

Genome-wide Association Study Identifies Five Susceptibility Loci for Follicular Lymphoma outside the HLA Region

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1. SUPPLEMENTAL FIGURES

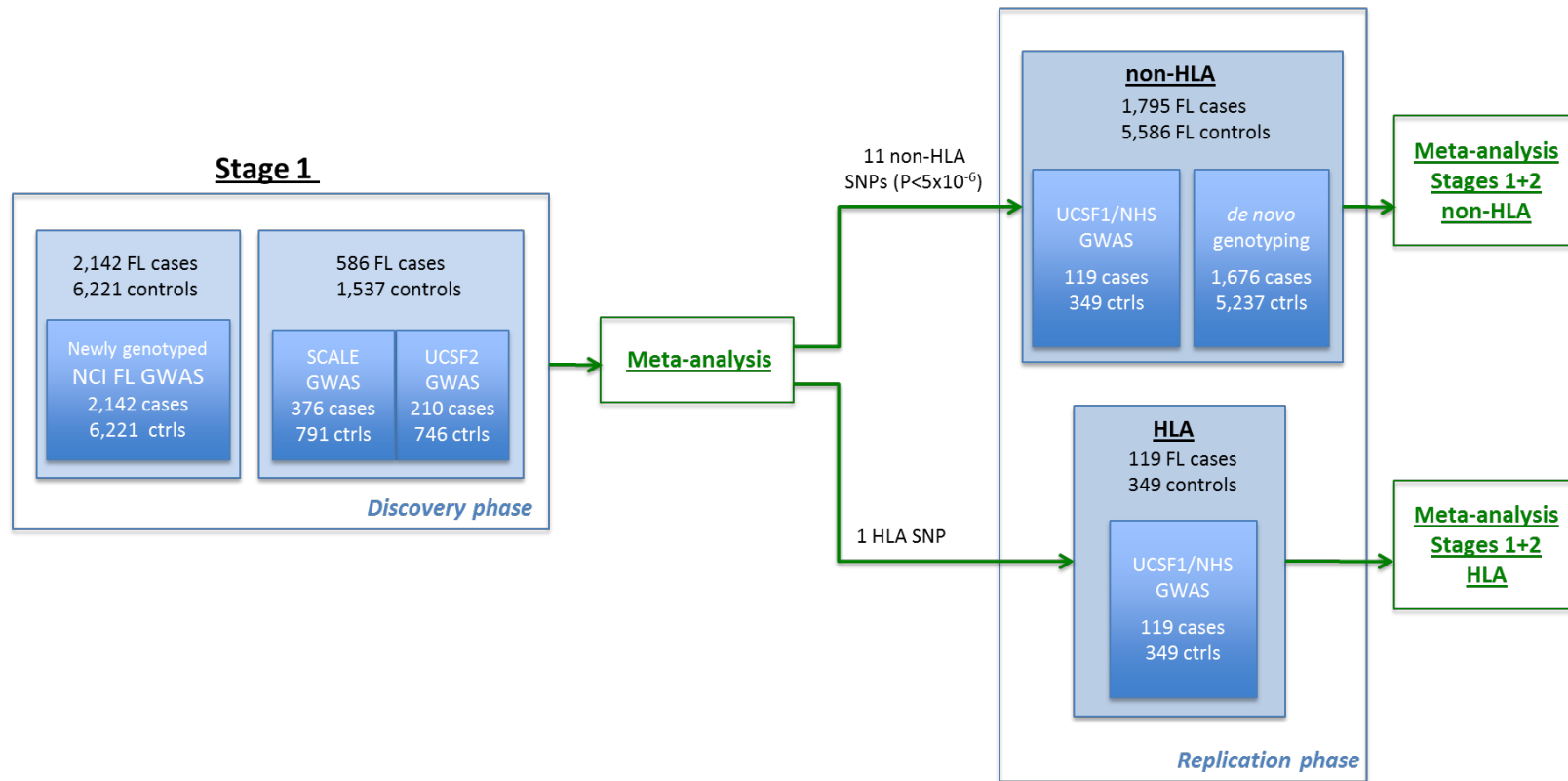


Figure S1. Schematic of the study design.

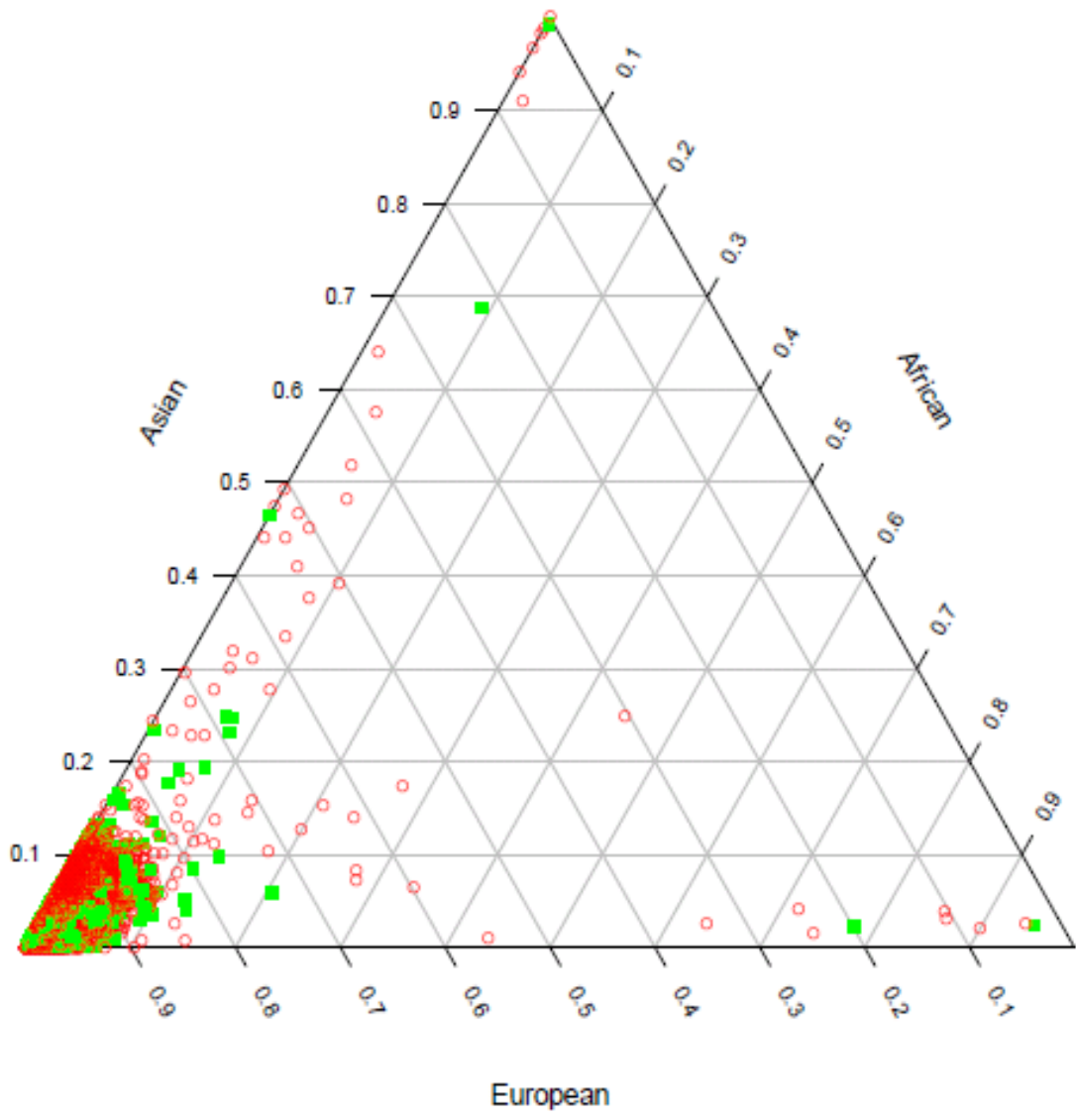
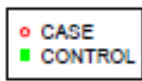


Figure S2. Plot of estimated admixture for individuals genotyped in the NCI FL GWAS. Individuals with <80% European ancestry were excluded.

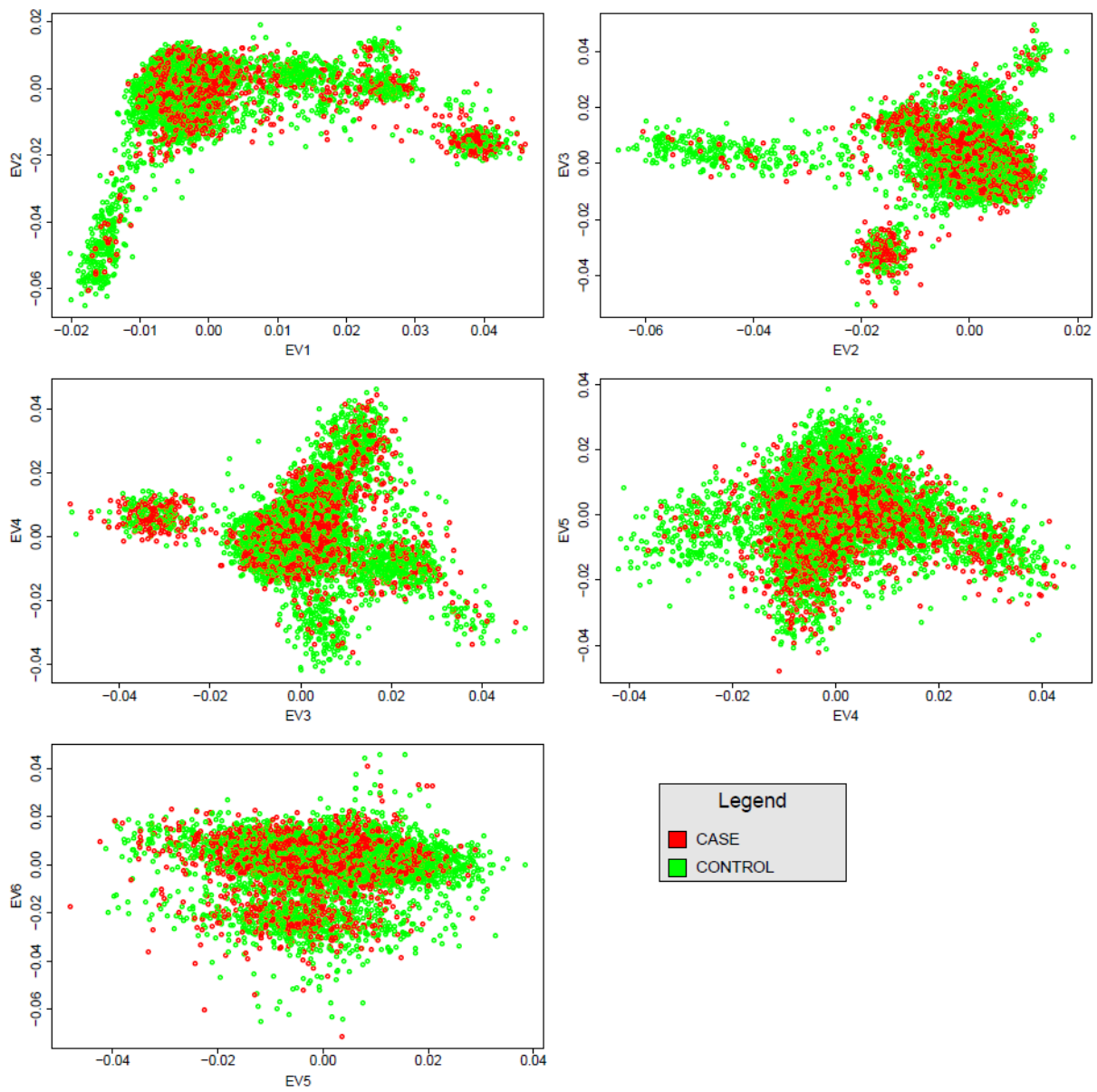


Figure S3: Plot of top eigenvectors from the NCI FL GWAS based on principal components analysis.

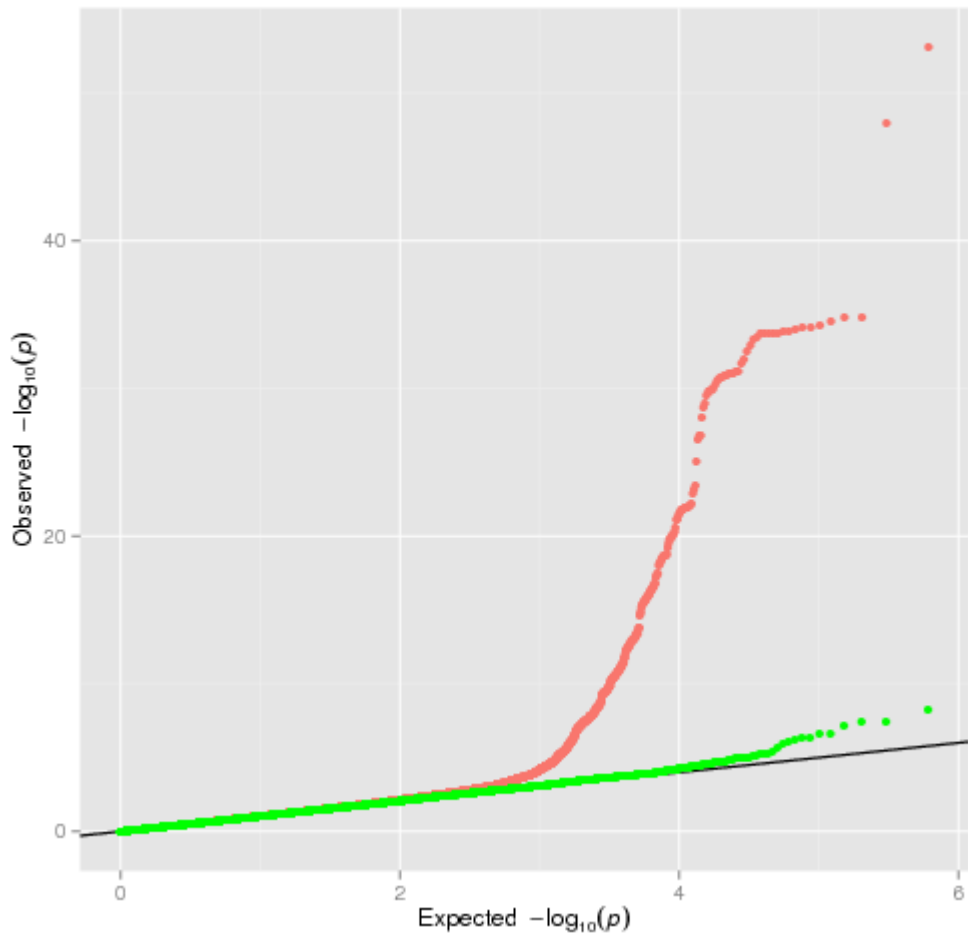


Figure S4. Quantile-quantile (Q-Q) plot of the association results for the genotyped SNPs for follicular lymphoma from the NCI FL GWAS before (red) and after removing SNPs located in the HLA region (green).

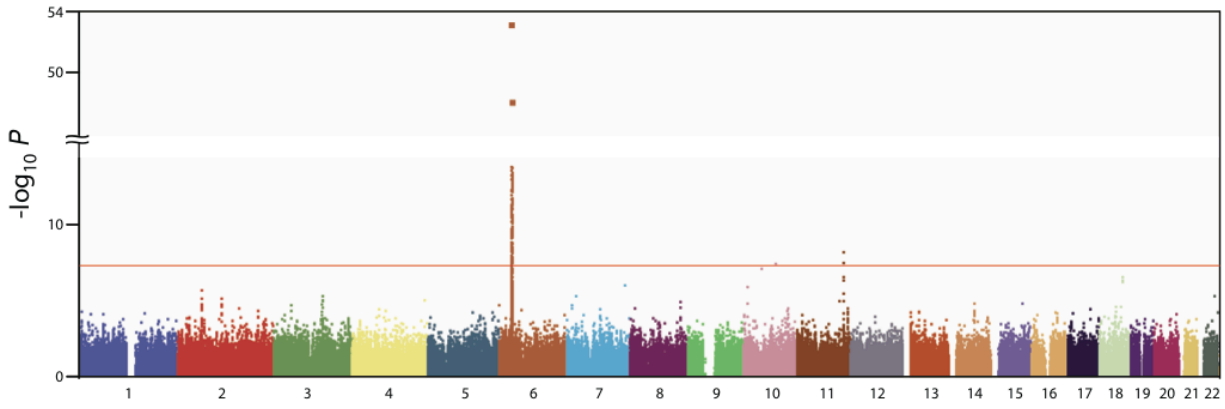
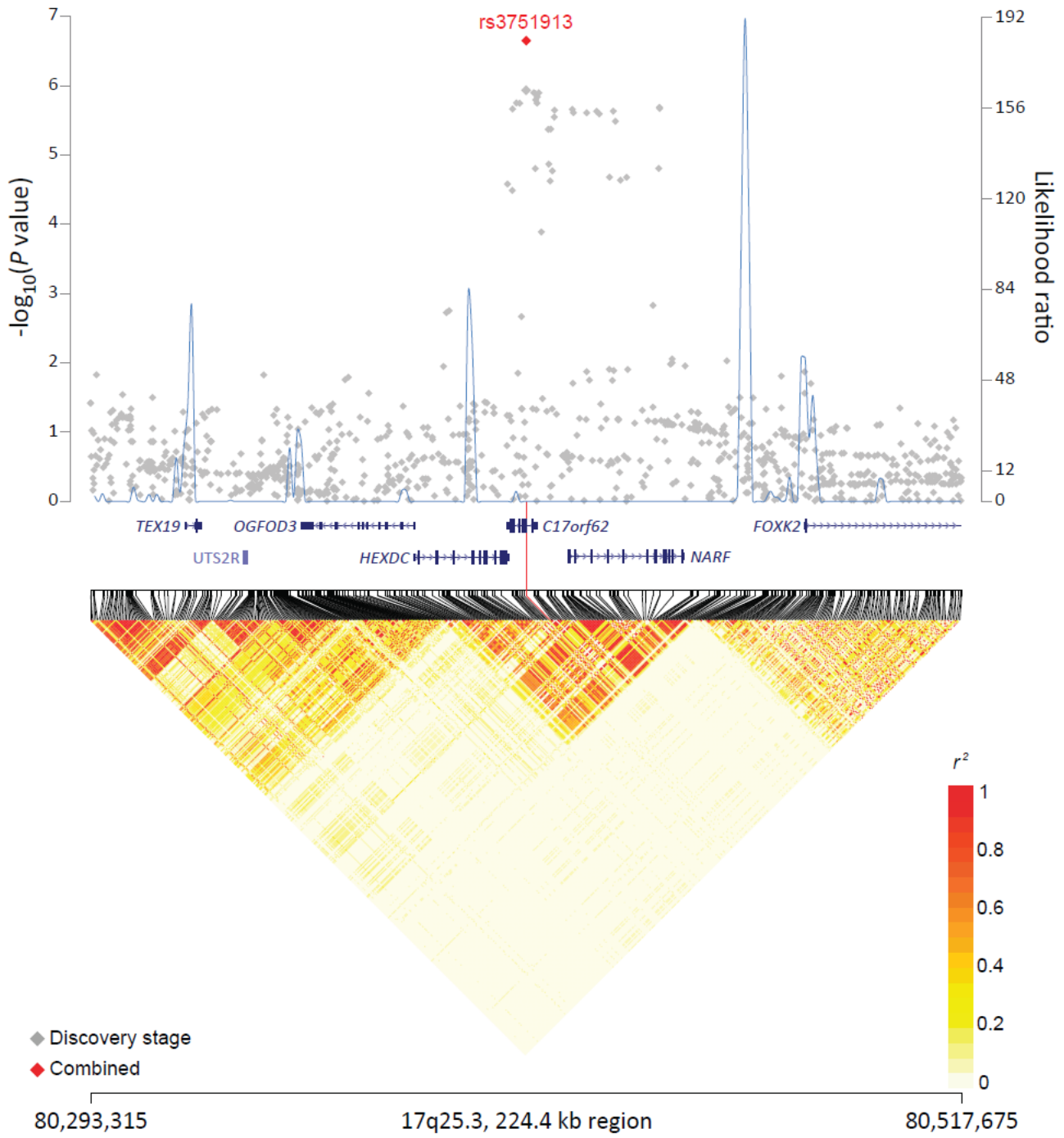
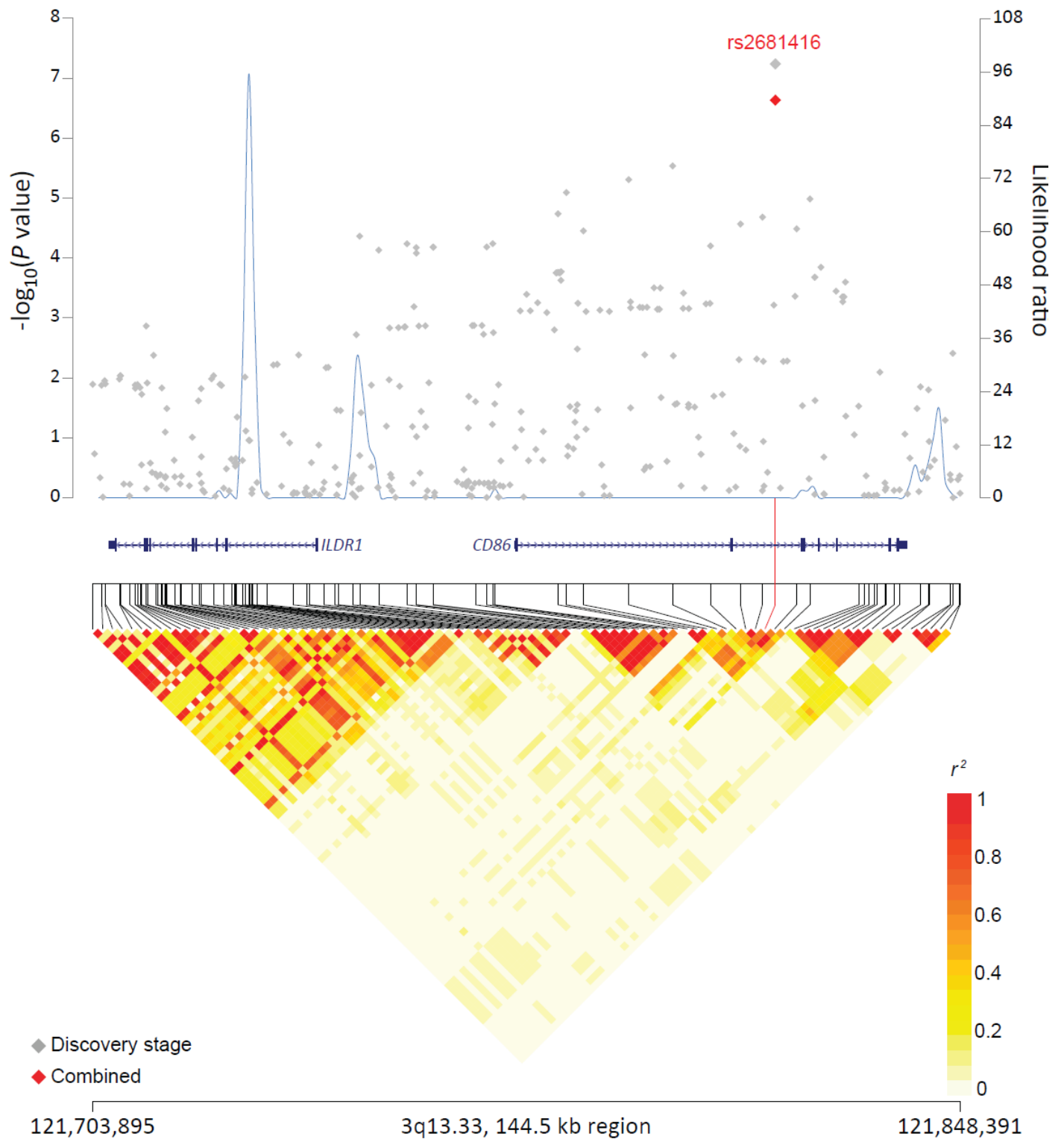


Figure S5. Genome-wide P -values for the association results from the NCI FL GWAS plotted against their respective chromosomal positions. Shown are the two-sided P -values obtained using the Cochran–Armitage trend test from 611,844 autosomal SNPs in 2,142 cases and 6,221 controls. The red horizontal line represents the genome-wide significance threshold level ($P < 5.0 \times 10^{-8}$).

A.



B.



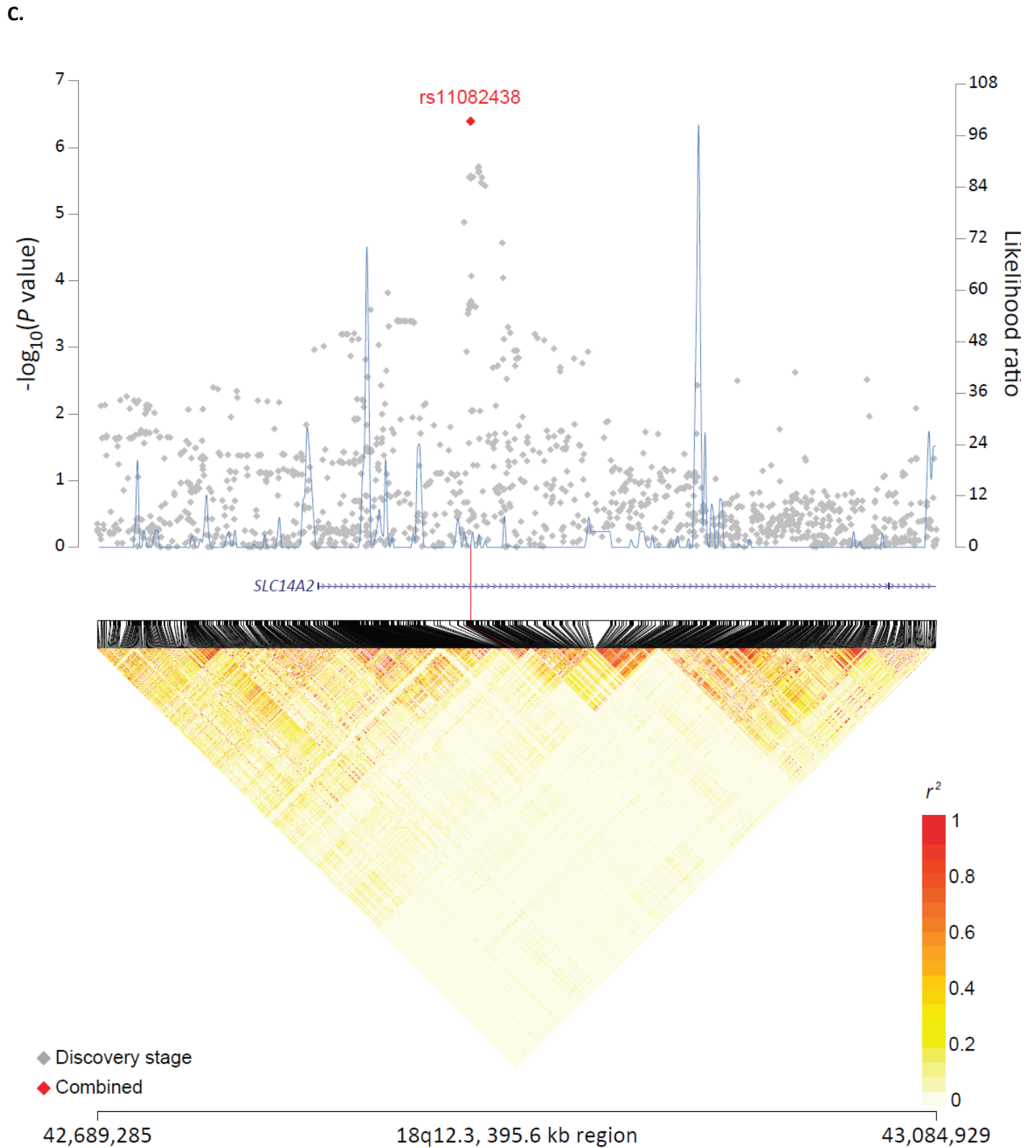


Figure S6A-C. Regional plots of the non-HLA regions approaching significance with risk of follicular lymphoma. The figure shows the association results from stage 1 (gray dots) and stages 1+2 combined (red diamond), recombination hotspots and LD plots for the associated loci: rs3751913 in 17q25.3 (A), rs2681416 in 3q13.33 (B), and rs11082438 in 18q12.3 (C).

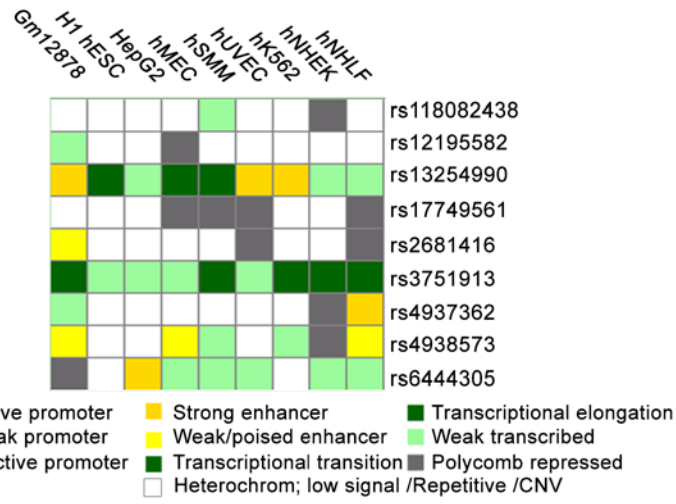
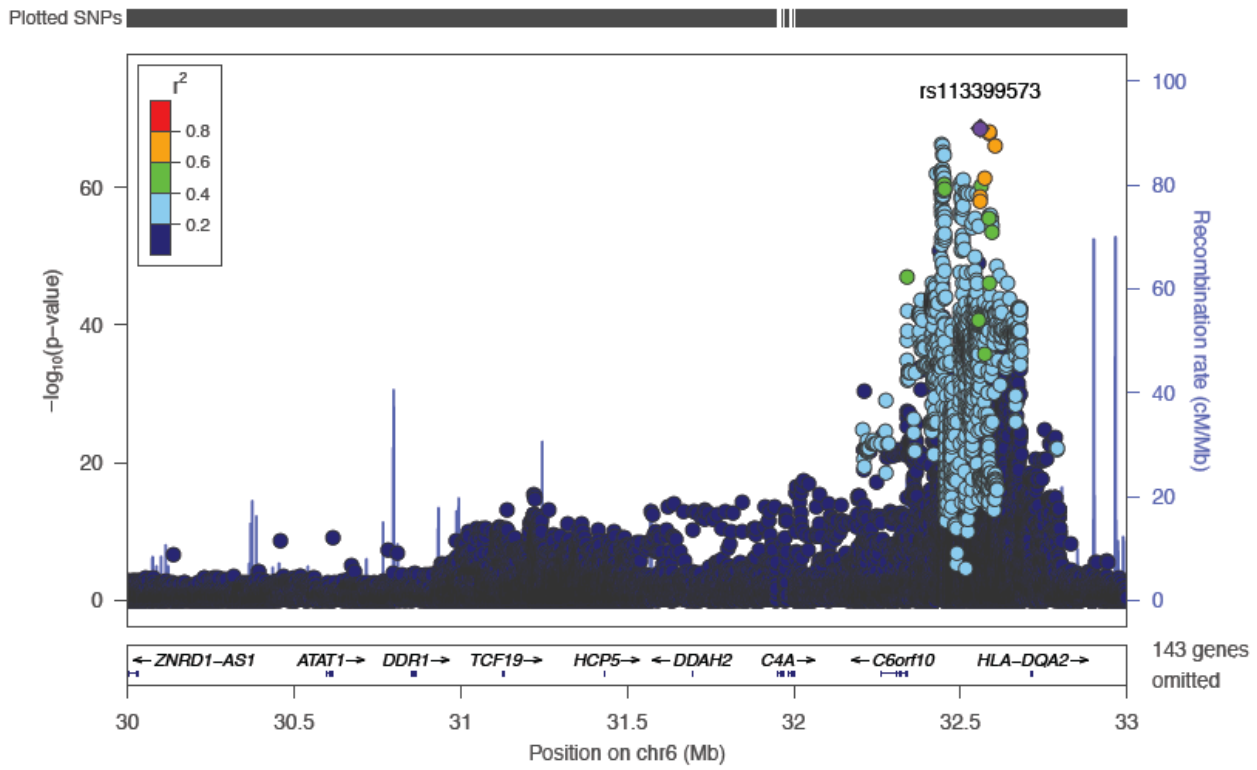


Figure S7. Chromatin states affected by follicular lymphoma associated SNPs.

A.

HLA region



B.

HLA Class I

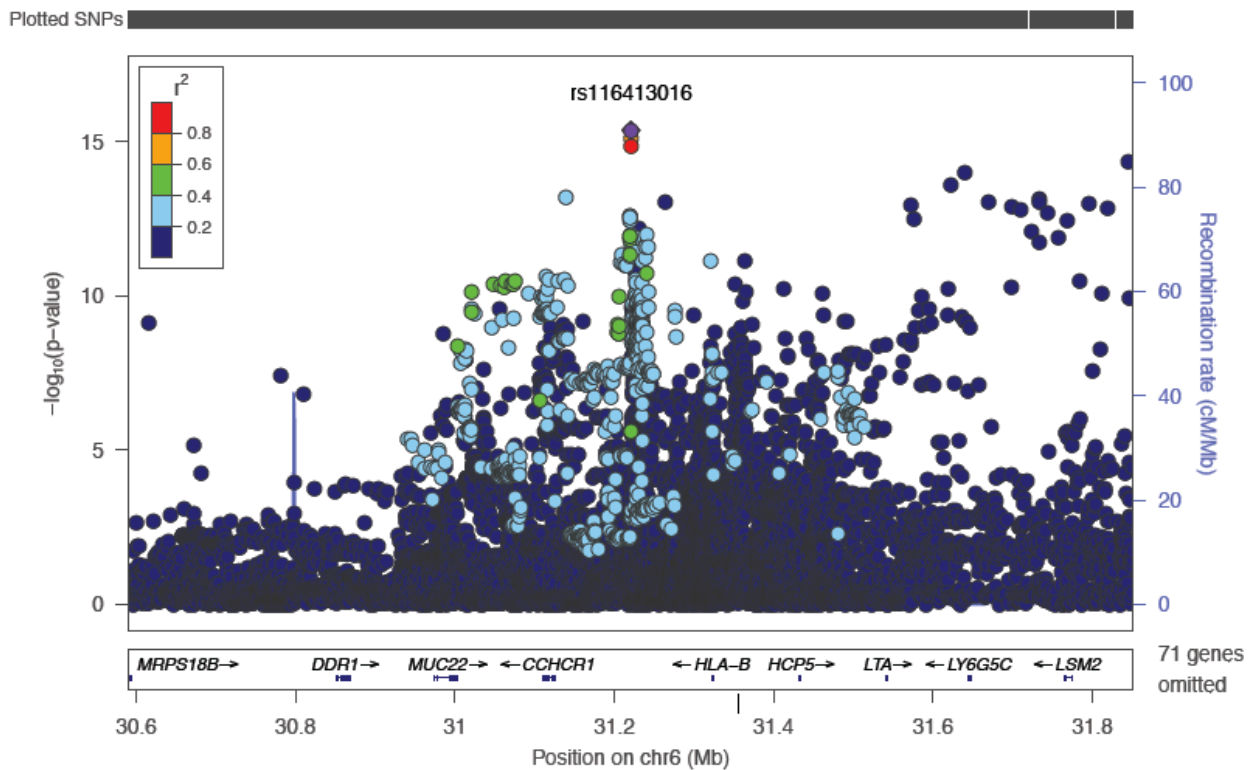


Figure S8A-B. Regional plots of the FL associated loci in the HLA region. Figure shows the association results for the HLA region (30-33Mb) (A), where the main association peak can be observed in the HLA Class II (32-33Mb), as well a zoom-in on the HLA Class I region (B), where a secondary peak can be observed approximately at 31-31.4Mb. SNPs are colored based on LD with the most significantly associated SNP in the region.

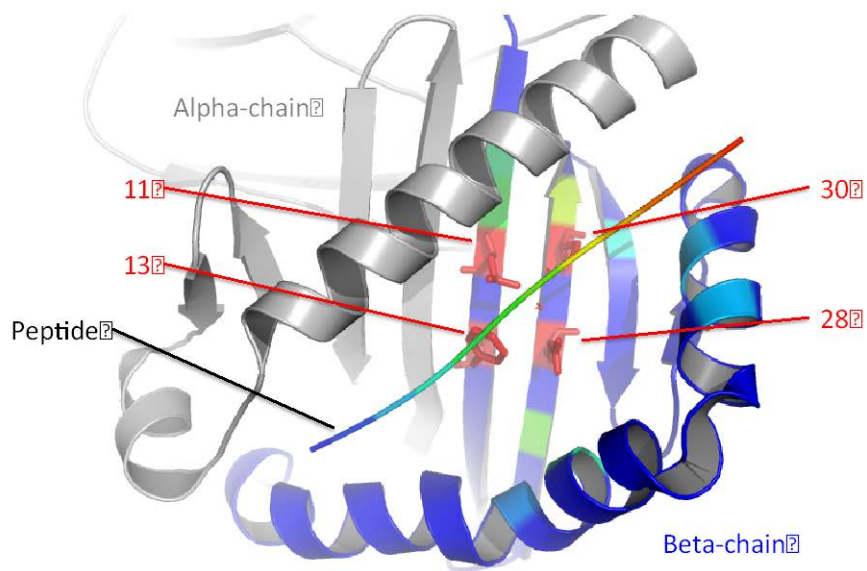


Figure S9. 3D-structural configuration of HLA-DRβ1 residues around the peptide binding groove. Amino acid residues at DRβ1 positions 11, 13, 28, and 30 are labeled and all have direct contact with the peptide in the binding groove.

2. SUPPLEMENTAL TABLES

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
Stage 1 – NCI FL GWAS						
Cohort Studies						
Alpha-Tocopherol, Beta-Carotene Lung Cancer Prevention Study ¹	ATBC	24	240 ^b	Nested case-control, Finland	Identified through linkage to the Finnish Cancer Registry	Cohort participants without a diagnosis of cancer
American Cancer Society Cancer Prevention Study-II Nutrition Cohort ²	CPS-II	161	220 ^b	Nested case-control, USA	Self-report through biannual questionnaires (starting in 1997). Verified by medical records or linkage to state cancer registry.	Cohort participants alive at time of case diagnosis without cancer
European Prospective Investigation into Cancer, Chronic Diseases, Nutrition and Lifestyles ^{3;4}	EPIC	53	773	Nested case-control, multiple European countries	Cases identified through population cancer registries in seven of the participating countries (Denmark, Italy, The Netherlands, Norway, Spain, Sweden and the UK) and through a combination of methods including health insurance records, cancer and pathology registries, and by active follow-up through study subjects and their next-of-kin in three countries (France, Germany and Greece).	Cohort participants matched by age, sex and study center who were alive and cancer-free at the time of diagnosis of the corresponding case
Health Professionals Follow-up Study ⁵	HPFS	5	86	Nested case-control, USA	Self-report through bi-annual questionnaires. Verified by medical records and pathology report	Cohort participants alive at time of case diagnosis without cancer, matched on date of birth, ethnicity, date and time of day of blood collection, and fasting status

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
The Melbourne Collaborative Cohort Study ⁶	MCCS	59	246	Nested case-control, Australia	Incident cases ascertained through national cancer registries	Controls were unaffected cohort participants
Nurses' Health Study ^{7;8}	NHS	25	90	Nested case-control, USA	Self-report through bi-annual questionnaires. Verified by medical records and pathology report	Cohort participants alive at time of case diagnosis without cancer, matched on date of birth, ethnicity, date and time of day of blood collection, and fasting status
New York University Women's Health Study ^{9;10}	NYU-WHS	13	56	Nested case-control, USA	Self-report through questionnaires every 2-4 years, confirmed by medical and pathology records; and linkages to tumor registries of NY, NJ and Florida and NDI	Cohort participants selected by incidence density sampling (alive and free of cancer at time of case diagnosis)
Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial ^{11;12}	PLCO	120	3076 ^b	Nested case-control, USA	Self-report through annual questionnaires. Verified by medical records and pathology report	Cohort participants alive at time of case diagnosis without cancer diagnosis

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
Women's Health Initiative ¹³	WHI	176	395	Nested case-control, USA	Self-report through semi-annual clinic visits or annual contact. Verified through medical records	Cohort participants without a diagnosis of cancer
Population-based case-control studies						
British Columbia Non-Hodgkin Lymphoma Study ¹⁴	BCCA	106	390	Population-based case-control study, Canada	First primary NHL diagnosis from Vancouver and Victoria metropolitan areas identified through the BC Cancer Registry (excluding HIV-infected and post-transplant cases)	Controls from the same areas, matched on area, age, and sex ascertained from the British Columbia Health Insurance files
Epidemiology & Genetics Unit Lymphoma Case-Control study ¹⁵⁻¹⁷	ELCCS	188	461	Population-based case-control study, UK	Cases were patients aged between 18-69 residing in predefined geographic areas and newly diagnosed with NHL between 1998 and 2003. Diagnoses were pathologically confirmed and coded to the WHO Classification for Oncology	For each case, one age- and sex-matched control was randomly selected from population based General practice registers
Multicenter Italian study on gene-environment interactions in lymphoma etiology: translational aspects	Italian GxE	11	54	Population-based case-control study, Italy	First primary NHL diagnosis identified in the Hematology Departments of the participating centres	Cohort participants alive at time of case diagnosis without cancer

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
National Cancer Institute-Surveillance, Epidemiology, and End Results Interdisciplinary Case-Control Study of Non-Hodgkin's Lymphoma ^{18;19}	NCI-SEER	235	689	Population-based case-control study, USA	First primary NHL diagnosis identified through 4 SEER registries (excluding HIV-infected cases)	Controls from the same areas, matched on area, age, and race ascertained through random digit dialing (<64 years of age) and CMMS files (≥65 years of age)
NSW non-Hodgkin lymphoma study ²⁰	NSW	158	397	Population-based case-control study, New South Wales (NSW) and Australian Capital Territory (ACT), Australia	Incident NHL diagnosis identified through NSW or ACT cancer registry (excluding HIV-infected cases and transplant recipients)	Controls randomly selected from electoral rolls, matched on age, sex and State of residence at diagnosis
Scandinavian Lymphoma Etiology Study ²¹	SCALE	0	301	Population-based case-control study, Scandinavia	Patients with incident primary NHL diagnosed through rapid case-ascertainment network in Sweden and Denmark	Frequency matched (age in 10 year intervals, sex and country) population controls prospectively identified every 6 months in nationwide population registers (incidence density sampling).
Molecular Epidemiology of non-Hodgkin lymphoma ²²	UCSF	7	10	Population-based case-control study, USA	RCA/SEER Incident NHL diagnosis for patients diagnosed in hospitals in 6 San Francisco Bay Area Counties and who were residents of the Bay Area at the time of diagnosis	Controls ascertained through RDD were frequency matched to cases on age in 5-year groups, sex and county of residence; Random sampling of CMS lists for person residing in the same 6 Bay Area counties were used to supplement recruitment of controls aged 65+

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
Population-based case-control study in Connecticut women ²³	Yale	104	504	Population-based case-control study, USA	First primary NHL diagnosis identified through the Rapid Case Shared Resources from all the hospitals in Connecticut	Population-based controls through random digit dialing for cases <65 years and Medicare files for ≥65 years
Clinic or hospital-based or mixed case-control studies						
Environmental and genetic risks factors study in adult lymphoma ²⁴	ENGELA	34	278	Hospital-based case-control study, France	Recent diagnosis of a NHL as per the WHO classification (ICD-O-3) / Cases with AIDS or on immunosuppressant drugs were not eligible. Path reports for 100%, slides review for selected NHL	Hospitalized in the same hospitals as the cases, for any reason except cancer, an accident or a disease directly related to the subject's occupation, smoking, or alcohol consumption. HIV negative.
EpiLymph case-control study in six European countries ²⁵	EpiLymph	136	1172	Multicenter case-control study, hospital-based and population-based, Europe	First primary lymphoma diagnosis (according to the 2001 WHO classification of lymphoma)	Controls from Germany and Italy were randomly selected by sampling from the general population, matched to cases on gender, 5-year age-group, and residence area. The rest of the centers used matched hospital controls, with eligibility criteria limited to diagnoses other than cancer, infectious diseases and immunodeficient diseases
Iowa-Mayo SPORE Molecular Epidemiology Resource ²⁶	Iowa-Mayo SPORE	233	0	Clinic-based case registry, USA	Consecutive patients with newly diagnosed, histologically-confirmed non-Hodgkin lymphoma (excluding HIV-infected cases) who were residents of US	N/A

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
Mayo Clinic Case-Control Study of NHL ²⁷	Mayo Case-Control	261	911	Clinic-based case-control study, USA	Consecutive patients with newly diagnosed, histologically-confirmed non-Hodgkin lymphoma (excluding HIV-infected cases) who were residents of Minnesota, Iowa or Wisconsin	Controls were selected from patients seen in the general medicine clinics at Mayo with a pre-scheduled general medical examination, frequency on age, sex, and geographic region
Memorial-Sloan Kettering Lymphoproliferative disorders Study ²⁸	MSKCC	206	9	Hospital-based case-study and NYCP controls, USA	Hospital clinic based ascertainment in a tertiary referral center	NYCP controls from same geographic area
Stage 1 - Previous GWAS						
Scandinavian Lymphoma Etiology Study ²¹	SCALE	580	800	Population-based case-control study, Scandinavia	Patients with incident primary NHL diagnosed through rapid case-ascertainment network in Sweden and Denmark	Frequency matched (age in 10 year intervals, sex and country) population controls prospectively identified every 6 months in nationwide population registers (incidence density sampling).

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
Molecular Epidemiology of non-Hodgkin lymphoma ²²	UCSF2	215	753	Population-based case-control study, USA	RCA/SEER Incident NHL diagnosis for patients diagnosed in hospitals in 6 San Francisco Bay Area Counties and who were residents of the Bay Area at the time of diagnosis	Controls ascertained through RDD were frequency matched to cases on age in 5-year groups, sex and county of residence; Random sampling of CMS lists for person residing in the same 6 Bay Area counties were used to supplement recruitment of controls aged 65+
Stage 2 - Replication studies						
Iowa-Mayo SPORE Molecular Epidemiology Resource ²⁶	Iowa-Mayo SPORE	105	0 ^c	Clinic-based case registry, USA	Consecutive patients with newly diagnosed, histologically-confirmed non-Hodgkin lymphoma (excluding HIV-infected cases) who were residents of US	N/A
Mayo Clinic Case-Control Study of NHL ²⁷	Mayo Case-Control	145	388	Clinic-based case-control study, USA	Consecutive patients with newly diagnosed, histologically-confirmed non-Hodgkin lymphoma (excluding HIV-infected cases) who were residents of Minnesota, Iowa or Wisconsin	Controls were selected from patients seen in the general medicine clinics at Mayo with a pre-scheduled general medical examination, frequency on age, sex, and geographic region
MD Anderson lymphoma case-control study	MD Anderson	541	542	Case-control, USA	MD Anderson Cancer Center	Kelsey Seybold Clinics
Memorial-Sloan Kettering Lymphoproliferative disorders Study ²⁹	MSKCC	403	376	Hospital-based case-study and NYCP controls, USA	Hospital clinic based ascertainment in a tertiary referral center	NYCP controls from same geographic area
NCI Replication Study ^{1-28; 30}	NCI Rep	605	4296	Mixed study of population, trial and hospital-based cases and controls	Follicular cases from the stage 1 studies that did not have sufficient DNA for scanning or failed in scanning due to low completion. Also includes 402 FL cases from a randomized clinical trial of advanced follicular lymphoma evaluating maintenance therapy with rituximab after induction of response with chemotherapy plus rituximab in comparison without maintenance therapy (PRIMA)	Controls from the stage 1 studies that were not scanned or failed scanning due to low completion.

Study Name	Study Abbreviation	No. FL Cases ^a	No. Controls ^a	Design, location	Source of cases	Source of controls
Molecular Epidemiology of non-Hodgkin lymphoma ^{22; 31; 32}	UCSF1/NHS	120	349	Case series with population controls	RCA/SEER Incident NHL diagnosis for patients diagnosed in hospitals in 6 San Francisco Bay Area Counties and who were residents of the Bay Area at the time of diagnosis	Participants from the Nurses' Health Study that were selected for a GWAS of endometrial cancer.

^aNumber of cases and controls with DNA available; however, not all subjects had sufficient DNA for scanning and/or Taqman genotyping. Only a subset of controls with DNA was selected for scanning in stage 1.

^bControls scanned previously on the Illumina Omni2.5.

^cNo controls were ascertained for this study. For the replication, the Iowa-Mayo SPORE and the Mayo Case-Control studies were considered to be a single study.

Table S1. Description and study design of studies included in stages 1 and 2.

This GWAS of FL was part of a larger initiative that included participants of European descent from 22 NHL studies including 9 prospective cohort studies, and 8 population-based and 5 clinic- or hospital-based case-control studies. All studies obtained informed consent from participants and approval from the respective Institutional Review Boards for this study. Cases were ascertained from cancer registries, clinics or hospitals or through self-report verified by medical and pathology reports. The phenotype information for all NHL cases was reviewed centrally at the International Lymphoma Epidemiology Consortium (InterLymph) Data Coordinating Center and harmonized according to the hierarchical classification proposed by the InterLymph Pathology Working Group based on the World Health Organization (WHO) classification (2008)^{33; 34}

Study	Sample QC				Genotyping and Imputation							
	No. of cases /controls in file	Inclusion/exclusion criteria		No.cases /controls after exclusions	Platform	Inclusion criteria for Imputation				SNPs that met QC criteria	Imputation Software	SNPs in meta-analysis
Minimum sample call rate for inclusion		Exclusions	Genotype calling algorithm			MAF	SNP Call rate*	P for HWE				
Stage 1: Discovery												
NCI	2301/6390 ^a	>=93%	1) Abnormal heterozygosity; 2) gender discordance; 3) unexpected duplicates; 4) Non CEU	2142/6221	Illumina OmniExpress	BeadStudio (GenCall)	>= 0.01	>=0.95	>=1e-6	611844	IMPUTE2	21554489 ^b
SCALE	379/791	>=95%	Unexpected duplicates	376/791	Illumina HumanHap 317K	BeadStudio (GenCall)	>= 0.01	>=0.95	>=1e-6	298045	IMPUTE2	14205416
UCSF2	213/751	>=95%	1) Abnormal heterozygosity; 2) PCA outlier	210/746	Illumina HumanCNV370-Duo	BeadStudio (GenCall)	>= 0.01	>=0.95	>=1e-6	290523	IMPUTE2	15085856
Stage 2: Replication												
UCSF1/NHS	120/349	>=95%	Incomplete phenotype	119/349	Illumina OmniExpress	BeadStudio (GenCall)	>= 0.01	>=0.95	>=1e-6	614320	IMPUTE2	12776022

^aA total of 3536 control subjects from ATBC, CPSII and PLCO cohorts that previously genotyped on Illumina Omni 2.5M chips were pooled into the NCI set.

^bUse both MAF>0.0001 and INFO>0.3 for post imputation SNP filtering. NCI set resulted in more SNPs being retained for analysis.

Table S2. Information on genotyping methods, quality control, imputation, and analysis for GWAS.

Study	Genotyped Subjects		Exclusions										Previously scanned		Final subjects included in the analysis		
			High missing rate		Heterozygosity		Gender discordance		Unexpected duplicates		Non CEU						
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls	Total
Cohort studies																	
ATBC	20		3											240	17	240	257
CPS-II	161		16				1		2		1			220	141	220	361
EPIC	47	275	1	9				1							46	265	311
HPFS	5	86		0								1			5	85	90
MCCS	59	76	1	1											58	75	133
NHS	25	90	1	2											24	88	112
NYU-WHS	13	56	1	3					1						11	53	64
PLCO	120		4						1					3076	115	3076	3191
WHI	176	250	13	19					1		1	3			161	228	389
Subtotal	626	833	40	34			1	1	5		2	4		3536	578	4330	4908
Population-based case-control studies																	
BCCA	106	110	7	1			1								98	109	207
ELCCS	188	251	6	5				1							182	245	427
Italian GxE	16	54		8				1							16	45	61
NCI-SEER	234	298	14	23	1		1	2			1	3			217	270	487
NSW	152	157	3	2			2	1			1				146	154	300
SCALE		299		6								2				291	291
UCSF	7	10		0											7	10	17
YALE	102	149	4	3											98	146	244
Subtotal	805	1328	34	48	1		4	5			2	5			764	1270	2034
Clinic or hospital-based or mixed case-control studies																	
ENGELA	34	77	4	14											30	63	93
EpiLymph	136	250	12	35						1	1	3			123	211	334
Iowa-Mayo SPORE	233		2	0								3			228		228
Mayo Case- Control	261	357	12	12					2	1	2	1			245	343	588
MSKCC	206	9	25	5			1					6			174	4	178
Subtotal	870	693	55	66			1		2	2	12	4			800	621	1421
Grand total	2301	2854	129	148	1		6	6	7	2	16	13		3536	2142	6221	8363

Table S3. Subjects genotyped, quality control exclusions, and final subjects included in the NCI FL GWAS

Study	No. of subjects		% Male		Mean age (SD)	
	Cases	Controls	Cases	Controls	Cases	Controls
STAGE 1: NCI FL GWAS						
ATBC	17	240	100.00%	100.00%	67.59 (6.00)	68.35 (7.67)
BCCA	98	109	44.90%	55.96%	58.68 (11.50)	60.70 (12.66)
CPSII	141	220	58.87%	49.55%	71.10 (6.75)	68.41 (6.28)
EPIC	46	265	39.13%	45.28%	60.48 (8.46)	62.65 (8.42)
Engela	30	63	53.33%	65.08%	51.83 (11.31)	55.25 (11.34)
Epilymph	123	211	44.72%	54.03%	57.19 (11.31)	59.31 (12.96)
HPFS	5	85	100.00%	100.00%	61.80 (6.82)	70.56 (8.43)
Iowa-Mayo SPORE	228	0	63.16%	NA	59.79(12.68)	NA
Italian GxE	16	45	37.50%	62.22%	52.44 (12.90)	55.38 (11.68)
Mayo case-control	245	343	52.24%	61.22%	59.93 (13.37)	60.90 (13.35)
MCCS	58	75	39.66%	52.00%	64.72 (10.86)	70.96 (7.85)
MSKCC	174	4	54.60%	0.00%	57.46 (12.19)	41.25 (9.36)
NCI-SEER	217	270	47.47%	54.07%	55.30 (12.07)	56.57 (11.94)
NHS	24	88	0.00%	0.00%	63.67 (5.80)	64.01 (6.91)
NSW	146	154	60.96%	60.39%	54.95 (9.93)	57.19 (11.13)
NYU-WHS	11	53	0.00%	0.00%	64.36 (9.40)	76.17 (9.20)
PLCO	115	3076	55.65%	95.68%	69.03 (6.73)	69.54 (6.19)
SCALE	0	291	0.00%	57.73%	NA	60.01(12.12)
UCSF	7	10	42.86%	60.00%	62.14 (10.67)	43.40 (14.83)
ELCCS	182	245	47.80%	50.61%	53.61 (7.33)	53.19 (8.19)
WHI	161	228	0.00%	0.00%	70.53 (6.41)	77.66 (6.58)
YALE	98	146	0.00%	0.00%	60.30 (12.33)	61.68 (13.47)
Total	2142	6221	45.75%	72.77%	60.30 (12.08)	66.04 (10.44)
STAGE 1: PREVIOUS GWAS						
SCALE	376	791	49.47%	31.73%	57.06 (9.47)	50.77 (11.56)
UCSF2	210	746	52.38%	57.64%	60.83 (11.88)	61.44 (13.00)
STAGE 2: REPLICATION						
UCSF1/NHS	119	349	51.26%	0.00%	58.81 (12.87)	62.52 (8.60)
MD Anderson	541	542	52.50%	52.40%	56.70 (10.87)	59.74 (10.48)
MSKCC	375	376	48.53%	18.09%	56.08 (12.53)	57.72 (11.77)
MAYO	250	385	52.80%	57.66%	60.58 (12.44)	62.32 (11.85)
NCI Replication	510	3934	50.59%	44.81%	57.82(12.11)	60.67(14.52)

Table S4. Characteristics of the cases and controls included in the final analysis for stages 1-2.

SNP	SNP location	SNP location with respect to nearest gene(s)	Observations
rs4938573	11q23.3	12.6kb upstream of <i>CXCR5</i>	<ul style="list-style-type: none"> <i>CXCR5</i> augments B-cell migration³⁵ and activation during B-cell receptor signaling³⁶ A previous study reported a suggestive association between FL risk and a weakly correlated SNP in the <i>CXCR5</i> region, rs1790192 ($r^2=0.25$)³⁷. In our study, mutual adjustment for both loci showed that rs4938573 is independently associated with FL risk (adjusted OR=1.30, $P=4.7 \times 10^{-12}$).
rs4937362	11q24.3	35kb upstream of <i>ETS1</i>	<ul style="list-style-type: none"> <i>ETS1</i> is a transcription factor and member of the ETS family. It is a negative regulator of Th17 and B-cell differentiation, is expressed in lymphoid cells and regulates the expression of several genes involved in lymphocyte survival and proliferation³⁸.
rs6444305	3q28	Overlapping <i>LPP</i> , 836.4 kb upstream of <i>BCL6</i>	<ul style="list-style-type: none"> <i>LPP</i> encodes a LIM domain-containing protein and participates in cell adhesion, cell migration, proliferation and transcription dynamics³⁹. rs6444305 is located 650.5kb from rs6773854 ($r^2=0.04$), a SNP in the <i>BCL6/LPP</i> region previously linked with risk of B-cell lymphoma and diffuse large B-cell lymphoma (DLBCL) in East Asian populations⁴⁰. In the current study, rs6773854 was not strongly associated with FL (OR=1.11, $P=0.01$).
rs17749561	18q21.33	7.4kb downstream of <i>BCL2</i>	<ul style="list-style-type: none"> <i>BCL2</i> is an anti-apoptotic oncogene, and a partner gene in the hallmark FL translocation t(14;18)(q32;q21) associated with <i>BCL2</i> over-expression⁴¹. rs17749561 is located near the major translocation breakpoint within the 3'UTR and it is in high linkage disequilibrium (LD) with rs4987855 ($r^2=0.86$), a chronic lymphocytic leukemia (CLL) risk allele⁴².
rs13254990	8q24.21	Intronic to <i>PVT1</i>	<ul style="list-style-type: none"> <i>PVT1</i> is a frequent site of translocations for Burkitt lymphoma, plasmacytomas⁴³ and aggressive B-cell lymphomas⁴⁴. Whereas rs13254990 is weakly correlated ($r^2 \leq 0.2$) with other nearby SNPs associated with Hodgkin lymphoma⁴⁵, CLL⁴⁶, and numerous solid cancers⁴⁷⁻⁵¹, it is in high LD with a DLBCL risk locus, rs13255292 ($r^2=0.93$) (<i>manuscript submitted</i>), suggesting a common susceptibility locus for FL and DLBCL.

Table S5. Characteristics of the non-HLA loci that showed genome-wide significance.

chr	pos (hg19)	LD (r ²)	LD (D')	variant	Ref	Alt	EUR freq	GERP cons	SiPhy cons	Promoter histone marks	Enhancer histone marks	DNAse	Proteins bound	eQTL tissues	Motifs changed	GENCODE genes	dbSNP func annot	
11	118725660	0.86	0.94	rs4936441	C	G	0.83									Evi-1, Nanog, PEBP	19kb 3' of Y_RNA	
11	118726753	0.87	-0.94	rs11217066	T	G	0.17									4 altered motifs	20kb 3' of Y_RNA	
11	118726843	0.87	-0.94	rs10892299	C	T	0.17										20kb 3' of Y_RNA	
11	118729456	0.89	0.95	rs10790269	C	T	0.82									Gfi1,HDAC2,Irf	23kb 3' of Y_RNA	
11	118734000	0.9	-0.96	rs11217074	T	C	0.17									4 altered motifs	20kb 5' of CXCR5	
11	118738298	0.96	0.99	rs7119044	G	C	0.83									8 altered motifs	16kb 5' of CXCR5	
11	118739056	0.95	0.98	rs7122669	A	G	0.82										15kb 5' of CXCR5	
11	118740104	0.93	0.98	rs201150316	AT	A	0.83									21 altered motifs	14kb 5' of CXCR5	
11	118740418	0.96	0.99	rs7951740	G	C	0.83			HepG2	HMEC, NHLF		HAE2F1			Ets,Zbtb3	14kb 5' of CXCR5	
11	118740864	0.96	0.99	rs4936443	C	T	0.82			HepG2, K562, GM12878	4 cell types	4 cell types	POL2, MAX			Zfx	14kb 5' of CXCR5	
11	118740931	0.96	0.99	rs4938572	C	T	0.82			HepG2, K562, GM12878	4 cell types	60 cell types	POL2, PBX3, MAX			4 altered motifs	14kb 5' of CXCR5	

11	118741157	0.97	1	rs7117261	T	C	0.83	HepG2, GM12878, HSMM	4 cell types	HepG2	GR, POL2	EWSR1-FLI1, Ets, NF- kappaB	13kb 5' of CXCR5
11	118741842	1	1	rs4938573	C	T	0.82	GM12878, HMEC, NHLF		Th1		4 altered motifs	13kb 5' of CXCR5
11	118742724	0.83	0.99	rs7125333	T	C	0.8	GM12878				6 altered motifs	12kb 5' of CXCR5
11	118742800	0.98	-1	rs74541740	G	A	0.18	GM12878				23 altered motifs	12kb 5' of CXCR5
11	118743286	0.82	-0.99	rs12365699	G	A	0.15	GM12878	13 cell types		7 bound proteins	HNF4, NRSF, ZID	11kb 5' of CXCR5
11	118743338	0.97	0.99	rs4936444	T	C	0.82	GM12878	9 cell types		4 bound proteins		11kb 5' of CXCR5
11	118743772	0.96	0.98	rs6421571	T	C	0.82	GM12878	AG04449				11kb 5' of CXCR5
11	118744396	0.94	0.97	rs7117313	C	G	0.82					NRSF, TATA, Zfx	10kb 5' of CXCR5
11	118744701	0.83	0.95	rs13825239 3	A	AAA AG	0.81					EWSR1-FLI1, HDAC2, p300	9.8kb 5' of CXCR5
11	118745243	0.96	1	rs7481797	A	G	0.83					LXR, Nkx2	9.2kb 5' of CXCR5
11	118745278	0.96	1	rs7481819	C	T	0.83					4 altered motifs	9.2kb 5' of CXCR5
11	118745884	0.95	0.99	rs10790275	G	C	0.83					Znf143	8.6kb 5' of CXCR5
11	128488322	0.8	0.98	rs2156698	G	A	0.56						RP11- 264E20.1

11	128489380	0.99	1	rs4245081	C	T	0.61	GM12878	iPS		HNF4, RXR::LXR	RP11- 264E20.1	
11	128489535	0.92	1	rs4245082	C	T	0.59	GM12878			7 altered motifs	RP11- 264E20.1	
11	128489818	0.99	1	rs4492838	C	T	0.6	GM12878	7 cell types	NFKB, GATA2	BDP1,Hsf	RP11- 264E20.1	
11	128491023	0.98	0.99	rs11221396	C	T	0.61	GM12878, HSMM	GM19240		4 altered motifs	RP11- 264E20.1	
11	128492401	0.99	1	rs10893897	T	C	0.6	NHLF, HSMM	6 cell types		Gfi1,RFX5	689bp 5' of RP11- 264E20.1	
11	128492571	1	1	rs11221397	G	T	0.61	NHLF, HSMM			6 altered motifs	859bp 5' of RP11- 264E20.1	
11	128492739	1	1	rs4937362	T	C	0.61	NHLF	LNCaP, 8988T, Adult_CD4_ Th0		5 altered motifs	1kb 5' of RP11- 264E20.1	
11	128494441	0.9	0.97	rs7105899	G	A	0.61	GM12878, H1	15 cell types	NFKB,CEBPB	9 altered motifs	2.7kb 5' of RP11- 264E20.1	
3	188298562	0.98	0.99	rs9878956	C	G	0.72		HL-60,NH-A		9 altered motifs	LPP	intronic
3	188298688	0.98	0.99	rs9823790	T	C	0.72		HL-60		Sox	LPP	intronic
3	188298989	0.99	1	rs1849913	G	A	0.72	HepG2			4 altered motifs	LPP	intronic
3	188299423	0.99	1	rs1849911	A	C	0.72	HepG2	RPTEC	HNF4A, HNF4G, P300	Myc,Pax- 5,Pax-8	LPP	intronic
3	188299793	0.99	1	rs6444303	A	G	0.72	HepG2	5 cell types			LPP	intronic

3	188299819	0.99	1	rs6444304	C	A	0.72		HepG2	4 cell types		COMP1	LPP	intronic
3	188299902	1	1	rs6444305	G	A	0.72		HepG2			PRDM1,TATA	LPP	intronic
3	188300051	0.96	1	rs13063967	C	A,T	0.71		HepG2				LPP	intronic
18	60783211	1	1	rs17749561	G	A	0.11					Irf,NF-kappaB	7.4kb 3' of BCL2	
18	60783729	1	1	rs17676919	A	G	0.11					Brachyury,FA C1,Myc	6.8kb 3' of BCL2	
18	60785638	1	1	rs17676949	G	A	0.11						4.9kb 3' of BCL2	
18	60788745	0.96	1	rs77551289	A	G	0.11					Foxp1,GATA	1.8kb 3' of BCL2	
18	60793494	0.95	0.99	rs4987856	C	T	0.11		CD34+_Mobilized, HIPEpiC			Pax-5	BCL2	3'-UTR
18	60793549	0.95	0.99	rs4987855	C	T	0.11		CD34+_Mobilized, HIPEpiC			4 altered motifs	BCL2	3'-UTR
18	60795188	0.92	0.96	rs4987845	C	T	0.11					Pax-5,RXRA	BCL2	3'-UTR
8	129076451	1	1	rs13254990	C	T	0.36		K562, Huvec, GM12878	6 cell types	USF2, NFKB, CMYC	Pax-5,Pou3f1	PVT1	intronic
8	129076573	0.92	0.98	rs13255292	C	T	0.37		K562, Huvec, GM12878	14 cell types	8 bound proteins	Arnt,SP1	PVT1	intronic
17	80402045	0.93	0.98	rs67228117	T	C	0.13		HMEC			ERalpha-a,Esr2,Rad21	C17orf62	intronic
17	80403059	0.99	1	rs60482040	C	G	0.12		LNCaP,Ishikawa		ERALPHA_A, POL2	4 altered motifs	C17orf62	intronic

17	80403894	0.98	0.99	rs2291394	G	A	0.12	HSMM	10 altered motifs	C17orf62	intronic			
17	80405552	1	1	rs3751913	T	C	0.12		6 altered motifs	C17orf62	intronic			
17	80407480	0.99	1	rs60529510	C	T	0.12	4 cell types	4 cell types	11 cell types	19 bound proteins	GR	C17orf62	5'-UTR
17	80407948	0.98	0.99	rs12450191	C	T	0.12	9 cell types				9 altered motifs	C17orf62	intronic
17	80407978	0.98	0.99	rs12450192	C	T	0.12	9 cell types		GM12864,H L-60		Myc	C17orf62	intronic
17	80408348	0.98	0.99	rs9911854	A	G	0.12	9 cell types		30 cell types	5 bound proteins	BHLHE40	C17orf62	intronic
17	80408419	0.98	0.99	rs9912066	A	C	0.12	9 cell types		31 cell types	8 bound proteins	NRSF,Sin3Ak- 20	C17orf62	5'-UTR
17	80408815	0.96	0.99	rs9303029	C	T	0.12	8 cell types	H1	80 cell types	15 bound proteins	11 altered motifs	109bp 5' of C17orf62	
17	80410445	0.96	0.99	rs20202010 0	G	GAC T	0.12		K562	Th1		ATF3,HNF6	1.7kb 3' of RP13-20L14.6	
17	80410447	0.96	0.99	rs14596373 5	C	CTA A	0.12		K562	Th1		ATF3,HNF6	1.7kb 3' of RP13-20L14.6	
17	80411207	0.92	0.99	rs9896620	C	G	0.13		K562	K562	TAL1	NF-AT,YY1	941bp 3' of RP13-20L14.6	
17	80411883	0.93	0.98	rs58441535	A	G	0.13			HCT- 116,WERI- Rb-1			265bp 3' of RP13-20L14.6	
17	80412797	0.94	0.99	rs79487483	A	G	0.13					E2F,TBX5,Zfx	RP13-20L14.6	
17	80412867	0.96	0.99	rs72857495	A	C	0.12						RP13-20L14.6	

17	80417443	0.98	0.99	rs72859113	G	C	0.12	8 cell types Huvec GM12878 Huvec, HepG2, K562 K562	K562	NARF	intronic	
17	80417729	0.98	0.99	rs78720068	C	G	0.12		STAT,TR4	NARF	intronic	
17	80421110	0.95	0.99	rs72859120	C	T	0.12		Cart1,Hsf,Pdx 1	NARF	intronic	
17	80423712	0.95	0.99	rs12450240	G	T	0.12		NARF	intronic		
17	80424386	0.96	0.99	rs9891900	T	G	0.12		5 altered motifs	NARF	intronic	
17	80427975	0.96	0.99	rs72859125	G	A	0.12		Crx,Pitx2	NARF	intronic	
17	80428532	0.96	0.99	rs12600876	G	A	0.12		4 altered motifs	NARF	intronic	
17	80429066	0.96	0.99	rs11153377 g	TC	T	0.12		6 altered motifs	NARF	intronic	
17	80439907	0.94	0.98	rs9898723	A	G	0.12		HL-60,SAEC	Fibrobl	NARF	intronic
17	80439925	0.94	0.98	rs9905527	T	C	0.12	Fibrobl	NARF	intronic		
3	121817613	1	1	rs2681416	G	A	0.28	GM12878	Th2	Zbtb12	CD86	intronic
18	42865210	1	1	rs11082438	G	T	0.05		FibroP	5 altered motifs	217kb 3' of SETBP1	intronic
18	42866471	0.94	1	rs11660485	A	C	0.04			Pou1f1	218kb 3' of SETBP1	intronic

Table S6. Results from HaploReg analysis of newly discovered and promising follicular lymphoma risk loci outside HLA and their correlated ($r^2 > 0.80$) surrogates.

AA/Allele/SNP	Study	Effect allele ^a	Other allele ^a	EAf ^b	Information ^c	OR	95% CI	P	P _{het}
AA DRβ1 28 Asp	NCI	P	A	0.684	0.999	0.51	(0.47-0.55)	1.54E-61	
AA DRβ1 28 Asp	UCSF2	P	A	0.676	1.003	0.68	(0.54-0.86)	0.001	
AA DRβ1 28 Asp	SCALE	P	A	0.712	0.976	0.60	(0.49-0.74)	1.34E-06	
AA DRβ1 28 Asp	UCSF1/NHS	P	A	0.683	0.990	0.42	(0.29-0.60)	2.61E-06	
AA DRβ1 28 Asp	Combined					0.53	(0.50-0.57)	6.10E-72	0.03
AA DRβ1 28 Glu	NCI	P	A	0.304	1.006	1.95	(1.80-2.11)	1.78E-60	
AA DRβ1 28 Glu	UCSF2	P	A	0.315	0.996	1.45	(1.15-1.82)	0.002	
AA DRβ1 28 Glu	SCALE	P	A	0.262	0.995	1.57	(1.27-1.94)	2.28E-05	
AA DRβ1 28 Glu	UCSF1/NHS	P	A	0.308	1.007	2.32	(1.61-3.34)	5.92E-06	
AA DRβ1 28 Glu	Combined					1.86	(1.74-2.00)	7.99E-69	0.02
HLA-DRB1*01	NCI	P	A	0.137	1.003	1.89	(1.71-2.10)	9.56E-35	
HLA-DRB1*01	UCSF2	P	A	0.144	1.025	1.68	(1.27-2.24)	0.0003	
HLA-DRB1*01	SCALE	P	A	0.125	0.992	1.71	(1.30-2.25)	0.0001	
HLA-DRB1*01	UCSF1/NHS	P	A	0.129	1.044	1.92	(1.22-3.03)	0.005	
HLA-DRB1*01	Combined					1.85	(1.70-2.03)	2.57E-42	0.81

^aP=presence of allele, A=absence of allele

^bEAf=effect allele frequency

^cInformation is the imputation quality score (r^2) from Beagle

Table S7. Top HLA amino acid and allele associations from the univariate analysis of HLA imputations.

AA Position	df	P_upperbound	P_lowerbound
AA DRB1 11	5	8.35e-70	5.41e-70
AA DRB1 13	5	4.11e-70	2.67e-70
AA DRB1 28	2	3.84e-67	2.49e-67
AA DRB1 30	4	4.20e-66	2.72e-66

Table S8. Global omnibus tests for associations between follicular lymphoma risk and DR β 1 AA positions at 11, 13, 28 and 30.

DRB1 Allele	Frequency	Amino acid position				FL association model			<i>P</i>
		11	13	28	30	OR	95% CI lower	95% CI upper	
*01	0.137	L	F	E	C	1.85	1.70	2.02	2.91E-42
*03:01	0.119	S	S	D	Y	0.89	0.81	0.99	2.55E-02
*04	0.16	V	H	D	Y	1.04	0.96	1.14	3.20E-01
*07:01	0.14	G	Y	E	L	1.52	1.39	1.66	1.59E-20
*08:01	0.024	S	G	D	Y	0.82	0.66	1.03	8.28E-02
*09:01	0.012	D	F	H	G	1.34	1	1.79	5.03E-02
*10:01	0.009	V	F	E	R	NA	NA	NA	NA
*11	0.09	S	S	D	Y	0.62	0.55	0.71	3.59E-13
*12:01	0.018	S	S	E	H	1.21	0.96	1.52	1.12E-01
*13	0.112	S	S	D	Y	0.56	0.50	0.63	5.32E-22
*14:01	0.022	S	S	D	Y	0.80	0.62	1.02	7.22E-02
*15:01	0.124	P	R	D	Y	0.67	0.60	0.74	1.01E-13
*16:01	0.015	P	R	D	Y	0.88	0.66	1.18	3.95E-01

Table S9. Follicular lymphoma (FL)-associated amino acid positions in HLA-DRβ1. Residue combinations of the DRβ1 amino acid positions 11, 13, 28, and 30 were associated with an increased risk of FL. Each DRB1 allele is shown with the observed frequency in controls and the amino acids carried by that allele, found in the IMMunoGeneTics/HLA Database, Release 3.15.0 (<http://www.ebi.ac.uk/ipd/imgt/hla/>).

LOCUS	GROUP	EFFECT ALLELE	REF ALLELE	EFFECT ALLELE FREQ	INFO	OR	95%CI lower	95%CI upper	P	P heterog.	I ²
Step 0: Unconditional association analysis											
AA DRB1 Glu-28	NCI	P	A	0.3039	1.0065	1.946	1.797	2.107	1.63E-60		
AA DRB1 Glu-28	SF	P	A	0.3149	0.996	1.45	1.152	1.824	0.00155		
AA DRB1 Glu-28	SCALE	P	A	0.2621	0.9946	1.565	1.27	1.928	2.62E-05		
AA DRB1 Glu-28	SF2	P	A	0.3087	1.0049	2.329	1.618	3.352	5.38E-06		
AA DRB1 Glu-28	NCI+SCALE+SF+SF2					1.861	1.736	1.995	7.89E-69	1.98E-02	69.56
AA DRB1 His-28	NCI	P	A	0.0122	0.9688	1.211	0.864	1.697	0.2661		
AA DRB1 His-28	SCALE	P	A	0.0253	0.9618	1.78	0.999	3.174	0.05048		
AA DRB1 His-28	NCI+SCALE					1.336	0.998	1.787	5.16E-02	2.59E-01	21.56
rs17203612	NCI	A	T	0.488	0.9648	1.903	1.759	2.059	9.39E-58		
rs17203612	SF	A	T	0.5092	0.9752	1.439	1.15	1.802	0.00148		
rs17203612	SCALE	A	T	0.5025	0.8121	1.769	1.431	2.187	1.34E-07		
rs17203612	SF2	A	T	0.4952	0.9015	1.833	1.271	2.643	0.00117		
rs17203612	NCI+SCALE+SF+SF2					1.837	1.715	1.968	4.57E-67	1.43E-01	44.79
rs3130437	NCI	A	C	0.6162	1.0059	1.288	1.192	1.393	1.72E-10		
rs3130437	SF	A	C	0.6429	1.0312	1.673	1.309	2.139	3.91E-05		
rs3130437	SCALE	A	C	0.5857	0.9768	1.296	1.069	1.57	0.00811		
rs3130437	SF2	A	C	0.6585	1.0378	1.859	1.278	2.703	0.00118		
rs3130437	NCI+SCALE+SF+SF2					1.332	1.244	1.425	1.59E-16	6.77E-02	57.96
Step 1: Conditional association analysis (conditioning on both AA DRB1 Glu-28 and AA DRB1 His-28)											
rs17203612	NCI	A	T	0.488	0.9647	1.469	1.328	1.624	6.55E-14		
rs17203612	SF	A	T	0.5092	0.9752	1.247	0.941	1.652	0.1245		
rs17203612	SCALE	A	T	0.5025	0.8121	1.504	1.166	1.939	0.00164		
rs17203612	SF2	A	T	0.4952	0.9015	1.087	0.678	1.743	0.7278		
rs17203612	NCI+SCALE+SF+SF2					1.435	1.315	1.566	4.59E-16	4.53E-01	0
rs3130437	NCI	A	C	0.6162	1.006	1.191	1.1	1.29	1.72E-05		
rs3130437	SF	A	C	0.6429	1.0312	1.675	1.308	2.145	4.45E-05		
rs3130437	SCALE	A	C	0.5857	0.9768	1.225	1.007	1.491	0.04234		
rs3130437	SF2	A	C	0.6585	1.0378	1.617	1.098	2.38	0.01487		
rs3130437	NCI+SCALE+SF+SF2					1.241	1.157	1.33	1.32E-09	3.75E-02	64.53

Step 2: Conditional association analysis (conditioning on AA DRB1 Glu-28, AA DRB1 His-28 and rs114137077)										
rs3130437	NCI	A	C	0.6162	1.006	1.179	1.088	1.277	5.82E-05	
rs3130437	SF	A	C	0.6429	1.0312	1.672	1.305	2.144	4.94E-05	
rs3130437	SCALE	A	C	0.5857	0.9768	1.208	0.992	1.472	0.06061	
rs3130437	SF2	A	C	0.6585	1.0378	1.629	1.105	2.401	0.01371	
rs3130437	NCI+SCALE+SF+SF2					1.229	1.145	1.318	8.23E-09	2.92E-02 66.7

Table S10. Results of HLA forward stepwise conditional analysis.

SNP	Position	Study	Genotyped or imputed (info)	No. of cases/ controls	Effect allele/ other allele	EAF	OR	(95%CI)	P	<i>P</i> conditioned on DRB1 position 28, rs17203612 and rs3130437	Reference
rs6457327	31074030	NCI	g	2142/6221	C/A	0.617	1.21	(1.12-1.31)	1.22E-06	0.10	(OR=1.68, P=4.7x10 ⁻¹¹) ⁵²
		UCSF2	g	210/746	C/A	0.636	1.56	(1.25-1.96)	0.0001		
		SCALE	g	376/791	C/A	0.560	1.23	(1.02-1.48)	0.03		
		UCSF1/NHS	i (0.998)	118/349	C/A	0.638	1.58	(1.12-2.24)	0.01		
		Combined		2846/8107			1.25	(1.17-1.34)	3.96E-11		
rs3132453	31604044	NCI	g	2142/6221	G/T	0.933	1.24	(1.06-1.44)	0.006	0.26	(OR=1.69, P=1.26x10 ⁻⁶) ⁵³
		UCSF2	g	210/746	G/T	0.937	1.71	(1.05-2.78)	0.03		
		SCALE	g	376/791	G/T	0.920	1.34	(0.94-1.92)	0.11		
		UCSF1/NHS	i (0.862)	119/348	G/T	0.943	1.18	(0.56-2.47)	0.66		
		Combined		2847/8106			1.28	(1.12-1.46)	0.0003		
rs9268853	3242643	NCI	g	2142/6221	C/T	0.306	1.4	(1.29-1.51)	3.03E-17	0.03	(OR=1.56, P=2.48x10 ⁻¹⁰) ²⁹
		UCSF2	i (0.999)	210/746	C/T	0.339	1.05	(0.84-1.32)	0.66		
		SCALE	i (0.998)	376/790	C/T	0.310	1.31	(1.09-1.58)	0.005		
		UCSF1/NHS	i (0.997)	119/348	C/T	0.306	1.72	(1.19-2.48)	0.004		
		Combined		2847/8105			1.36	(1.27-1.45)	2.71E-19		
rs2647012	32664458	NCI	i (1)	2142/6221	C/T	0.601	1.58	(1.46-1.71)	1.14E-31	0.34	(OR=1.56, P=1.56x10 ⁻²¹) ⁵⁴
		UCSF2	g	210/746	C/T	0.637	1.35	(1.07-1.70)	0.01		
		SCALE	g	376/791	C/T	0.564	1.62	(1.34-1.96)	6.45E-07		
		UCSF1/NHS	i (0.992)	119/348	C/T	0.603	1.77	(1.25-2.51)	0.001		
		Combined		2847/8106			1.57	(1.47-1.68)	2.95E-40		
rs10484561	32665420	NCI	i (1)	2141/6221	G/T	0.121	1.87	(1.68-2.07)	3.11E-31	0.02	(OR=1.95, P=1.12x10 ⁻²⁹) ⁵⁵
		UCSF2	i (1)	210/746	G/T	0.131	1.83	(1.35-2.47)	9.66E-05		
		SCALE	g	376/791	G/T	0.114	1.71	(1.31-2.23)	7.61E-05		
		UCSF1/NHS	i (1)	119/349	G/T	0.109	2.11	(1.32-3.38)	0.002		
		Combined		2846/8107			1.85	(1.69-2.03)	5.15E-40		

rs2621416	32741868	NCI	g	2142/6221	C/T	0.276	1.42	(1.31-1.55)	3.21E-17		
		UCSF2	i (0.981)	210/745	C/T	0.272	1.3	(1.01-1.65)	0.04		
		SCALE	i (0.979)	376/790	C/T	0.281	1.36	(1.11-1.67)	0.003		
		UCSF1/NHS	i (0.950)	119/349	C/T	0.262	1.59	(1.08-2.35)	0.02		
		Combined		2847/8105			1.41	(1.31-1.51)	4.96E-21	0.60	(OR=1.57, P=2.41×10 ⁻⁹) ²⁹
rs241447	32796751	NCI	g	2142/6221	C/T	0.269	1.32	(1.21-1.43)	3.55E-11		
		UCSF2	g	210/746	C/T	0.265	1.34	(1.06-1.71)	0.02		
		SCALE	g	376/791	C/T	0.243	1.19	(0.96-1.48)	0.11		
		UCSF1/NHS	g	119/349	C/T	0.274	1.6	(1.10-2.32)	0.01		
		Combined		2847/8107			1.32	(1.22-1.41)	5.48E-14	0.67	(OR=1.82, P=6.9 × 10 ⁻⁸) ⁵⁶
DRB1*0101		NCI	i (0.975)	2142/6221	P/A	0.107	1.92	(1.71-2.16)	1.32E-28		
		UCSF2	i (1.000)	210/746	P/A	0.102	1.68	(1.20-2.36)	0.003		
		SCALE	i (1.005)	376/791	P/A	0.114	1.66	(1.26-2.20)	0.0004		
		UCSF1/NHS	i (1.009)	119/349	P/A	0.090	1.84	(1.07-3.17)	0.03		
		Combined		2847/8107	P/A		1.86	(1.69-2.06)	4.28E-34	5.45E-03	(OR=2.14, P<0.001) ⁵⁷
DPB1*0301		NCI	i (0.898)	2142/6221	P/A	0.102	0.49	(0.40-0.60)	6.78E-13		
		UCSF2	i (0.952)	210/746	P/A	0.094	0.55	(0.30-1.02)	0.06		
		SCALE	i (0.899)	376/791	P/A	0.094	0.59	(0.39-0.91)	0.02		
		UCSF1/NHS	i (0.785)	119/349	P/A	0.110	0.7	(0.33-1.49)	0.35		
		Combined		2847/8107	P/A		0.52	(0.44-0.61)	6.83E-15	5.58E-05	(OR=0.39, P=4.61× 10 ⁻⁴) ⁵⁸
DRB1*13 (*1301, *1302, *1303)		NCI	i (0.985)	2142/6221	P/A	0.112	0.55	(0.48-0.63)	8.26E-18		
		UCSF2	i (0.984)	210/746	P/A	0.096	0.7	(0.46-1.05)	0.08		
		SCALE	i (0.987)	376/791	P/A	0.119	0.53	(0.38-0.74)	0.0002		
		UCSF1/NHS	i (0.906)	119/349	P/A	0.106	0.59	(0.33-1.08)	0.09		
		Combined		2847/8107	P/A		0.56	(0.50-0.63)	5.79E-22	4.91E-05	(OR=0.48, P=0.008) ⁵⁸
AA_DRB1_13 32660109_YF		NCI	i (0.998)	2142/6221	P/A	0.297	1.96	(1.81-2.13)	1.20E-60		

	UCSF2	i (1.024)	210/746	P/A	0.304	1.49	(1.18-1.87)	0.0007		
	SCALE	i (0.966)	376/791	P/A	0.264	1.67	(1.35-2.06)	2.26E-06		
	UCSF1/NHS	i (1.028)	119/349	P/A	0.292	2.18	(1.53-3.12)	1.89E-05		
	Combined		2847/8107	P/A		1.88	(1.76-2.02)	1.61E-70	0.37	(OR=1.76, P=2.00×10 ⁻¹⁴) ⁵⁹
AA_DRB1_13 32660109_SR	NCI	i (1.031)	2142/6221	P/A	0.491	0.56	(0.52-0.60)	1.37E-51		
	UCSF2	i (0.981)	210/746	P/A	0.477	0.75	(0.60-0.94)	0.01312		
	SCALE	i (1.012)	376/791	P/A	0.463	0.57	(0.47-0.69)	1.38E-08		
	UCSF1/NHS	i (1.012)	119/349	P/A	0.502	0.48	(0.34-0.68)	4.43E-05		
	Combined		2847/8107	P/A		0.57	(0.53-0.61)	5.11E-62	3.40E-01	(OR=0.60, P=6.51×10 ⁻¹⁴) ⁵⁹

Table S11. HLA SNPs, HLA alleles and amino acids previously reported as associated with risk of follicular lymphoma and p-values after conditioning on DRB1 position 28, rs17203612 and rs3130437.

PROXY	SNP IN LD	POS	A1/A2	r ² SNP- PROXY	PROBE	P	FDR	rho
rs12194148	rs12194148	6:32444198	G/T	NA	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs12194148	6:32444198	G/T	NA	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs12194148	6:32444198	G/T	NA	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs12194148	6:32444198	G/T	NA	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs12194148	6:32444198	G/T	NA	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs12194148	6:32444198	G/T	NA	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs12194148	6:32444198	G/T	NA	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs12194148	6:32444198	G/T	NA	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs1964995	6:32449411	T/C	1	<i>HLA-DRB6:NR_001298</i>	2.48E-15	1.37E-12	-0.91
rs12194148	rs1964995	6:32449411	T/C	1	<i>HLA-DRB1:NM_002124</i>	5.60E-06	4.28E-04	0.66
rs12194148	rs1964995	6:32449411	T/C	1	<i>HLA-DQA2:NM_020056</i>	6.83E-06	4.75E-04	-0.66
rs12194148	rs1964995	6:32449411	T/C	1	<i>HLA-DQB1:NM_002123</i>	1.23E-04	5.55E-03	0.58
rs12194148	rs1964995	6:32449411	T/C	1	<i>HLA-DRB5:NM_002125</i>	5.40E-04	1.80E-02	0.53
rs12194148	rs1964995	6:32449411	T/C	1	<i>HLA-DQA1:NM_002122</i>	5.51E-04	1.81E-02	0.53
rs12194148	rs1964995	6:32449411	T/C	1	<i>C6orf25:NM_138274</i>	1.64E-03	4.36E-02	0.49
rs12194148	rs1964995	6:32449411	T/C	1	<i>C6orf25:NM_138275</i>	1.64E-03	4.36E-02	0.49
rs12194148	rs3998157	6:32678477	C/A	0.86	<i>HLA-DRB6:NR_001298</i>	6.04E-11	1.32E-08	-0.87
rs12194148	rs3998157	6:32678477	C/A	0.86	<i>HLA-DRB1:NM_002124</i>	1.23E-06	1.22E-04	0.73
rs12194148	rs3998157	6:32678477	C/A	0.86	<i>HLA-DQA2:NM_020056</i>	2.65E-05	1.36E-03	-0.66
rs12194148	rs3998157*	6:32678477	C/A	0.86	<i>HLA-DQB1:NM_002123</i>	3.12E-05	1.59E-03	0.66
rs12194148	rs3998157	6:32678477	C/A	0.86	<i>HLA-DQA1:NM_002122</i>	7.86E-05	3.64E-03	0.63
rs12194148	rs3998157	6:32678477	C/A	0.86	<i>HLA-DRB5:NM_002125</i>	6.90E-04	2.21E-02	0.56
rs12194148	rs4273729	6:32678597	C/G	0.85	<i>HLA-DRB6:NR_001298</i>	9.79E-13	3.00E-10	-0.86
rs12194148	rs4273729	6:32678597	C/G	0.85	<i>HLA-DRB1:NM_002124</i>	4.92E-07	7.28E-05	0.69
rs12194148	rs4273729*	6:32678597	C/G	0.85	<i>HLA-DQB1:NM_002123</i>	7.84E-07	9.77E-05	0.68
rs12194148	rs4273729	6:32678597	C/G	0.85	<i>HLA-DQA1:NM_002122</i>	7.26E-06	4.75E-04	0.64
rs12194148	rs4273729	6:32678597	C/G	0.85	<i>HLA-DQA2:NM_020056</i>	7.35E-06	4.75E-04	-0.64
rs12194148	rs4273729	6:32678597	C/G	0.85	<i>HLA-DRB5:NM_002125</i>	2.51E-04	1.01E-02	0.54
rs12194148	rs4273729	6:32678597	C/G	0.85	<i>HLA-DQB2:NR_003937</i>	3.36E-04	1.22E-02	-0.53
rs12194148	rs4410767	6:32448129	T/C	1	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs4410767	6:32448129	T/C	1	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs4410767	6:32448129	T/C	1	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs4410767	6:32448129	T/C	1	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs4410767	6:32448129	T/C	1	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54

rs12194148	rs4410767	6:32448129	T/C	1	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs4410767	6:32448129	T/C	1	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs4410767	6:32448129	T/C	1	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs5007260	6:32379047	G/A	0.8	<i>HLA-DRB6:NR_001298</i>	5.40E-12	1.38E-09	-0.85
rs12194148	rs5007260	6:32379047	G/A	0.8	<i>HLA-DRB1:NM_002124</i>	1.25E-06	1.22E-04	0.68
rs12194148	rs5007260	6:32379047	G/A	0.8	<i>HLA-DQA2:NM_020056</i>	1.23E-05	7.60E-04	-0.63
rs12194148	rs5007260	6:32379047	G/A	0.8	<i>HLA-DQB1:NM_002123</i>	1.01E-04	4.62E-03	0.58
rs12194148	rs5007260	6:32379047	G/A	0.8	<i>HLA-DQA1:NM_002122</i>	1.34E-04	5.96E-03	0.57
rs12194148	rs5007260	6:32379047	G/A	0.8	<i>HLA-DRB5:NM_002125</i>	2.75E-04	1.03E-02	0.55
rs12194148	rs5020946	6:32450089	G/T	1	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs5020946	6:32450089	G/T	1	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs5020946	6:32450089	G/T	1	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs5020946	6:32450089	G/T	1	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs5020946	6:32450089	G/T	1	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs5020946	6:32450089	G/T	1	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs5020946	6:32450089	G/T	1	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs5020946	6:32450089	G/T	1	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>HLA-DRB6:NR_001298</i>	2.66E-11	6.10E-09	-0.84
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>HLA-DQA2:NM_020056</i>	8.31E-07	9.77E-05	-0.7
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>HLA-DRB1:NM_002124</i>	9.11E-07	9.77E-05	0.7
rs12194148	rs6932517*	6:32678182	C/G	0.84	<i>HLA-DQB1:NM_002123</i>	2.78E-06	2.45E-04	0.67
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>HLA-DQA1:NM_002122</i>	2.06E-05	1.18E-03	0.63
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>HLA-DRB5:NM_002125</i>	4.92E-04	1.76E-02	0.53
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>HLA-DQB2:NR_003937</i>	7.68E-04	2.45E-02	-0.52
rs12194148	rs6932517	6:32678182	C/G	0.84	<i>BTNL2:NM_019602</i>	9.28E-04	2.88E-02	0.51
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs7748270	6:32448599	C/T	0.97	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9271586	6:32590899	G/T	0.84	<i>HLA-DRB6:NR_001298</i>	1.64E-08	3.43E-06	-0.82
rs12194148	rs9271586	6:32590899	G/T	0.84	<i>HLA-DRB1:NM_002124</i>	2.18E-04	9.25E-03	0.62
rs12194148	rs9271586	6:32590899	G/T	0.84	<i>HLA-DQA2:NM_020056</i>	1.51E-03	4.11E-02	-0.55

rs12194148	rs9271588	6:32590953	T/C	0.91	<i>HLA-DRB6:NR_001298</i>	5.28E-13	2.20E-10	-0.88
rs12194148	rs9271588	6:32590953	T/C	0.91	<i>HLA-DQA2:NM_020056</i>	1.15E-05	7.30E-04	-0.65
rs12194148	rs9271588	6:32590953	T/C	0.91	<i>HLA-DRB1:NM_002124</i>	1.21E-05	7.60E-04	0.65
rs12194148	rs9271588*	6:32590953	T/C	0.91	<i>HLA-DQB1:NM_002123</i>	1.62E-04	7.08E-03	0.57
rs12194148	rs9271588	6:32590953	T/C	0.91	<i>HLA-DRB5:NM_002125</i>	8.46E-04	2.68E-02	0.52
rs12194148	rs9271588	6:32590953	T/C	0.91	<i>HLA-DQA1:NM_002122</i>	8.96E-04	2.80E-02	0.52
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>HLA-DRB6:NR_001298</i>	8.60E-12	2.08E-09	-0.88
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>HLA-DQA2:NM_020056</i>	3.85E-06	3.10E-04	-0.7
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>HLA-DRB1:NM_002124</i>	3.96E-06	3.13E-04	0.7
rs12194148	rs9275517*	6:32674649	A/G	0.88	<i>HLA-DQB1:NM_002123</i>	6.49E-06	4.75E-04	0.69
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>HLA-DQA1:NM_002122</i>	2.63E-05	1.36E-03	0.65
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>HLA-DRB5:NM_002125</i>	2.35E-04	9.89E-03	0.59
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>HLA-DQB2:NR_003937</i>	1.03E-03	2.91E-02	-0.54
rs12194148	rs9275517	6:32674649	A/G	0.88	<i>BTNL2:NM_019602</i>	1.11E-03	3.07E-02	0.54
rs12194148	rs9275524	6:32675109	T/C	0.88	<i>HLA-DRB6:NR_001298</i>	3.63E-12	9.79E-10	-0.86
rs12194148	rs9275524*	6:32675109	T/C	0.88	<i>HLA-DQB1:NM_002123</i>	2.12E-06	1.91E-04	0.68
rs12194148	rs9275524	6:32675109	T/C	0.88	<i>HLA-DRB1:NM_002124</i>	3.23E-06	2.75E-04	0.68
rs12194148	rs9275524	6:32675109	T/C	0.88	<i>HLA-DQA2:NM_020056</i>	3.63E-06	2.97E-04	-0.67
rs12194148	rs9275524	6:32675109	T/C	0.88	<i>HLA-DQA1:NM_002122</i>	2.16E-05	1.18E-03	0.63
rs12194148	rs9275524	6:32675109	T/C	0.88	<i>HLA-DRB5:NM_002125</i>	2.08E-04	8.92E-03	0.57
rs12194148	rs9275524	6:32675109	T/C	0.88	<i>HLA-DQB2:NR_003937</i>	6.83E-04	2.21E-02	-0.53
rs12194148	rs9275565	6:32677938	T/C	0.85	<i>HLA-DRB6:NR_001298</i>	9.79E-13	3.00E-10	-0.86
rs12194148	rs9275565	6:32677938	T/C	0.85	<i>HLA-DRB1:NM_002124</i>	4.92E-07	7.28E-05	0.69
rs12194148	rs9275565*	6:32677938	T/C	0.85	<i>HLA-DQB1:NM_002123</i>	7.84E-07	9.77E-05	0.68
rs12194148	rs9275565	6:32677938	T/C	0.85	<i>HLA-DQA1:NM_002122</i>	7.26E-06	4.75E-04	0.64
rs12194148	rs9275565	6:32677938	T/C	0.85	<i>HLA-DQA2:NM_020056</i>	7.35E-06	4.75E-04	-0.64
rs12194148	rs9275565	6:32677938	T/C	0.85	<i>HLA-DRB5:NM_002125</i>	2.51E-04	1.01E-02	0.54
rs12194148	rs9275565	6:32677938	T/C	0.85	<i>HLA-DQB2:NR_003937</i>	3.36E-04	1.22E-02	-0.53
rs12194148	rs9275572	6:32678999	A/G	0.88	<i>HLA-DRB6:NR_001298</i>	3.63E-12	9.79E-10	-0.86
rs12194148	rs9275572*	6:32678999	A/G	0.88	<i>HLA-DQB1:NM_002123</i>	2.12E-06	1.91E-04	0.68
rs12194148	rs9275572	6:32678999	A/G	0.88	<i>HLA-DRB1:NM_002124</i>	3.23E-06	2.75E-04	0.68
rs12194148	rs9275572	6:32678999	A/G	0.88	<i>HLA-DQA2:NM_020056</i>	3.63E-06	2.97E-04	-0.67
rs12194148	rs9275572	6:32678999	A/G	0.88	<i>HLA-DQA1:NM_002122</i>	2.16E-05	1.18E-03	0.63
rs12194148	rs9275572	6:32678999	A/G	0.88	<i>HLA-DRB5:NM_002125</i>	2.08E-04	8.92E-03	0.57
rs12194148	rs9275572	6:32678999	A/G	0.88	<i>HLA-DQB2:NR_003937</i>	6.83E-04	2.21E-02	-0.53
rs12194148	rs9275573	6:32679146	C/G	0.85	<i>HLA-DRB6:NR_001298</i>	9.79E-13	3.00E-10	-0.86

rs12194148	rs9275573	6:32679146	C/G	0.85	<i>HLA-DRB1:NM_002124</i>	4.92E-07	7.28E-05	0.69
rs12194148	rs9275573*	6:32679146	C/G	0.85	<i>HLA-DQB1:NM_002123</i>	7.84E-07	9.77E-05	0.68
rs12194148	rs9275573	6:32679146	C/G	0.85	<i>HLA-DQA1:NM_002122</i>	7.26E-06	4.75E-04	0.64
rs12194148	rs9275573	6:32679146	C/G	0.85	<i>HLA-DQA2:NM_020056</i>	7.35E-06	4.75E-04	-0.64
rs12194148	rs9275573	6:32679146	C/G	0.85	<i>HLA-DRB5:NM_002125</i>	2.51E-04	1.01E-02	0.54
rs12194148	rs9275573	6:32679146	C/G	0.85	<i>HLA-DQB2:NR_003937</i>	3.36E-04	1.22E-02	-0.53
rs12194148	rs9378212	6:32445691	C/T	1	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs9378212	6:32445691	C/T	1	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs9378212	6:32445691	C/T	1	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs9378212	6:32445691	C/T	1	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs9378212	6:32445691	C/T	1	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs9378212	6:32445691	C/T	1	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs9378212	6:32445691	C/T	1	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9378212	6:32445691	C/T	1	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9378213	6:32448398	T/G	1	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs9378213	6:32448398	T/G	1	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs9378213	6:32448398	T/G	1	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs9378213	6:32448398	T/G	1	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs9378213	6:32448398	T/G	1	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs9378213	6:32448398	T/G	1	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs9378213	6:32448398	T/G	1	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9378213	6:32448398	T/G	1	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9378264	6:32443451	G/A	1	<i>HLA-DRB6:NR_001298</i>	2.48E-15	1.37E-12	-0.91
rs12194148	rs9378264	6:32443451	G/A	1	<i>HLA-DRB1:NM_002124</i>	5.60E-06	4.28E-04	0.66
rs12194148	rs9378264	6:32443451	G/A	1	<i>HLA-DQA2:NM_020056</i>	6.83E-06	4.75E-04	-0.66
rs12194148	rs9378264	6:32443451	G/A	1	<i>HLA-DQB1:NM_002123</i>	1.23E-04	5.55E-03	0.58
rs12194148	rs9378264	6:32443451	G/A	1	<i>HLA-DRB5:NM_002125</i>	5.40E-04	1.80E-02	0.53
rs12194148	rs9378264	6:32443451	G/A	1	<i>HLA-DQA1:NM_002122</i>	5.51E-04	1.81E-02	0.53
rs12194148	rs9378264	6:32443451	G/A	1	<i>C6orf25:NM_138274</i>	1.64E-03	4.36E-02	0.49
rs12194148	rs9378264	6:32443451	G/A	1	<i>C6orf25:NM_138275</i>	1.64E-03	4.36E-02	0.49
rs12194148	rs9378266	6:32448189	G/T	1	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs9378266	6:32448189	G/T	1	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs9378266	6:32448189	G/T	1	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs9378266	6:32448189	G/T	1	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs9378266	6:32448189	G/T	1	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs9378266	6:32448189	G/T	1	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52

rs12194148	rs9378266	6:32448189	G/T	1	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9378266	6:32448189	G/T	1	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9380318	6:32677669	C/T	0.85	<i>HLA-DRB6:NR_001298</i>	9.79E-13	3.00E-10	-0.86
rs12194148	rs9380318	6:32677669	C/T	0.85	<i>HLA-DRB1:NM_002124</i>	4.92E-07	7.28E-05	0.69
rs12194148	rs9380318*	6:32677669	C/T	0.85	<i>HLA-DQB1:NM_002123</i>	7.84E-07	9.77E-05	0.68
rs12194148	rs9380318	6:32677669	C/T	0.85	<i>HLA-DQA1:NM_002122</i>	7.26E-06	4.75E-04	0.64
rs12194148	rs9380318	6:32677669	C/T	0.85	<i>HLA-DQA2:NM_020056</i>	7.35E-06	4.75E-04	-0.64
rs12194148	rs9380318	6:32677669	C/T	0.85	<i>HLA-DRB5:NM_002125</i>	2.51E-04	1.01E-02	0.54
rs12194148	rs9380318	6:32677669	C/T	0.85	<i>HLA-DQB2:NR_003937</i>	3.36E-04	1.22E-02	-0.53
rs12194148	rs9391786	6:32448561	A/G	1	<i>HLA-DRB6:NR_001298</i>	2.98E-15	1.37E-12	-0.9
rs12194148	rs9391786	6:32448561	A/G	1	<i>HLA-DRB1:NM_002124</i>	9.58E-07	9.77E-05	0.68
rs12194148	rs9391786	6:32448561	A/G	1	<i>HLA-DQA2:NM_020056</i>	2.24E-05	1.18E-03	-0.61
rs12194148	rs9391786	6:32448561	A/G	1	<i>HLA-DQB1:NM_002123</i>	6.45E-05	3.02E-03	0.58
rs12194148	rs9391786	6:32448561	A/G	1	<i>HLA-DQA1:NM_002122</i>	2.66E-04	1.01E-02	0.54
rs12194148	rs9391786	6:32448561	A/G	1	<i>HLA-DRB5:NM_002125</i>	5.26E-04	1.77E-02	0.52
rs12194148	rs9391786	6:32448561	A/G	1	<i>C6orf25:NM_138274</i>	1.05E-03	2.91E-02	0.49
rs12194148	rs9391786	6:32448561	A/G	1	<i>C6orf25:NM_138275</i>	1.05E-03	2.91E-02	0.49
rs3130439	rs11962994	6:31219289	A/G	0.94	<i>PSORS1C3:NR_026816</i>	3.18E-07	5.40E-05	0.73
rs3130439	rs11967600	6:31199573	T/C	0.82	<i>PSORS1C3:NR_026816</i>	1.60E-04	7.05E-03	0.61
rs3130439	rs11967600	6:31199573	T/C	0.82	<i>PSORS1C2:NM_014069</i>	3.52E-04	1.27E-02	0.58
rs3130439	rs2394892	6:31205382	A/G	0.89	<i>PSORS1C3:NR_026816</i>	2.79E-07	4.93E-05	0.72
rs3130439	rs28397299	6:31207704	A/G	0.83	<i>PSORS1C3:NR_026816</i>	1.64E-05	9.89E-04	0.64
rs3130439	rs3130439	6:31221023	G/A	NA	<i>PSORS1C3:NR_026816</i>	1.32E-05	8.10E-04	0.65
rs3130439	rs3130439	6:31221023	G/A	NA	<i>PSORS1C2:NM_014069</i>	1.39E-03	3.81E-02	0.51
rs3130439	rs3130439	6:31221023	G/A	NA	<i>DPCR1:NM_080870</i>	1.55E-03	4.21E-02	-0.5
rs3130439	rs3869117	6:31205923	G/C	0.93	<i>PSORS1C3:NR_026816</i>	1.38E-06	1.31E-04	0.68
rs3130439	rs3869117	6:31205923	G/C	0.93	<i>PSORS1C2:NM_014069</i>	8.94E-04	2.80E-02	0.5
rs3130439	rs6457350	6:31204109	C/T	0.87	<i>PSORS1C3:NR_026816</i>	1.79E-06	1.68E-04	0.68
rs3130439	rs6908994	6:31198709	T/C	0.89	<i>PSORS1C3:NR_026816</i>	2.79E-07	4.93E-05	0.72
rs3130439	rs7745906	6:31204008	A/G	0.89	<i>PSORS1C3:NR_026816</i>	2.77E-07	4.93E-05	0.73
rs3130439	rs7768431	6:31202665	A/G	0.89	<i>PSORS1C3:NR_026816</i>	2.36E-07	4.71E-05	0.71

A1/A2 = minor/major allele in HapMap-CEU r28. Gene expression changes were estimated for the minor allele.

*The highlighted eQTLs also showed significant correlation with lower methylation levels in the same gene.

Table S12. Results from the eQTL analysis of rs12194148 and rs3130439, proxies, respectively, for the independent markers in the HLA forward stepwise analysis, rs17203612 and rs3130437. eQTL analysis was performed using a publicly available RNA Seq dataset (GEO accession number GSE16921) containing

whole-genome gene expression data in transformed lymphoblastoid cell lines from 41 HapMap-CEU samples. Whole-genome genotyping data for the same HapMap-CEU individuals (release #28) were directly downloaded from HapMap. As the two SNPs that remained statistically significant in the stepwise conditional analysis, rs17203612 and rs3130439, were not available in HapMap, rs12194148 ($r^2 = 0.98$ with rs17203612) and rs3130439 ($r^2 = 0.93$ with rs3130437) were selected as proxies, and the eQTL analysis was conducted on these two proxies and SNPs in LD ($r^2 > 0.8$) by correlating genotype and expression levels of probes within 1Mb of the SNPs. Correlation between expression and genotype for each SNP-probe pair was tested using the Spearman's rank test with t-distribution approximation and were estimated with respect to the minor allele in HapMap-CEU. *P*-values were adjusted for multiple comparisons using the Benjamini-Hochberg false-discovery rate (FDR) and eQTL were considered statistically significant at an FDR *P*-value threshold < 0.05 .

PROXY	SNP in LD	POS	A1/A2 ^a	PROBE	GENE	RHO	P	FDR
rs12194148	rs3998157*	6:32678477	C/A	cg01889448	HLA-DQB1	-0.48	7.15E-06	3.86E-05
rs12194148	rs4273729*	6:32678597	C/G	cg01889448	HLA-DQB1	-0.45	8.53E-06	4.19E-05
rs12194148	rs6932517*	6:32678182	C/G	cg01889448	HLA-DQB1	-0.46	1.36E-05	5.46E-05
rs12194148	rs9271586	6:32590899	G/T	cg01889448	HLA-DQB1	-0.48	1.42E-05	5.46E-05
rs12194148	rs9271588*	6:32590953	T/C	cg01889448	HLA-DQB1	-0.47	9.33E-06	4.20E-05
rs12194148	rs9275517*	6:32674649	A/G	cg01889448	HLA-DQB1	-0.47	1.63E-05	5.86E-05
rs12194148	rs9275524*	6:32675109	T/C	cg01889448	HLA-DQB1	-0.45	2.43E-05	7.72E-05
rs12194148	rs9275565*	6:32677938	T/C	cg01889448	HLA-DQB1	-0.47	3.74E-06	2.79E-05
rs12194148	rs9275572*	6:32678999	A/G	cg01889448	HLA-DQB1	-0.45	2.43E-05	7.72E-05
rs12194148	rs9275573*	6:32679146	C/G	cg01889448	HLA-DQB1	-0.47	3.74E-06	2.79E-05
rs12194148	rs9380318*	6:32677669	C/T	cg01889448	HLA-DQB1	-0.47	4.12E-06	2.79E-05
rs3130439	rs11962994	6:31219289	A/G	cg10409680	HLA-C	0.43	6.10E-05	1.65E-04
rs3130439	rs11967600	6:31199573	T/C	cg10409680	HLA-C	0.4	4.70E-04	1.21E-03
rs3130439	rs2394892	6:31205382	A/G	cg10409680	HLA-C	0.49	3.98E-06	2.79E-05
rs3130439	rs28397299	6:31207704	A/G	cg10409680	HLA-C	0.49	4.13E-06	2.79E-05
rs3130439	rs3130439	6:31221023	G/A	cg10409680	HLA-C	0.43	3.28E-05	9.85E-05
rs3130439	rs3869117	6:31205923	G/C	cg10409680	HLA-C	0.47	2.58E-06	2.79E-05
rs3130439	rs6457350	6:31204109	C/T	cg10409680	HLA-C	0.43	3.56E-05	1.01E-04
rs3130439	rs6908994	6:31198709	T/C	cg10409680	HLA-C	0.49	3.98E-06	2.79E-05
rs3130439	rs7745906	6:31204008	A/G	cg10409680	HLA-C	0.5	3.25E-06	2.79E-05
rs3130439	rs7768431	6:31202665	A/G	cg10409680	HLA-C	0.46	5.37E-06	3.22E-05

^aA1/A2 = minor/major allele in HapMap-CEU r28. Methylation changes were estimated for the minor allele.

*The highlighted meQTLs also showed significant correlation with higher expression levels in the same gene

Table S13. Results from the meQTL analysis of rs12194148 and rs3130439, proxies, respectively, for the independent markers in the conditional analysis, rs17203612 and rs3130437. meQTL analysis was performed using a publicly available dataset (GEO accession number GSE27146) that contained 27,578 DNA methylation measurements near the transcription start sites of 14,000 genes in 180 HapMap samples. Methylation probes were mapped to the human genome sequence (hg19) using BLAT and those that mapped to multiple locations with up to two mismatches were discarded, leaving 26,375 probes for analysis. Only the 90 samples of CEU origin were used in this study, and only SNPs and methylation probes that were located within 50kb were tested for association. Correlation between SNP genotypes and methylation levels was tested using the Spearman's rank correlation test and estimated with respect to the minor allele in HapMap-CEU. meQTL were considered significant at an FDR adjusted *P*-value < 0.05.

SNP	Gene transcript	Effect allele	Other allele	Beta for NHL SNP ^a	P for NHL SNP ^a	P for NHL SNP conditioned on peak SNP ^b	Peak SNP for transcript ^c	Beta for Peak SNP ^d	P for Peak SNP ^d	P for peak SNP conditioned on NHL SNP ^e
rs3130437	<i>HCG22</i>	C	A	-2.215	2.03E-12	0.82	rs116195588	-2.034	7.56E-27	4.58E-20
rs3130437	<i>HCG27</i>	C	A	1.650	7.10E-10	0.42	rs116794933	-0.615	5.86E-14	2.36E-07
rs3130437	<i>HLA-C</i>	C	A	0.882	1.13E-07	0.007	rs116398710	0.556	1.21E-11	1.13E-07
rs3130437	<i>HLA-C</i>	C	A	0.760	4.24E-07	0.08	rs149683222	-0.198	3.85E-10	3.11E-05
rs3130437	<i>TCF19</i>	C	A	0.847	5.74E-06	0.002	rs140242258	0.830	1.05E-28	8.51E-28
rs3130437	<i>HLA-B</i>	C	A	0.617	2.53E-05	0.002	rs140242258	0.461	3.51E-15	1.03E-13

^aBeta and p-value for the association between the NHL SNP and gene transcript.

^bp-value for the association between the NHL SNP and gene transcript after adjustment for the peak SNP

^cPeak SNP is the most significant SNP associated with the gene transcript

^dBeta and p-value for the association between the peak SNP and the gene transcript

^eP-value for the association between the peak SNP and the gene transcript after adjustment for the NHL SNP

Table S14. Expression quantitative trait loci (eQTL) associations with FDR < 1% from the childhood asthma dataset in the HLA region. eQTL analysis was conducted using a publicly available childhood asthma microarray dataset (GEO accession number GSE8052). As described previously for this dataset, peripheral blood lymphocytes were transformed into lymphoblastoid cell lines for 830 parents and offspring from 206 families of European ancestry. Using extracted RNA, gene expression was assessed with the Affymetrix HG-U133 Plus 2.0 chip. Genotyping was conducted using the Illumina Human1M Beadchip and Illumina HumanHap300K Beadchip, and imputation performed using data from 1000 Genomes Project. All SNPs selected for replication were tested for *cis* associations (defined as gene transcripts within 1 Mb), assuming an additive genetic model, adjusting for non-genetic effects in the gene expression value. To gain insight into the relative importance of eQTL associations with our SNPs compared to other SNPs in the region with stronger eQTL associations, we also conducted conditional analyses, in which both the FL SNP and the most significant SNP for the particular gene transcript (i.e., the peak SNP) were included in the same model. Only *cis* associations that reached $P < 6.8 \times 10^{-5}$, which corresponds to a FDR of 1% are reported.

chr	pos (hg19)	LD (r ²)	LD (D')	variant	Ref	Alt	EUR freq	Enhancer Histone marks	DNase	Proteins bound	eQTL tissues	Motifs changed	GENCODE genes	dbSNP func annot
6	31220895	1	1	rs3130437	A	C	0.61					4 altered motifs	16kb 3' of HLA-C	
6	31221153	0.93	0.98	rs2394946	G	A	0.61					Ncx,Pou1f1,Sox	15kb 3' of HLA-C	
6	32442836	0.83	0.97	rs13211921	T	G	0.43					13 altered motifs	30kb 3' of HLA-DRA	
6	32443172	0.92	0.97	rs9391879	C	T	0.45					SZF1-1,Spz1	30kb 3' of HLA-DRA	
6	32443451	0.89	0.95	rs9378264	G	A	0.45	K562					31kb 3' of HLA-DRA	
6	32443666	0.8	0.97	rs28895242	G	C	0.42					CEBPA,STAT	31kb 3' of HLA-DRA	
6	32444198	0.92	0.97	rs12194148	G	T	0.45						31kb 3' of HLA-DRA	
6	32444330	0.9	0.97	rs12207473	A	C	0.44					7 altered motifs	32kb 3' of HLA-DRA	
6	32444544	0.89	0.94	rs12195582	C	T	0.46						32kb 3' of HLA-DRA	
6	32444733	0.9	0.96	rs113660101	T G	T	0.45					GATA,SIX5	32kb 3' of HLA-DRA	
6	32445079	0.92	0.98	rs28895255	C	T	0.45					NF-kappaB,Rad21	32kb 3' of HLA-DRA	
6	32445114	0.87	0.98	rs28895257	A	G	0.43					Foxp3	32kb 3' of HLA-DRA	
6	32445117	0.87	0.98	rs28895258	C	T	0.43					AP-1,p53	32kb 3' of HLA-DRA	
6	32445306	0.88	0.99	rs28895261	G	A	0.43					AhR::Arnt,Arnt,BDP1	32kb 3' of HLA-DRA	
6	32445691	0.92	0.96	rs9378212	C	T	0.46		MCF-7	CTCF		5 altered motifs	33kb 3' of HLA-DRA	
6	32445992	0.91	0.98	rs17209866	G	A	0.44					Pitx2	33kb 3' of HLA-DRA	
6	32446010	0.91	0.96	rs17209873	T	C	0.46					Pbx-1,Rhox11	33kb 3' of HLA-DRA	
6	32446051	0.93	0.98	rs17209887	A	C	0.45						33kb 3' of HLA-DRA	
6	32446071	0.95	0.98	rs17203514	C	G	0.45					Hoxa5	33kb 3' of HLA-DRA	
6	32446307	0.86	0.96	rs17203549	T	C	0.44					Pax-5	33kb 3' of HLA-DRA	
6	32446425	0.83	0.98	rs139916710	G AA T	G	0.42					4 altered motifs	34kb 3' of HLA-DRA	

6	32446459	0.86	0.99	rs17203563	G	A, C, T	0.42			34kb 3' of HLA-DRA
6	32446853	1	1	rs17203612	A	T	0.46		8 altered motifs	34kb 3' of HLA-DRA
6	32446922	0.89	1	rs17203619	T	C	0.43			34kb 3' of HLA-DRA
6	32446994	0.81	1	rs17203626	G	A, T	0.41			34kb 3' of HLA-DRA
6	32447014	0.95	1	rs17203636	G	A	0.45		Pou3f2,Sox	34kb 3' of HLA-DRA
6	32447111	0.95	1	rs29001652	A	G	0.45	H7-hESC	Glis2,NERF1a	34kb 3' of HLA-DRA
6	32447162	0.96	0.99	rs29001478	G	A	0.45	H7-hESC	4 altered motifs	34kb 3' of HLA-DRA
6	32447216	0.96	0.99	rs29001620	A	T	0.45	H7-hESC	NRSF,Sin3Ak-20	34kb 3' of HLA-DRA
6	32447219	0.96	0.99	rs28732246	G	A	0.45	H7-hESC	NRSF,PU.1,Sin3Ak-20	34kb 3' of HLA-DRA
6	32447341	0.96	0.99	rs29001568	G	A	0.45		Maf,Nkx2,RXRA	35kb 3' of HLA-DRA
6	32447715	0.92	0.99	rs4994859	A	G	0.44		4 altered motifs	35kb 3' of HLA-DRA
6	32447873	0.92	0.99	rs4994855	A	G	0.44		6 altered motifs	35kb 3' of HLA-DRA
6	32447900	0.91	0.99	rs4994854	T	C	0.44		Pax-4,Sox	35kb 3' of HLA-DRA
6	32448129	0.81	0.99	rs4410767	T	C	0.41		GATA,Irf	35kb 3' of HLA-DRA
6	32449138	0.9	0.97	rs9394098	C	T	0.44		Smad3	36kb 3' of HLA-DRB5
6	32449160	0.87	0.97	rs9394099	G	T	0.44		6 altered motifs	36kb 3' of HLA-DRB5
6	32449188	0.86	0.96	rs9394100	G	A	0.47		Pou5f1	36kb 3' of HLA-DRB5
6	32449198	0.85	0.94	rs9394101	A	G	0.46		Irf,TEF	36kb 3' of HLA-DRB5
6	32449293	0.87	0.97	rs5018660	A	G	0.44		Dmbx1,Mef2,OTX	36kb 3' of HLA-DRB5
6	32449411	0.85	0.97	rs1964995	T	C	0.43		5 altered motifs	36kb 3' of HLA-DRB5
6	32450089	0.87	0.98	rs5020946	G	T	0.43	GM12878	AP-2,STAT	35kb 3' of HLA-DRB5
6	32450678	0.83	0.96	rs34452456	T	C	0.44	GM12878	Pax-4	34kb 3' of HLA-DRB5
6	32451570	0.81	0.92	rs13194770	C	T	0.45		5 altered motifs	34kb 3' of HLA-DRB5

Table S15. Results from HaploReg analysis of HLA follicular lymphoma risk loci and their correlated ($r^2 > 0.80$) surrogates.

3. SUPPLEMENTAL NOTES

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