot for the P-values in the $-\log_{10}$ scale for the discovery GWAS meta-analysis. The meta-analysis for the discovery GWAS was conducted using the fixed effects model with 1816 cases and 7877 controls. HLA region (chr6, 25,000,000–35,000,000) and variants with I^2 values ≥ 75% indicative of significant heterogeneity were excluded when calculating the inflation factor (λ) and creating the Q-Q plot. The inflation factor (λ_{1000}) excluding the HLA region normalized to 1000 cases and 1000 controls = 1.03. The red line represents concordance of observed and expected values. The shaded area indicates a 99% concentration band. We examined over-dispersion using P-values from the meta-analysis to generate Q-Q plots and estimate an inflation factor λ, calculated as a ratio of the median of the observed chi-square statistics for association from the Wald tests over the median (= 0.455) of the chi-square distribution with 1 df[54].

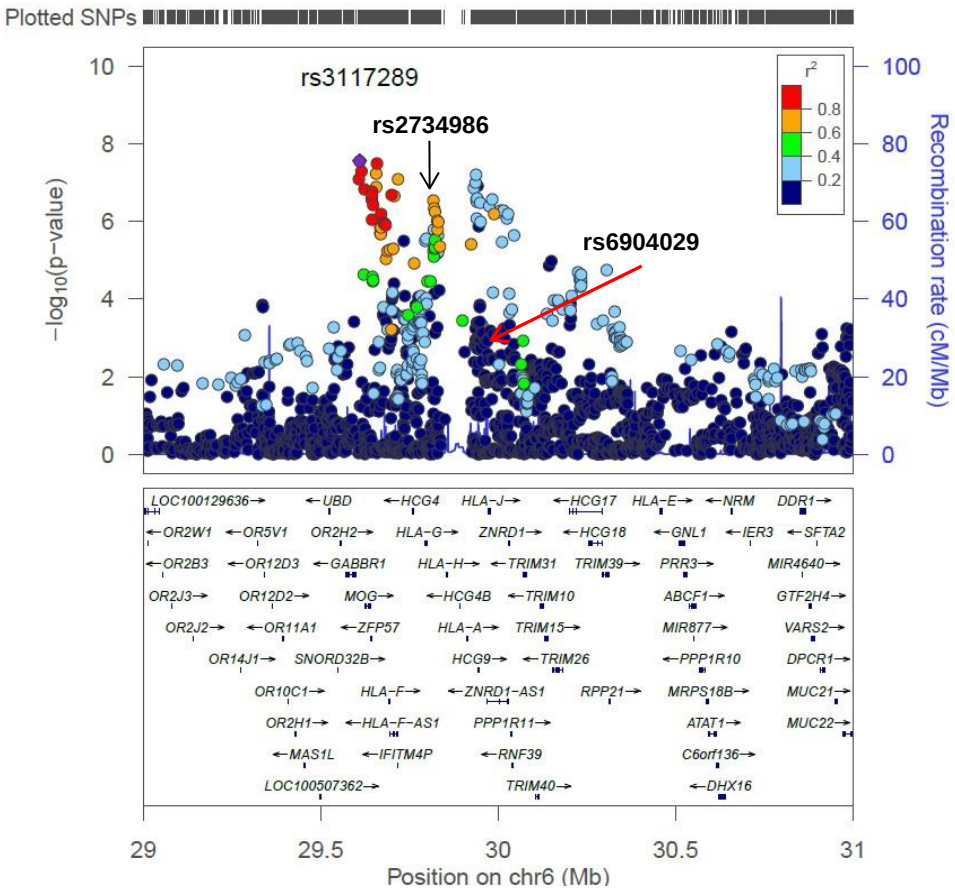

A
Plotted SNPs
rs13034020
rs1432295
r2
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
BCL11A
PAPOLG
PUS10
C2orf74
SNORA70B
FAM161A
REL
PEX13
AHSA2
XPO1
CCT4
KIAA1841
COMMD1
USP34
Position on chr2 (Mb)


B
Plotted SNPs
rs12493245
rs3806624
r2
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
EOMES
Position on chr3 (Mb)

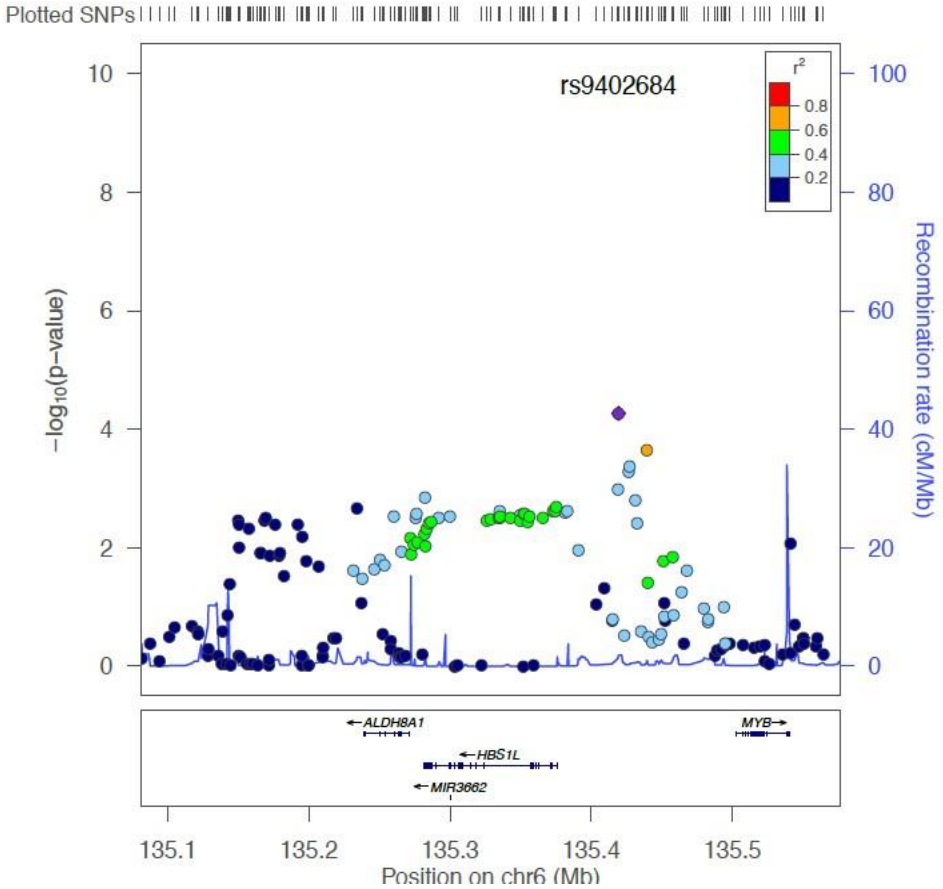
C


Plotted SNPs
rs2069757
rs20541
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
C5orf56
IL5
RAD50
IL4
KIF3A
SEPT8
SOWAHA
IRF1
IL13
CCNI2
SHROOM1
131.8
131.9
132
132.1
Position on chr5 (Mb)

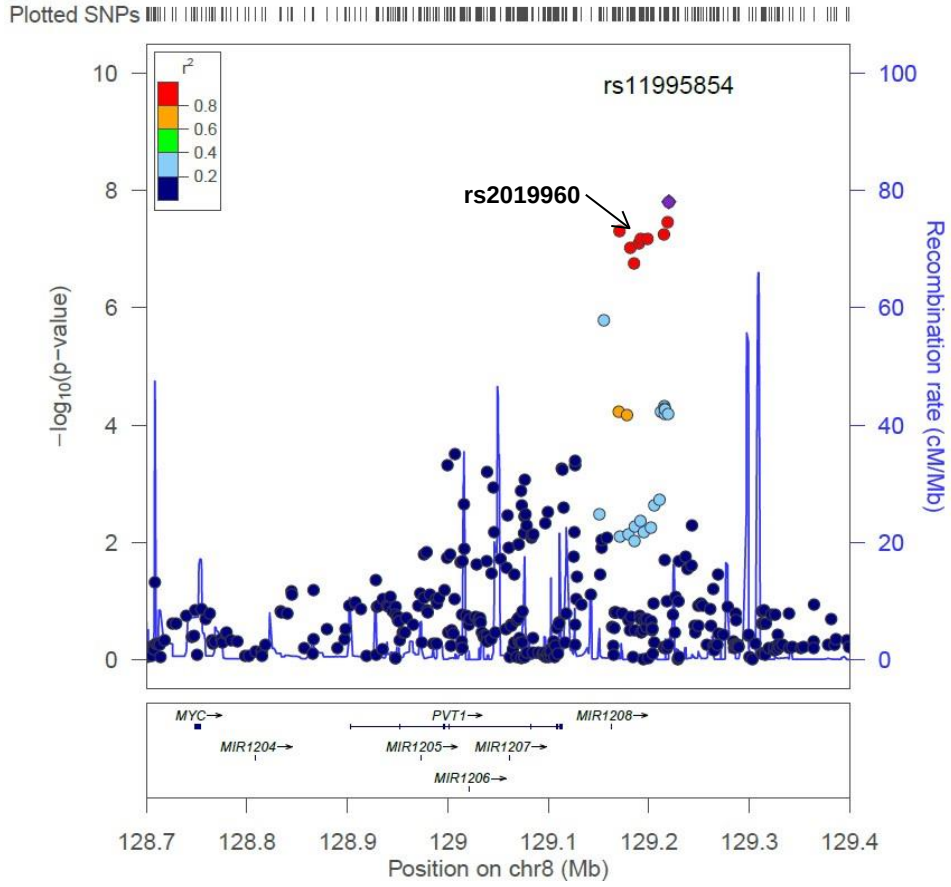
D

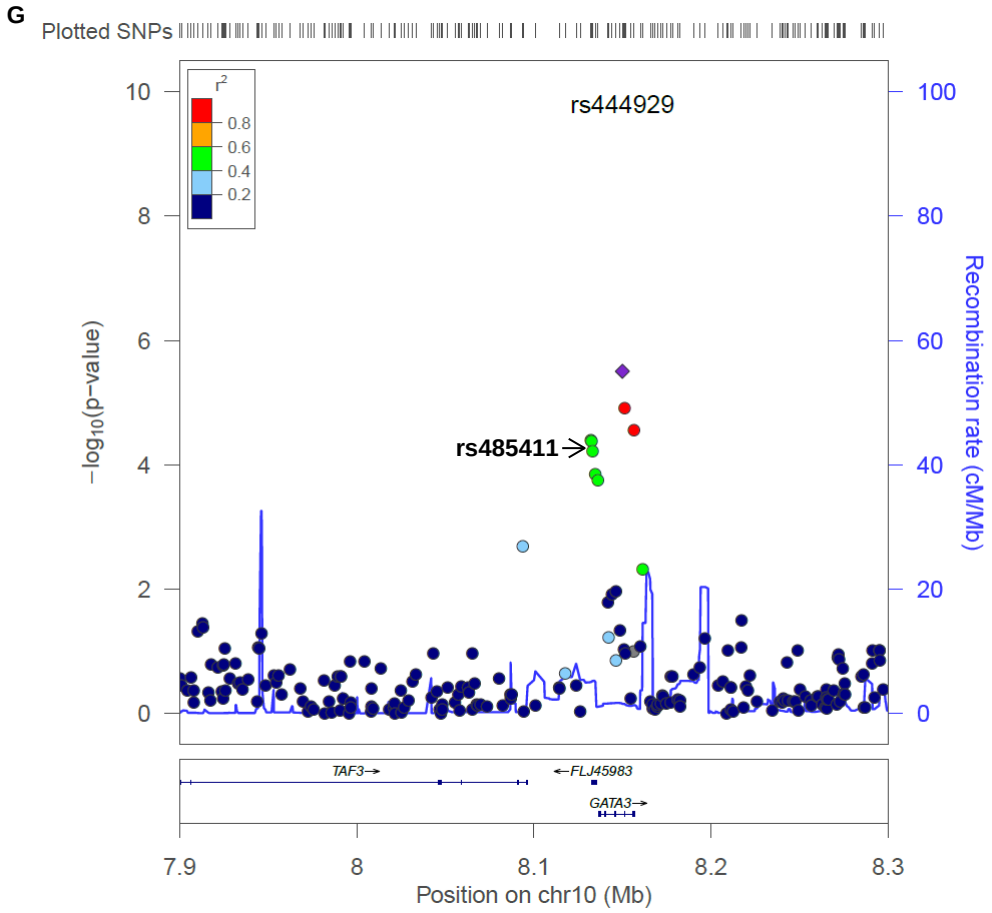

Plotted SNPs
rs3117289
rs2734986
rs6904029
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
LOC100129636
UBD
HCG4
HLA−J
HCG17
HLA−E
NRM
DDR1
OR2W1
OR5V1
OR2H2
HLA−G
ZNRD1
HCG18
GNL1
IER3
SFTA2
OR2B3
OR12D3
GABBR1
HLA−H
TRIM31
TRIM39
PRR3
MIR4640
OR2J3
OR12D2
MOG
HCG4B
TRIM10
ABCF1
GTF2H4
OR2J2
OR11A1
ZFP57
HLA−A
TRIM15
MIR877
VARS2
OR14J1
SNORD32B
HCG9
TRIM26
PPP1R10
DPCR1
OR10C1
HLA−F
ZNRD1−AS1
RPP21
MRPS18B
MUC21
OR2H1
HLA−F−AS1
PPP1R11
ATAT1
MUC22
MAS1L
IFITM4P
RNF39
C6orf136
LOC100507362
TRIM40
DHX16
29
29.5
30
30.5
31
Position on chr6 (Mb)

E

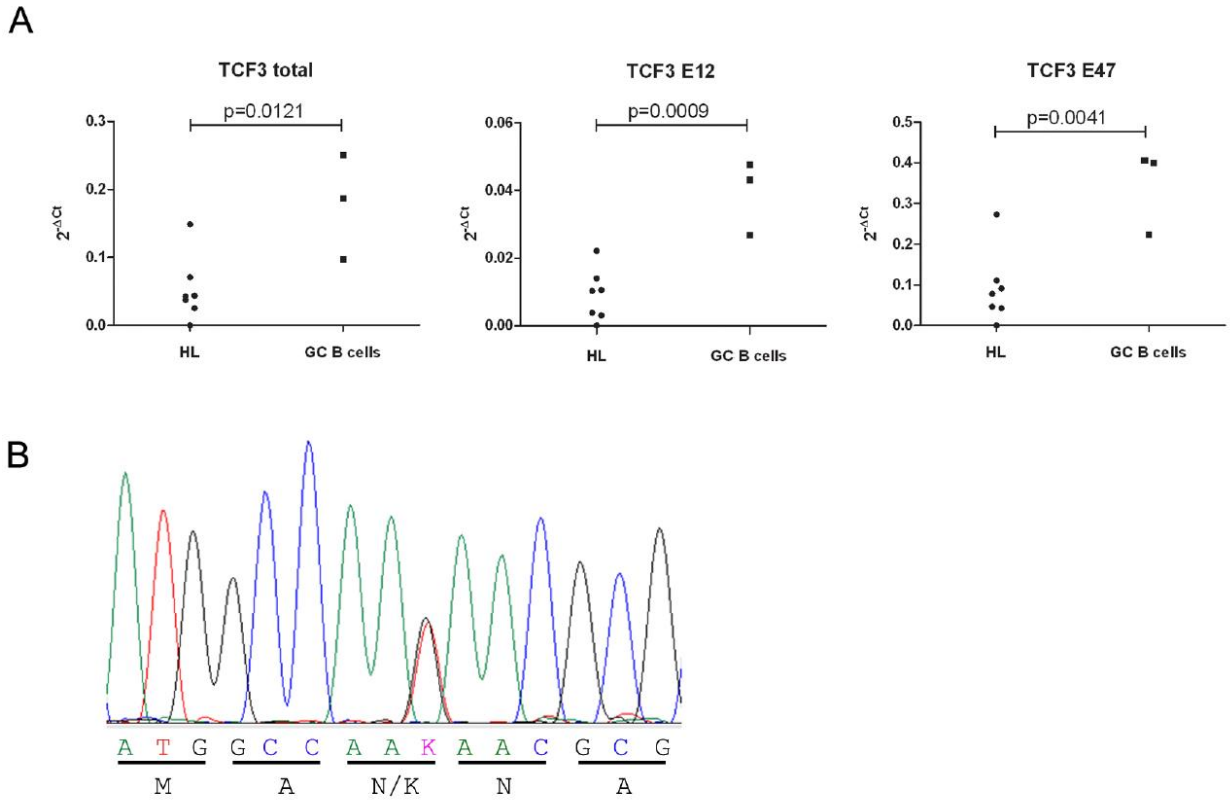

Plotted SNPs
rs9402684
r2
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
ALDH8A1
MYB
HBS1L
MIR3662
135.1
135.2
135.3
135.4
135.5
Position on chr6 (Mb)

F

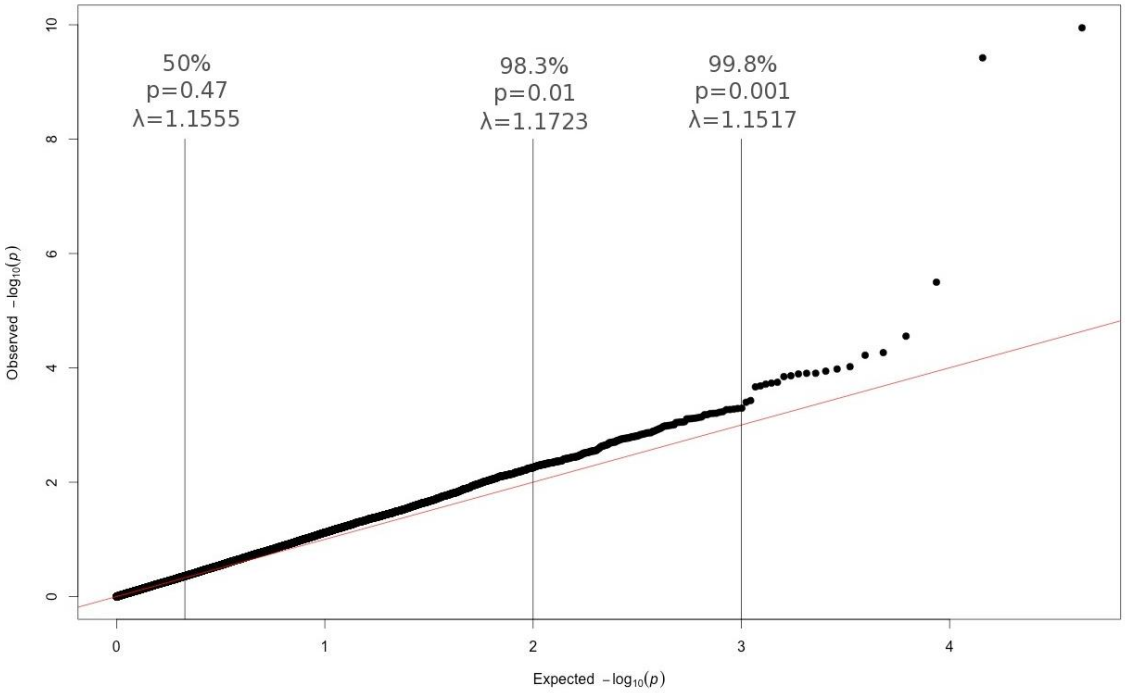

Plotted SNPs
rs11995854
rs2019960
r2
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
MYC
PVT1
MIR1208
MIR1204
MIR1205
MIR1207
MIR1206
128.7
128.8
128.9
129
129.1
129.2
129.3
129.4
Position on chr8 (Mb)



Supplementary Figure 3. Regional plots of the previously identified loci associated with Hodgkin lymphoma. Results ($-\log_{10}P$) for all Hodgkin lymphoma combined from the meta-analysis of 1816 cases and 7877 controls using a fixed effects model are shown for SNPs genotyped and imputed within the region. The most significant SNP in the locus is shown diamond-shaped and the r^2 values for the rest of the SNPs are indicated by different colors depending on the LD level in the CEU population. The genes within the region are annotated and shown as arrows at 2p16.1 (A), 3p24.1 (B), 5q31 (C), HLA region on 6p21.32 (D), 6q23.3 (E), 8q24.21 (F) 10p14 (G) are annotated and shown as arrows.



Supplementary Figure 4. TCF3 expression and mutation analysis in seven Hodgkin lymphoma derived cell lines. (A) Quantitative RT-PCR of the total, E12 and E47 TCF3 splice variants in seven Hodgkin lymphoma (HL) cell lines compared to germinal center (GC) B cells. Germinal center B cells (CD19+CD38+IgD-) were sorted from three different tonsils. A T-test was used to determine significant differences between the two groups. (B) A mutation in the *TCF3* gene was observed in in SUPHD1 cell line in an ongoing exome-sequencing analysis. We confirmed this mutation at the mRNA level by RT-PCR followed by Sanger sequencing of the resulting PCR product. The c.1653 T>G mutation results in an amino acid change at position 551, i.e. p.N551K.



Supplementary Figure 5. Quantile-Quantile (Q-Q) plot for the 21608 eQTL b-cell SNP, Lambda (λ) values at differing P values. The line represents concordance of observed and expected values. λ was calculated as a ratio of the median of the observed chi-square statistics for association from the Wald tests over the median (= 0.455) of the chi-square distribution with 1 df[54].

Supplementary Table 1. Participating studies and number of subjects by Hodgkin lymphoma subtype.

	Discovery								Replication												Combined	
Subtype	European Collaborative Study		USC		UC		Discovery Combined		EPILYMPH replication set		French replication series		UK replication series		SCALE		Mayo Clinic		Replication Combined			
	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co	Ca	Co
All Subtypes Combined	1241	5726	366	1137	209	1014	1816	7877	64	141	366	1696	499	520	118	638	234	223	1281	3218	3097	11095
Classical	1200	5726	334	1137	160	1014	1694	7877	62	141	341	1696	471	520	118	638	206	223	1198	3218	2892	11095
Nodular Sclerosis	840	5726	251	1137	142	1014	1233	7877	43	141	304	1696	357	520	84	638	150	223	938	3218	2171	11095
Mixed Cellularity	230	5726	72	1137	18	1014	320	7877	8	141	32	1696	88	520	26	638	27	223	181	3218	501	11095
EBV-negative	669	5726	107	1137	n/a	n/a	776	6863	11	141	145	1696	269	520	81	638	88	223	594	3218	1370	10081
EBV-positive	265	5726	22	1137	n/a	n/a	287	6863	6	141	42	1696	108	520	34	638	21	223	211	3218	498	10081
Nodular Sclerosis 15-35 y/o	506	5726	199	1137	87	1014	792	7877	26	141	186	1696	220	520	50	638	73	223	555	3218	1347	11095
Nodular sclerosis 35+ y/o[1]	331	5726	52	n/a	0	n/a	383	5726	17	141	118	1696	137	520	34	638	n/a	n/a	306	2995	689	8721
Males	663	3061	198	0	60	464	921	3525	35	68	198	685	290	298	68	353	129	114	720	1518	1641	5043
Females	578	2665	168	1137	149	550	895	4352	29	73	168	1011	209	222	50	285	105	109	561	1700	1456	6052

[1]A separate analysis was not conducted with USC cases > 35 years old due to small numbers.

Supplementary Table 2. Association between previously reported loci and risk of Hodgkin lymphoma by subtype and GWAS study[*].

		European Collaborative Study				*USC*				*UC*				*Combined*			
SNP	Minor Allele	MAF (Ca)	MAF (Co)	OR(95%CI)‡	*P*	MAF (Ca)	MAF (Co)	OR(95%CI)‡	*P*	MAF (Ca)	MAF (Co)	OR(95%CI)‡	*P*	OR(95%CI)*	*P*	P_{hom}	*P*
All Subtypes Combined																	
rs6903608[a]	C	0.42	0.30	1.72(1.56-1.9)	4.3E-27	0.44	0.33	1.58(1.24-2.02)	2.04E-04	0.40	0.32	1.34(1.08-1.65)	7.8E-03	1.64(1.51-1.78)	7.0E-31	0.10	56
rs204999[b]	G	0.23	0.28	0.81(0.72-0.91)	1.8E-04	0.19	0.27	0.68(0.51-0.91)	0.01	0.21	0.28	0.66(0.51-0.87)	2.51×10^{-3}	0.77(0.7-0.85)	2E-07	0.26	25
rs2734986[c]	C	0.21	0.17	1.35(1.19-1.52)	3.1E-06	0.16	0.15	1.25(0.91-1.73)	0.17	0.18	0.15	1.26(0.95-1.67)	0.11	1.32(1.19-1.47)	3E-07	0.86	0
rs6904029[d]	A	0.27	0.29	0.86(0.77-0.95)	4.5E-03	0.24	0.30	0.74(0.55-0.98)	0.04	0.29	0.30	0.98(0.78-1.24)	0.86	0.86(0.79-0.94)	1E-03	0.31	15
rs20541[e]	A	0.24	0.18	1.4(1.25-1.57)	7.3E-09	0.26	0.21	1.26(0.96-1.66)	0.09	0.26	0.21	1.33(1.05-1.7)	0.02	1.37(1.25-1.51)	1E-10	0.76	0
rs2019960[f]	C	0.27	0.22	1.31(1.18-1.47)	1.2E-06	0.26	0.22	1.23(0.93-1.63)	0.14	0.24	0.20	1.27(0.99-1.63)	0.06	1.3(1.18-1.43)	7E-08	0.90	0
rs2069757[g]	A	0.11	0.07	1.66(1.41-1.94)	1.7E-09	0.12	0.08	1.98(1.36-2.87)	3.3E-04	0.09	0.08	1.04(0.72-1.51)	0.82	1.59(1.39-1.82)	2E-11	0.04	69
rs3806624[h]	G	0.50	0.47	1.11(1.01-1.22)	3.8E-02	0.56	0.47	1.5(1.18-1.91)	9.9E-04	0.48	0.43	1.24(1.01-1.54)	4.4E-02	1.17(1.08-1.27)	2.26E-04	0.06	64
rs9402684[i]	T	0.52	0.48	1.21(1.1-1.34)	1.2E-04	0.52	0.49	0.93(0.73-1.19)	5.7E-01	0.55	0.49	1.3(1.05-1.61)	0.02	1.19(1.09-1.29)	5.4E-05	0.10	57
rs13034020[¶]	G	0.18	0.16	1.23(1.09-1.4)	9.0E-04	0.18	0.164	1.34(0.99-1.8)	0.06	0.21	0.15	1.5(1.14-1.97)	3.3E-03	1.28(1.16-1.43)	3.2E-06	0.42	0
rs444929[#]	C	0.24	0.21	1.2(1.07-1.35)	2.3E-03	0.22	0.20	1.4(1.05-1.86)	0.02	0.28	0.21	1.48(1.16-1.89)	1.5E-03	1.26(1.14-1.39)	3.1E-06	0.24	31
classical HL																	
rs6903608[a]	C	0.42	0.30	1.7(1.58-1.93)	5.9E-28	0.45	0.33	1.62(1.26-2.09)	1.7E-04	0.42	0.32	1.4(1.12-1.81)	3.9E-03	1.69(1.55-1.84)	3E-32	0.28	22
rs204999[b]	G	0.24	0.28	0.8(0.73-0.92)	4.9E-04	0.18	0.27	0.65(0.47-0.88)	5.5E-03	0.20	0.28	0.6(0.46-0.84)	2.03E-03	0.78(0.7-0.86)	7E-07	0.11	54
rs2734986[c]	C	0.22	0.17	1.4(1.22-1.56)	6.2E-07	0.17	0.15	1.36(0.98-1.88)	0.07	0.18	0.15	1.3(0.96-1.81)	0.09	1.37(1.23-1.53)	2E-08	0.96	0
rs6904029[d]	A	0.27	0.29	0.8(0.76-0.94)	2.1E-03	0.23	0.30	0.69(0.51-0.94)	0.02	0.29	0.30	1(0.76-1.27)	0.90	0.85(0.77-0.93)	5E-04	0.23	33
rs20541[e]	A	0.24	0.18	1.4(1.26-1.59)	5.0E-09	0.26	0.21	1.27(0.96-1.69)	0.09	0.26	0.21	1.3(1.03-1.77)	0.03	1.39(1.26-1.53)	9E-11	0.77	0
rs2019960[f]	C	0.26	0.22	1.3(1.16-1.45)	5.3E-06	0.25	0.22	1.19(0.89-1.59)	0.23	0.23	0.20	1.2(0.91-1.6)	0.20	1.27(1.16-1.4)	1E-06	0.80	0
rs2069757[g]	A	0.11	0.07	1.7(1.44-1.99)	5.3E-10	0.12	0.08	2(1.36-2.92)	4.0E-04	0.10	0.08	1.2(0.8-1.77)	0.38	1.66(1.44-1.9)	1E-12	0.16	45
rs3806624[h]	G	0.50	0.47	1.11(1-1.22)	4.1E-02	0.56	0.47	1.51(1.17-1.94)	1.3E-03	0.48	0.43	1.24(0.98-1.57)	0.07	1.17(1.07-1.27)	4.4E-04	0.07	62
rs9402684[i]	T	0.52	0.48	1.23(1.11-1.35)	5.3E-05	0.52	0.49	0.98(0.76-1.26)	8.6E-01	0.54	0.49	1.23(0.97-1.56)	0.09	1.2(1.1-1.3)	5.1E-05	0.25	27
rs13034020[¶]	G	0.18	0.16	1.2(1.08-1.39)	1.4E-03	0.18	0.16	1.32(0.97-1.8)	0.08	0.21	0.15	1.5(1.12-2.04)	6.7E-03	1.27(1.14-1.42)	1.2E-05	0.44	0
rs444929[#]	C	0.24	0.21	1.2(1.1-1.39)	4.8E-04	0.22	0.20	1.32(0.97-1.78)	0.08	0.27	0.21	1.5(1.11-1.92)	6.3E-03	1.27(1.15-1.41)	3.2E-06	0.52	0
nodular sclerosis HL																	

rs6903608[a]	C	0.46	0.30	1.93(1.69-2.21)	6.5E-23	0.47	0.33	1.66(1.27-2.16)	1.7E-04	0.43	0.32	1.5(1.16-1.92)	1.8E-03	1.8(1.61-2)	1E-26	0.17	44
rs204999[b]	G	0.21	0.28	0.7(0.6-0.82)	7.4E-06	0.18	0.27	0.61(0.44-0.85)	3.3E-03	0.19	0.28	0.6(0.43-0.82)	1.47E-03	0.67(0.59-0.76)	1E-09	0.54	0
rs2734986[c]	C	0.19	0.17	1.19(1-1.42)	5.7E-02	0.16	0.15	1.31(0.93-1.85)	0.12	0.19	0.15	1.3(0.95-1.85)	0.09	1.23(1.07-1.42)	4E-03	0.78	0
rs6904029[d]	A	0.29	0.29	0.88(0.77-1.01)	6.6E-02	0.22	0.30	0.73(0.53-0.99)	0.04	0.30	0.30	1(0.77-1.32)	0.96	0.88(0.78-0.98)	3E-02	0.30	17
rs20541[e]	A	0.26	0.18	1.6(1.37-1.86)	1.4E-09	0.28	0.21	1.27(0.94-1.7)	0.12	0.26	0.21	1.3(0.99-1.75)	0.06	1.48(1.31-1.68)	3E-10	0.26	27
rs2019960[f]	C	0.27	0.22	1.36(1.17-1.57)	7.3E-05	0.24	0.22	1.16(0.85-1.57)	0.34	0.24	0.20	1.2(0.89-1.62)	0.22	1.29(1.15-1.46)	4E-05	0.58	0
rs2069757[g]	A	0.11	0.07	1.67(1.34-2.07)	4.4E-06	0.13	0.08	2.09(1.41-3.1)	2.4E-04	0.11	0.08	1.3(0.86-1.93)	0.23	1.66(1.4-1.98)	7E-09	0.24	29
rs3806624[h]	G	0.51	0.47	1.14(1-1.3)	5.0E-02	0.57	0.47	1.56(1.2-2.03)	9.8E-04	0.48	0.43	1.22(0.95-1.57)	0.12	1.22(1.09-1.35)	3.35E-04	0.12	53
rs9402684[I]	T	0.52	0.48	1.29(1.13-1.47)	1.7E-04	0.52	0.49	0.96(0.74-1.25)	7.5E-01	0.52	0.49	1.13(0.88-1.45)	0.33	1.2(1.08-1.33)	9.4E-04	0.13	52
rs13034020[¶]	G	0.18	0.16	1.2(1.01-1.42)	3.4E-02	0.18	0.16	1.34(0.97-1.85)	0.08	0.20	0.15	1.5(1.06-2)	2.1E-02	1.26(1.11-1.45)	6.3E-04	0.54	0
rs444929[#]	C	0.25	0.21	1.32(1.13-1.54)	5.8E-04	0.23	0.20	1.3(0.95-1.79)	0.01	0.26	0.21	1.4(1.06-1.9)	1.7E-02	1.33(1.18-1.51)	7.8E-06	0.89	0
mixed cellularity HL																	
rs6903608[a]	C	0.32	0.30	1.1(0.88-1.38)	3.9E-01	0.34	0.33	1.46(0.88-2.43)	0.1415	0.33	0.32	1(0.49-1.99)	9.7E-01	1.14(0.94-1.39)	2E-01	0.56	0
rs204999[b]	G	0.31	0.28	1.1(0.87-1.38)	4.4E-01	0.26	0.27	1.04(0.59-1.84)	0.8837	0.25	0.28	0.9(0.4-1.91)	7.31E-01	1.07(0.87-1.32)	5E-01	0.85	0
rs2734986[c]	C	0.30	0.17	2.15(1.65-2.8)	2.1E-08	0.22	0.15	1.79(0.97-3.28)	0.06	0.17	0.15	1.2(0.48-2.9)	0.71	2.01(1.59-2.54)	5E-09	0.42	0
rs6904029[d]	A	0.22	0.29	0.62(0.49-0.79)	8.2E-05	0.24	0.30	0.61(0.32-1.15)	0.12	0.25	0.30	0.8(0.37-1.69)	0.55	0.63(0.51-0.79)	4E-05	0.83	0
rs20541[e]	A	0.21	0.18	1.17(0.91-1.51)	2.2E-01	0.23	0.21	1.15(0.64-2.07)	0.64	0.31	0.21	1.6(0.79-3.32)	0.18	1.21(0.97-1.51)	1E-01	0.69	0
rs2019960[f]	C	0.24	0.22	1.22(0.96-1.56)	1.1E-01	0.30	0.22	1.2(0.67-2.15)	0.54	0.22	0.20	1.2(0.52-2.54)	0.72	1.21(0.98-1.51)	8E-02	0.99	0
rs2069757[g]	A	0.1	0.07	1.44(1-2.07)	5.5E-02	0.11	0.08	2.16(1.03-4.52)	4.1E-02	0.06	0.08	0.6(0.14-2.51)	0.48	1.49(1.08-2.04)	1E-02	0.28	22
rs3806624[h]	G	0.50	0.47	1.14(0.91-1.42)	2.5E-01	0.51	0.47	1.08(0.66-1.77)	7.6E-01	0.53	0.43	1.49(0.77-2.9)	0.24	1.15(0.95-1.4)	0.144319	0.72	0
rs9402684[I]	T	0.51	0.48	1.2(0.97-1.5)	9.4E-02	0.51	0.49	0.98(0.57-1.67)	0.93	0.69	0.49	2.37(1.16-4.88)	0.02	1.23(1.01-1.49)	0.035922	0.14	50
rs13034020[¶]	G	0.17	0.16	1.01(0.76-1.33)	9.7E-01	0.20	0.16	1(0.5-2)	1.00	0.25	0.15	2(0.94-4.41)	7.3E-02	1.08(0.84-1.38)	5.4E-01	0.24	30
rs444929[#]	C	0.2	0.21	0.97(0.73-1.27)	8.1E-01	0.18	0.20	1.06(0.55-2.05)	0.86	0.33	0.21	1.8(0.89-3.57)	1.0E-01	1.05(0.83-1.34)	6.8E-01	0.28	22
EBV negative HL																	
rs6903608[a]	C	0.46	0.30	2.05(1.82-2.31)	1.1E-31	0.51	0.33	1.79(1.14-2.81)	0.01	n/a	n/a	n/a	n/a	2.03(1.81-2.28)	7E-33	0.57	0
rs204999[b]	G	0.20	0.28	0.64(0.55-0.74)	3.7E-10	0.16	0.27	0.58(0.32-1.04)	0.07	n/a	n/a	n/a	n/a	0.64(0.55-0.73)	2E-10	0.75	0
rs2734986[c]	C	0.17	0.17	0.94(0.8-1.11)	4.9E-01	0.12	0.15	0.83(0.42-1.62)	0.58	n/a	n/a	n/a	n/a	0.94(0.8-1.1)	4E-01	0.70	0
rs6904029[d]	A	0.31	0.29	1.05(0.92-1.19)	4.7E-01	0.25	0.30	0.94(0.56-1.56)	0.80	n/a	n/a	n/a	n/a	1.04(0.92-1.18)	5E-01	0.67	0
rs20541[e]	A	0.26	0.18	1.48(1.3-1.7)	2.4E-08	0.29	0.21	1.51(0.91-2.49)	0.11	n/a	n/a	n/a	n/a	1.49(1.3-1.69)	3E-09	0.96	0
rs2019960[f]	C	0.28	0.22	1.41(1.24-1.61)	2.6E-07	0.25	0.22	1.5(0.9-2.49)	0.12	n/a	n/a	n/a	n/a	1.42(1.25-1.61)	5E-08	0.82	0
rs2069757[g]	A	0.12	0.07	1.74(1.44-2.09)	1.9E-08	0.12	0.08	1.99(0.99-4)	0.05	n/a	n/a	n/a	n/a	1.75(1.47-2.1)	8E-10	0.72	0
rs3806624[h]	G	0.49	0.47	1.05(0.93-1.18)	4.5E-01	0.57	0.47	1.49(0.95-2.34)	0.08	n/a	n/a	n/a	n/a	1.07(0.96-1.2)	0.24102	0.14	54

rs9402684[l]	T	0.52	0.48	1.2(1.07-1.35)	2.6E-03	0.52	0.49	0.97(0.61-1.53)	0.89	n/a	n/a	n/	n/a	1.18(1.06-1.33)	4.04E-03	0.37	0
rs13034020[¶]	G	0.19	0.16	1.27(1.1-1.48)	1.7E-03	0.17	0.16	1.12(0.62-2.02)	0.7114	n/a	n/a	n/	n/a	1.26(1.09-1.46)	1.4E-03	0.67	0
rs444929[#]	C	0.25	0.21	1.29(1.12-1.48)	4.0E-04	0.20	0.20	1.23(0.7-2.15)	0.4766	n/a	n/a	n/	n/a	1.28(1.12-1.47)	2.6E-04	0.87	0
EBV positive HL																	
rs6903608[a]	C	0.27	0.30	0.95(0.78-1.16)	6.5E-01	0.36	0.33	1.1(0.4-2.99)	0.86	n/a	n/a	n/	n/a	0.96(0.79-1.17)	7E-01	0.79	0
rs204999[b]	G	0.33	0.28	1.16(0.96-1.41)	1.4E-01	0.16	0.27	1.06(0.37-3.04)	0.92	n/a	n/a	n/	n/a	1.16(0.96-1.4)	1E-01	0.86	0
rs2734986[c]	C	0.34	0.17	2.2(1.78-2.72)	7.8E-13	0.23	0.15	2.1(0.63-7.05)	0.23	n/a	n/a	n/	n/a	2.2(1.78-2.71)	1E-13	0.94	0
rs6904029[d]	A	0.17	0.29	0.47(0.37-0.6)	4.6E-11	0.25	0.30	0.38(0.09-1.64)	0.19	n/a	n/a	n/	n/a	0.47(0.37-0.59)	4E-10	0.77	0
rs20541[e]	A	0.19	0.18	1.06(0.84-1.32)	6.4E-01	0.20	0.21	0.76(0.21-2.7)	0.67	n/a	n/a	n/	n/a	1.05(0.84-1.31)	7E-01	0.61	0
rs2019960[f]	C	0.26	0.22	1.24(1.02-1.52)	3.7E-02	0.20	0.22	0.49(0.11-2.25)	0.36	n/a	n/a	n/	n/a	1.22(1-1.5)	5E-02	0.24	29
rs2069757[g]	A	0.08	0.07	1.11(0.79-1.55)	5.4E-01	0.07	0.08	1.59(0.34-7.4)	5.5E-01	n/a	n/a	n/	n/a	1.13(0.81-1.57)	5E-01	0.65	0
rs3806624[h]	G	0.51	0.47	1.18(0.98-1.42)	0.08	0.48	0.47	1(0.4-2.5)	9.9E-01	n/a	n/a	n/	n/a	1.17(0.98-1.4)	0.084495	0.72	0
rs9402684[l]	T	0.51	0.48	1.19(0.99-1.43)	0.06	0.52	0.49	1.3(0.5-3.4)	5.9E-01	n/a	n/a	n/	n/a	1.19(1-1.43)	5.39E-02	0.86	0
rs13034020[¶]	G	0.16	0.16	1.04(0.81-1.32)	7.7E-01	0.09	0.16	0.71(0.16-3.1)	0.65	n/a	n/a	n/	n/a	1.03(0.81-1.31)	8.3E-01	0.62	0
rs444929[#]	C	0.21	0.21	0.99(0.79-1.24)	9.1E-01	0.22	0.20	1.37(0.44-4.27)	0..58	n/a	n/a	n/	n/a	1(0.8-1.25)	1.0E+00	0.58	0
nodular sclerosis HL in 15-35 year olds																	
rs6903608[a]	C	0.47	0.30	2.1(1.84-2.42)	1.3E-25	0.45	0.33	1.51(1.11-2.04)	0.00829	0.42	0.32	1.4(1.05-1.98)	2.2E-02	1.9(1.69-2.14)	6E-27	0.03	73
rs204999[b]	G	0.19	0.28	0.62(0.52-0.73)	1.7E-08	0.18	0.27	0.62(0.43-0.91)	0.01458	0.18	0.28	0.6(0.38-0.87)	7.86E-03	0.61(0.53-0.71)	6E-11	0.95	0
rs2734986[c]	C	0.18	0.17	1.13(0.94-1.36)	2.0E-01	0.16	0.15	1.23(0.82-1.84)	0.32	0.19	0.15	1.4(0.9-2.05)	0.14	1.18(1.01-1.38)	4E-02	0.70	0
rs6904029[d]	A	0.30	0.29	0.97(0.84-1.13)	7.3E-01	0.25	0.30	0.81(0.57-1.14)	0.22	0.26	0.30	0.9(0.61-1.22)	0.39	0.93(0.82-1.06)	3E-01	0.54	0
rs20541[e]	A	0.27	0.18	1.58(1.35-1.85)	1.6E-08	0.29	0.21	1.24(0.88-1.74)	0.22	0.27	0.21	1.4(0.97-1.96)	0.08	1.5(1.31-1.71)	2E-09	0.39	0
rs2019960[f]	C	0.29	0.22	1.52(1.3-1.77)	1.4E-07	0.25	0.22	1.15(0.81-1.63)	0.44	0.24	0.20	1.2(0.87-1.8)	0.23	1.42(1.25-1.62)	1E-07	0.27	23
rs2069757[g]	A	0.12	0.07	1.89(1.52-2.35)	5.9E-08	0.13	0.08	2.02(1.28-3.19)	2.4E-03	0.13	0.08	1.5(0.91-2.36)	0.11	1.84(1.53-2.21)	5E-11	0.58	0
rs3806624[h]	G	0.52	0.47	1.16(1.01-1.33)	0.04	0.58	0.47	1.62(1.2-2.19)	1.8E-03	0.52	0.43	1.47(1.08-2.01)	0.01	1.26(1.12-1.42)	1.02E-04	0.08	60
rs9402684[l]	T	0.53	0.48	1.27(1.11-1.46)	7.7E-04	0.52	0.49	0.95(0.7-1.29)	7.5E-01	0.50	0.49	1.06(0.78-1.45)	0.71	1.19(1.06-1.33)	0.004102	0.17	43
rs13034020[¶]	G	0.19	0.16	1.29(1.08-1.53)	5.3E-03	0.18	0.164	1.29(0.88-1.88)	0.19	0.19	0.15	1.3(0.87-1.94)	2.0E-01	1.29(1.11-1.49)	6.8E-04	1.00	0
rs444929[#]	C	0.27	0.21	1.44(1.23-1.69)	1.193E-05	0.23	0.20	1.16(0.8-1.69)	0.43	0.25	0.21	1.3(0.91-1.89)	1.4E-01	1.38(1.2-1.58)	3.6E-06	0.56	0

[*]Frequency for the European Collaborative Study is based on the genotyped results. The study was imputed against 1000 Genome[19] (release 2010-08) using minimac[15] and all missing observation were re-imputed for the meta-analysis, which was conducted which was conducted using a random effects[15, 33]. P for homogeneity across studies was calculated using Cochran's Q statistic. Sample sizes are: All HL= All subtypes of Hodgkin lymphoma combined (1816 cases, 7877 controls), NS = nodular sclerosis (1233 cases, 7877 controls), MC = mixed cellularity (320 cases, 7877 controls), NS_{young} = nodular sclerosis diagnosed in young adults15-35 years old (792 cases, 7877 controls), EBV-negative (776 cases, 6863 controls), EBV-positive (287 cases, 6863 controls).

*position is given according NCBI build 37

‡Per-allele effect estimates for the fixed effect model are presented.

[a] SNP at 6p21.32, intergenic HLA class II region, BP 32536263[11]

[b] SNP at 6p21.32, intergenic HLA class II region, BP 32217957[13]

[c]SNP at 6p21.32, intergenic HLA class II region, BP29926547[12]

[d] SNP at 6p21.32, exon, MICD-HCG9, BP30051046[12]

[e] SNP at 5q31, Q144R, exon IL13, BP132023863[12]

[f]SNP at q24.21, intergenic, P129261453[11]

[g]SNP at 5q31, intergenic, BP132026312, novel

[h]SNP at 3p24.1, predicted promoter, *EOMES,* BP27764623[17]

[I]SNP at 6q23.2, intergenic HBS1L and *MYB, BP* 135419305[17]

¶ SNP at 2p16.1, intergenic, BP 60897338, LD with the previously described rs1432295 r^2=0.30; D'=1.00[11]

SNP at 10p14, intron GATA3, BP 8150030, LD with the previously described rs501764 R^2=0.48; D'=0.82[11]

Supplementary Table 3. Association of previously and newly described markers at 2p16.1 and 10p14 loci mutually adjusted in conditional analysis on previously described risk variants at these loci*.

locus	model	rs_number	effect allele	reference allele	IARC GWAS OR (95% CI)‡	IARC GWAS P-value	USC GWAS OR (95% CI)‡	USC GWAS P-value	UC GWAS OR (95% CI)‡	UC GWAS P-value	Combined (fixed effect model) OR (95% CI)‡	Combined (fixed effect model) P-value	Combined (fixed effect model) Phom
2p16.1, *RFI*	rs1432295	rs1432295	G	A	1.13(1.02-1.24)	0.01	1.15(0.90-1.46)	0.2659	1.27(1.03-1.57)	0.03	1.15(1.06-1.25)	$9.0x10^{-4}$	0.61
	rs13034020 ¶	rs13034020	G	A	1.23(1.09-1.4)	$7.9x10^{-4}$	1.34(0.99-1.80)	0.0577	1.50(1.14-1.97)	$3.3x10^{-3}$	1.28(1.16-.43)	$3.2x10^{-o}$	0.42
	rs13034020 rs1432295	rs13034020	G	A	1.19(1.04-1.37)	0.01	1.26(0.76-2.07)	0.37	1.39(1.02-1.91)	0.04	1.23(1.08-1.39)	$1.2x10^{-3}$	0.68
	rs13034020 rs1432295	rs1432295	G	A	1.06(0.95-1.18)	0.32	0.73(0.49-1.09)	0.12	1.11(0.86-1.43)	0.39	1.04(0.94-1.15)	0.41	0.19
10p14, GATA3	rs485411 §	rs485411	T	C	1.14(1.02-1.26)	0.02	1.67(1.30-2.15)	$7x10^{-5}$	1.19(0.94-1.50)	0.15	1.20(1.10-1.32)	$6.1x10^{-5}$	0.02
	rs444929 #	rs444929	C	T	1.2(1.07-1.35)	$2.2x10^{-3}$	1.40(1.05-1.86)	0.0238	1.48(1.16-1.89)	$1.5x10^{-3}$	1.26(1.15-1.39)	$3.1x10^{-6}$	0.24
	rs444929 rs485411	rs444929	C	T	1.17(1-1.37)	0.05	1.28(0.75-2.20)	0.37	1.60(1.15-2.20)	$4.8x10^{-3}$	1.24(1.08-1.42)	$1.8x10^{-3}$	0.23
	rs444929 rs485411	rs485411	T	C	1.04(0.9-1.19)	0.63	1.30(0.77-2.18)	0.31	0.89(0.65-1.22)	0.47	1.02(0.90-1.16)	0.71	0.45

§proxy for the previously described rs501764, R2=1; D'=1[11]

¶LD with the previously described rs1432295 r^2=0.30; D'=1.00[11]

#LD with the previously described rs501764 R^2=0.48; D'=0.82[11]

*IARC, USC and UC GWAS consisted of 1,241 cases, 5,726 controls; 366 cases 1,137 controls; and 209 cases, 1,014 controls, respectively. Odds Ratios were calculated using logistic regression.

Supplementary Table 4. Association of rs6439924 (3q32, minor allele C) and rs2058613/rs6946457 (7p21, minor allele A) with the risk of Hodgkin lymphoma in the discovery and replication sets*.

	Discovery (1816 cases, 7877 controls)					*Replication (1281 cases, 3218 controls)*					*Combined (3097 cases and 11095 controls)*			
SNP	MAF† (Ca)	MAF† (Co)	OR (95% CI)*	*P*	P_{hom}	MAF† (Ca)	MAF† (Co)	OR (95% CI)*	*P*	P_{hom}	OR (95% CI)*	*P*	P_{hom}	I^2
rs6439924	0.20	0.16	1.33 (1.2-1.47)	8.3×10^{-8}	0.71	0.18	0.18	1.08 (0.95-1.23)	0.22	0.63	1.23 (1.13-1.33)	7.5×10^{-7}	0.15	40.0
rs2058613/rs6946457#	0.22	0.29	0.78 (0.7-0.86)	6.6×10^{-7}	0.52	0.24	0.26	0.98 (0.84-1.13)	0.74	0.43	0.84 (0.77-0.91)	1.8×10^{-5}	0.08	52.1

*Results for the fixed effects model are presented.

#No assay could be designed for rs2058613 and therefore a proxy variant (r^2=1.0, D'=1.0 in CEU) rs6946457 was genotyped in the replication set.

Supplementary Table 5. Genomic inflation factor lambda (λ) for the overall meta-analysis for the subgroup of variants in expression quantitative trait loci (eQTL) with B -cell expression

	#SNPs (excluding HLA)	λ	Random re-sampling with replacement
non eQTL SNPs		1.09	
eQTL b-cell SNPs	21608	1.16	1.07 - 1.13