Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

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Abbreviations: SJLIFE, St. Jude Lifetime Cohort Study; WGS, whole-genome sequencing; CCSS, Childhood Cancer Survivor Study; HL, Hodgkin lymphoma; SNP, single-nucleotide polymorphism; GWAS, genome-wide association study.
eFigure 2. Quantile-Quantile Plot for the $P$ Values in the $-\log_{10}$ Scale for the Discovery GWAS Meta-analysis
eFigure 3. Pair-wise Linkage Disequilibrium Among 3 Independent SNPs in HLA Region
### eTable 1. Meta-GWAS Results for Previously Published HL-Associated SNPs in HLA Region

| SNP     | Position† | Neighboring genes | Risk allele | OR    | 95% CI  | P       | \( P_{het} \) | \( I^2 \), % | Published Study PMID‡ |
|---------|-----------|-------------------|-------------|-------|---------|---------|-------------|-------------|------------------------|
| rs204999 | chr6:32142202:A:G | PRRT1           | A           | 1.46  | (1.31, 1.63) | 1.43E-11 | 6.73E-01 | 0.00        | 22086417               |
| rs1633096 | chr6:29739490:G:T | HLA-F            | T           | 1     | (0.9, 1.11)  | 9.99E-01 | 2.04E-01 | 37.05       | 29196614               |
| rs2248462 | chr6:31479019:G:A | MICB             | G           | 1.3   | (1.16, 1.46) | 6.22E-06 | 4.16E-01 | 0.00        | 22286212               |
| rs2281389 | chr6:33092019:A:G | HLA-DPB1         | G           | 1.53  | (1.38, 1.71) | 8.33E-15 | 2.97E-01 | 17.67       | 21596858               |
| rs2395185 | chr6:32465390:G:T | HLA-DRA          | G           | 1.11  | (1.01, 1.22) | 3.74E-02 | 6.73E-01 | 0.00        | 22286212               |
| rs2734986 | chr6:29850791:T:C | HLA-A            | T           | 1     | (0.89, 1.13)  | 9.37E-01 | 3.70E-01 | 0.00        | 22286212               |
| rs2858870 | chr6:132604474:A:G | HLA-DRA          | A           | 1.11  | (1.01, 1.22) | 2.41E-02 | 8.76E-01 | 0.00        | 22086417               |
| rs6457715 | chr6:33115411:A:G | HLA-DRA          | A           | 1.04  | (0.93, 1.15)  | 4.91E-01 | 7.41E-01 | 0.00        | 26404960               |
| rs6903608 | chr6:32460508:C:T | HLA-DRA          | C           | 1.44  | (1.31, 1.58) | 1.00E-14 | 5.26E-01 | 0.00        | 21037568, 21596858, 22086417, 22286212, 24149102 |
| rs6904029 | chr6:29975290:G:A | HcG9/HLA-A       | A           | 1.05  | (0.95, 1.15)  | 3.72E-01 | 1.04E-02 | 78.10       | 22286212               |
| rs9268528 | chr6:32415331:A:G | HLA-DRA          | G           | 1.37  | (1.25, 1.5)  | 1.19E-11 | 1.97E-01 | 38.44       | 22086417               |
| rs9268542 | chr6:32416944:A:G | HLA-DRA          | G           | 1.37  | (1.25, 1.49) | 1.34E-11 | 1.64E-01 | 44.65       | 22086417               |
| rs9269081 | chr6:32473323:A:C | HLA-DRA          | A           | 1.53  | (1.4, 1.69)  | 2.41E-19 | 2.90E-01 | 19.33       | 29196614               |
| rs13196329 | chr6:32357594:A:C | C6orf10          | C           | 1.47  | (1.07, 2.01) | 1.59E-02 | 5.73E-02 | 65.02       | 29196614               |

Abbreviations: GWAS, genome-wide association study; HL, Hodgkin Lymphoma; OR, odds ratio; CI, confidence interval.

†Position according to human reference GRCh38.

Heterogeneity between data sets was assessed by \( P \)-value \((P_{het})\) and inverse variance \((I^2)\) using the Cochran’s Q statistic.

‡PMID for studies previously published the HL-associated SNP in HLA region.
| Marker ID            | Position | Effect allele | Non effect allele | Imputed Z    | r² pred | Imputed P       |
|---------------------|----------|---------------|-------------------|--------------|---------|----------------|
| AA_DQB1_-5_32742280_L | 32634302 | P             | A                 | 8.64         | 0.90    | 5.65E-18       |
| AA_DQB1_-5_32742280_L | 32632598 | A             | P                 | 8.21         | 0.88    | 2.30E-16       |
| AA_DQB1_-5_32742280_L | 32632598 | P             | A                 | 8.11         | 0.89    | 5.23E-16       |
| AA_DQB1_-5_32742280_L | 32632745 | V             | A                 | -7.84        | 0.92    | 4.39E-15       |
| AA_DQB1_-5_32742280_L | 32632646 | P             | A                 | -7.77        | 0.91    | 7.78E-15       |
| AA_DQB1_-5_32742280_L | 32632688 | P             | A                 | 7.76         | 0.88    | 8.62E-15       |
| AA_DQB1_-5_32742280_L | 32632628 | R             | T                 | -7.69        | 0.91    | 1.48E-14       |
| AA_DQB1_-5_32742280_L | 32632634 | V             | L                 | -7.48        | 0.90    | 7.45E-14       |
| AA_DQB1_-5_32742280_L | 32632637 | A             | P                 | -7.48        | 0.90    | 7.45E-14       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -7.48        | 0.90    | 7.45E-14       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -7.28        | 0.94    | 3.22E-13       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -7.28        | 0.94    | 3.22E-13       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.98        | 0.89    | 2.91E-12       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.96        | 0.94    | 3.30E-12       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.69        | 0.90    | 2.24E-11       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.68        | 0.88    | 2.47E-11       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.55        | 0.94    | 5.81E-11       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.47        | 0.91    | 1.00E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.46        | 0.91    | 1.05E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.46        | 0.91    | 1.05E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.44        | 0.92    | 1.18E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.39        | 0.90    | 1.70E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | 6.34         | 0.91    | 2.31E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.29        | 0.95    | 3.26E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.23        | 0.90    | 4.59E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.21        | 0.95    | 5.21E-10       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.05        | 0.93    | 1.48E-09       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.00        | 0.93    | 1.98E-09       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.00        | 0.93    | 1.98E-09       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.00        | 0.93    | 1.98E-09       |
| AA_DQB1_-5_32742280_L | 32632646 | A             | P                 | -6.00        | 0.93    | 1.98E-09       |
| HLA Allele       | Position | AA        | r²     | Z score | Association |
|------------------|----------|-----------|--------|---------|-------------|
| AA_DQB1_27       | 32634368 | P         | A      | -6.00   | 1.98E-09    |
| AA_DQB1_30       | 32552080 | A         | P      | -5.93   | 3.04E-09    |
| AA_DQB1_14       | 32632817 | P         | A      | -5.91   | 3.33E-09    |
| AA_DQB1_45       | 32632724 | E         | G      |  5.91   | 3.35E-09    |
| AA_DQB1_14       | 32632817 | A         | P      | -5.87   | 4.41E-09    |
| AA_DQB1_116      | 32629962 | A         | P      | -5.86   | 4.63E-09    |
| AA_DQB1_125      | 32629935 | A         | P      | -5.85   | 4.85E-09    |
| AA_DQB1_224      | 32629129 | A         | P      | -5.78   | 7.56E-09    |
| AA_DQB1_125      | 32629935 | A         | P      |  5.69   | 1.32E-08    |
| AA_DRB1_28       | 32552086 | P         | A      | -5.61   | 1.36E-08    |
| AA_DRB1_78       | 32551936 | V         | Y      | -5.54   | 3.06E-08    |
| AA_DRB1_30       | 32552080 | P         | A      | -5.54   | 3.06E-08    |
| AA_DRB1_11       | 32552137 | P         | A      | -5.54   | 3.06E-08    |
| AA_DRB1_4        | 32557422 | P         | A      | -5.54   | 3.06E-08    |
| AA_DQB1_167      | 32629809 | A         | P      |  5.48   | 4.21E-08    |
| AA_DRB1_58       | 32551996 | A         | P      |  5.46   | 4.73E-08    |

Abbreviations: HL, Hodgkin Lymphoma.
† Position refers to the genomic coordinates based on GRCh37.
‡ Z score represents HL association.
*r² pred represents assessment of the imputation reliability at each HLA variant.
### eTable 3. Previously Reported HLA Alleles Associated With HL Susceptibility

| Marker ID       | Position ¹ | Effect allele | Non effect allele | Imputed Z $^{\dagger}$ | r² pred $^{*}$ | Imputed P  | Published Study PMID $^{‡}$ |
|-----------------|------------|---------------|-------------------|--------------------------|----------------|------------|-----------------------------|
| HLA_A_01        | 29911991   | Presence      | Absence           | 0.14                     | 0.97           | 8.88E-01   | 34830986                    |
| HLA_B_37        | 31323293   | Presence      | Absence           | 1.76                     | 0.75           | 7.77E-02   | 22808081                    |
| HLA_DPB1_0301   | 33049368   | Presence      | Absence           | 2.72                     | 0.88           | 6.61E-03   | 29196614                    |
| HLA_DQA1_0201   | 32608306   | Presence      | Absence           | -4.83                    | 0.92           | 1.35E-06   | 21596858                    |
| HLA_DQB1_0303   | 32631061   | Presence      | Absence           | -3.99                    | 0.82           | 6.51E-05   | 21596858                    |
| HLA_DQB1_0602   | 32631061   | Presence      | Absence           | 6.08                     | 0.88           | 1.17E-09   | 21596858                    |
| HLA_DRB1_0701   | 32552064   | Presence      | Absence           | -4.66                    | 0.92           | 3.17E-06   | 21596858                    |
| HLA_DRB1_1501   | 32552064   | Presence      | Absence           | 5.84                     | 0.89           | 5.28E-09   | 21596858                    |

Abbreviations: HL, Hodgkin Lymphoma.

¹ Position refers to the genomic coordinates based on GRCh37.

$^{\dagger}$ Z score represents HL association.

* r² pred represents assessment of the imputation reliability at each HLA variant.

‡ PMID for studies previously published the HL-associated HLA alleles.
| SNP       | Position    | Neighboring genes | Risk allele | OR   | 95% CI     | P       | Phet   | I², % | Published Study PMID² |
|-----------|-------------|-------------------|-------------|------|------------|---------|--------|-------|-----------------------|
| rs1432295 | chr2:60839531:G:A | REL             | G           | 1.20 | (1.10, 1.32) | 6.42E-05 | 4.36E-01 | 0.00 | 21037568              |
| rs2019960 | chr8:128180025:T:C | PVT1           | C           | 1.30 | (1.17, 1.44) | 7.05E-07 | 8.03E-01 | 0.00 | 21037568, 24920014    |
| rs20541   | chr5:132660272:A:G | IL13           | A           | 1.19 | (1.07, 1.32) | 1.52E-03 | 6.92E-01 | 0.00 | 22286212              |
| rs3806624 | chr3:27723132:A:G | EOMES          | G           | 1.21 | (1.11, 1.32) | 3.21E-05 | 7.56E-01 | 0.00 | 24149102              |
| rs7745098 | chr6:135093866:C:T | HBS1L, MYB     | C           | 1.05 | (0.96, 1.15) | 2.78E-01 | 2.41E-01 | 29.78 | 24149102              |
| rs2069757 | chr5:132662721:G:A | IL13           | A           | 1.19 | (1.03, 1.39) | 2.20E-02 | 3.36E-01 | 8.30 | 24920014              |
| rs1860661 | chr19:1650125:A:G | TCF3           | NA          | NA   | NA         | NA      | NA     | NA    | 24920014              |
| rs4459895 | chr3:188236626:A:C | LPP            | A           | 1.22 | (1.09, 1.37) | 4.89E-04 | 4.02E-01 | 0.00 | 29196614              |
| rs9482849 | chr6:127967391:T:C | PTPRK          | C           | 1.21 | (1.07, 1.36) | 1.80E-03 | 8.38E-01 | 0.00 | 29196614              |
| rs6928977 | chr6:135305210:T:G | AH1            | G           | 1.18 | (1.07, 1.29) | 4.89E-04 | 2.78E-01 | 21.81 | 29196614              |
| rs3781093 | chr10:8059964:T:C | GATA3          | T           | 1.44 | (1.26, 1.65) | 1.01E-07 | 1.75E-01 | 42.67 | 29196614              |
| rs112998813 | chr13:114294254:T:C | UPF3A         | T           | 1.12 | (0.94, 1.34) | 1.97E-01 | 7.84E-01 | 0.00 | 29196614              |
| rs34972832 | chr16:11105081:G:A | CLEC16A       | A           | 1.21 | (1.09, 1.35) | 3.44E-04 | 9.24E-01 | 0.00 | 29196614              |
| rs649775 | chr6:33716536:A:G | ITPR3, UQCC2, IP6K3 | A    | 1.30 | (1.12, 1.51) | 5.21E-04 | 4.83E-01 | 0.00 | 30194254              |
| rs1002658 | chr6:137660447:C:T | OLIG3, TNFAIP3 | T           | 1.13 | (1.01, 1.26) | 3.37E-02 | 2.54E-01 | 26.97 | 30194254              |
| rs7111520 | chr11:111378886:G:A | POU2AF1       | A           | 1.04 | (0.95, 1.15) | 3.81E-01 | 6.11E-01 | 0.00 | 30194254              |
| rs6565176 | chr16:30163605:T:C | MAPK3, CORO1A  | T           | 1.08 | (0.99, 1.18) | 9.10E-02 | 8.39E-01 | 0.00 | 30194254              |
| rs2425752 | chr20:46073481:T:C | NCOA5, CD40    | T           | 1.09 | (0.98, 1.21) | 1.21E-01 | 8.81E-01 | 0.00 | 30194254              |

Abbreviations: GWAS, genome-wide association study; HL, Hodgkin Lymphoma; OR, odds ratio; CI, confidence interval.

1 Position according to human reference GRCh38.

Heterogeneity between data sets was assessed by P-value (Phet) and inverse variance (I²) using the Cochran’s Q statistic.

²PMID for studies previously published the HL-associated SNP in non-HLA region.
eFigure 4. SNV rs117953624 near PDGFD