Supplementary info for:

# Functionally distinct ERAP1 and ERAP2 are a hallmark of HLA-A29-(Birdshot) Uveitis.

**J.J.W. Kuiper et al.**

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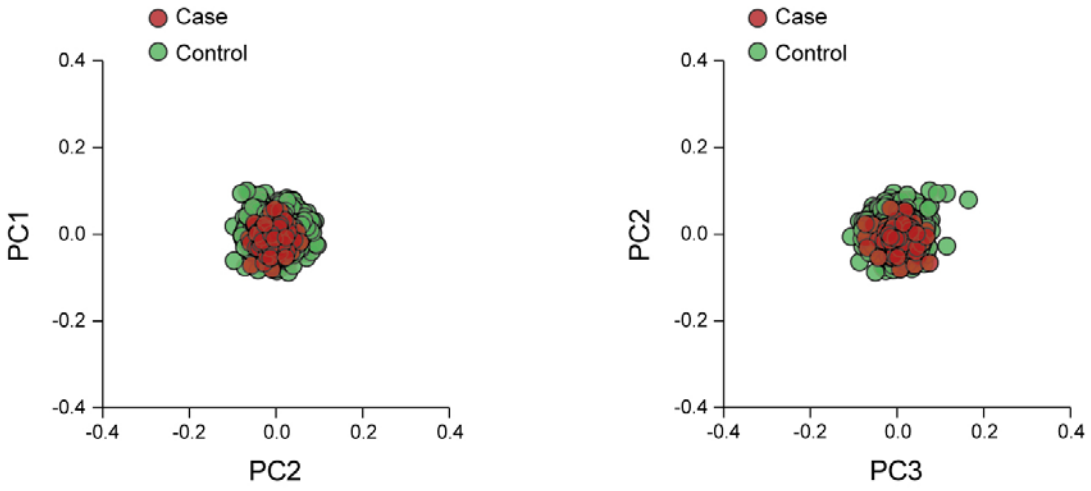
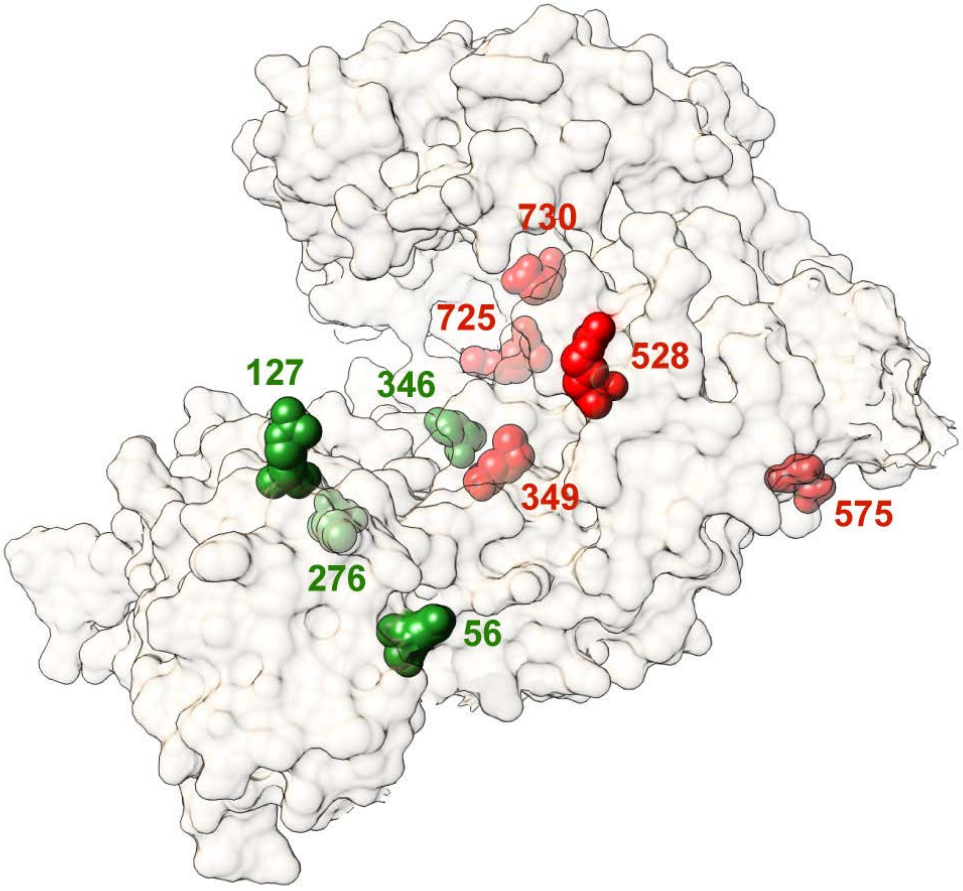
*Supplementary Figures 1-10*
*Supplementary Tables 1-6*

# Supplementary Figures

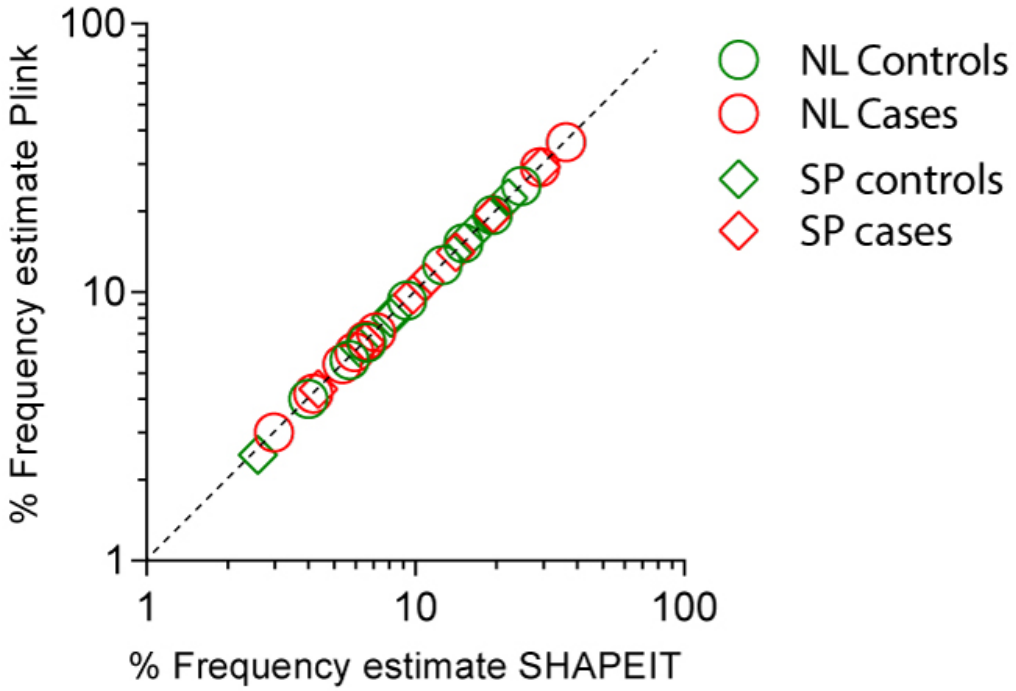
**Supplementary Figure 1 | Analysis of genetic matching of cases and controls using principal component analysis (PCA)**. PCA of the first versus second and second versus third component in cases and controls using genotype data from the Dutch collections as described in the Method section. We filtered SNPs with minor allele frequency (MAF) <0.1, excluding the *MHC*, two large inversions on chromosomes 8 and 17 and the *LCT* locus on chromosome 2. We further filtered out SNPs that are not in Hardy-Weinberg equilibrium ($p<10^{-4}$), or showed a pairwise LD of $r^2$ 0.2 or more. PCA was computed using a set of 75,239 random and independent SNPs autosome-wide (chr 1-22) in EIGENSOFT (*Price et al. Principal components analysis corrects for stratification in genome-wide association studies. Nat Genet. 2006 Aug;38(8):904-9*).



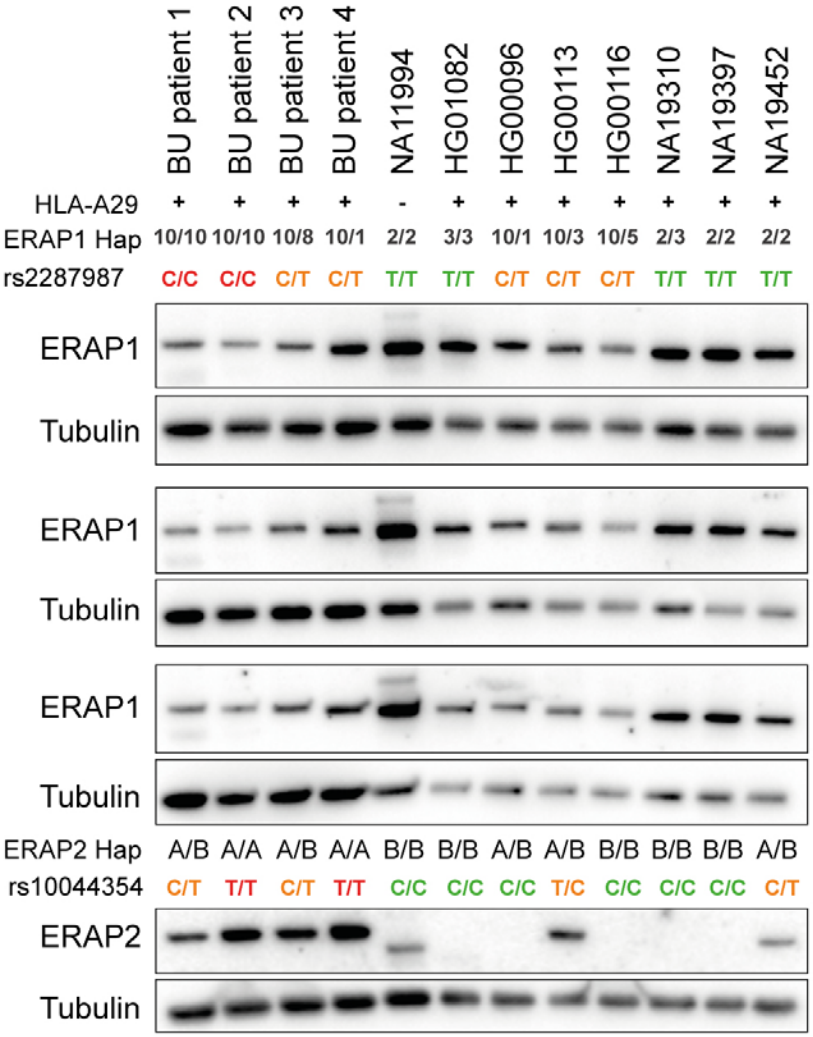
**Supplementary Figure 2 | Three-dimensional surface model for the ERAP1 allotype associated with Birdshot uveitis** (Protein Data Bank entry: 3MDJ). Common variant amino acid residues in ERAP1 are displayed as spheres; Ancestral amino acids are highlighted in green and non-ancestral amino acid positions are highlighted in red. 3D structure was produced using UCSF Chimera (*Pettersen, E. F. et al. UCSF Chimera - a visualization system for exploratory research and analysis. J. Comput. Chem. 25, 1605–1612 2004*).



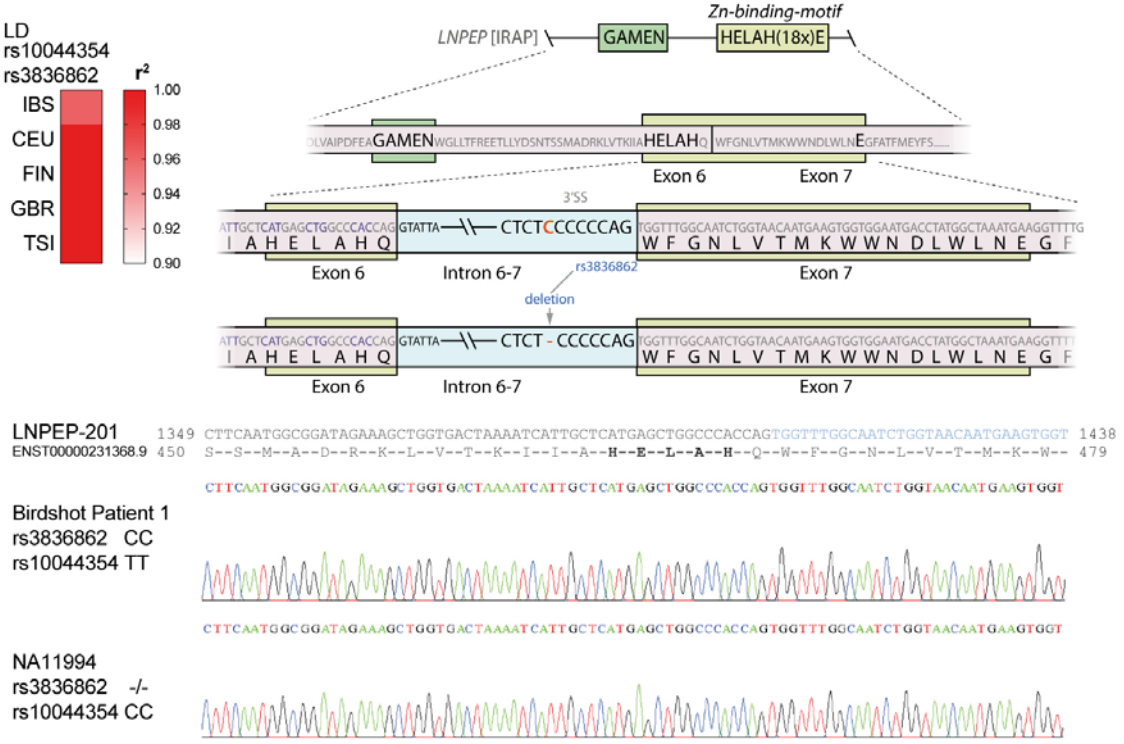
**Supplementary Figure 3 | The estimated haplotype frequency (%) for the 8 common ERAP1 haplotypes using Plink [44] and SHAPEIT [47] for cases (in red) and controls (in green).** The dotted diagonal line indicates perfect correlation between the estimated haplotype frequencies.



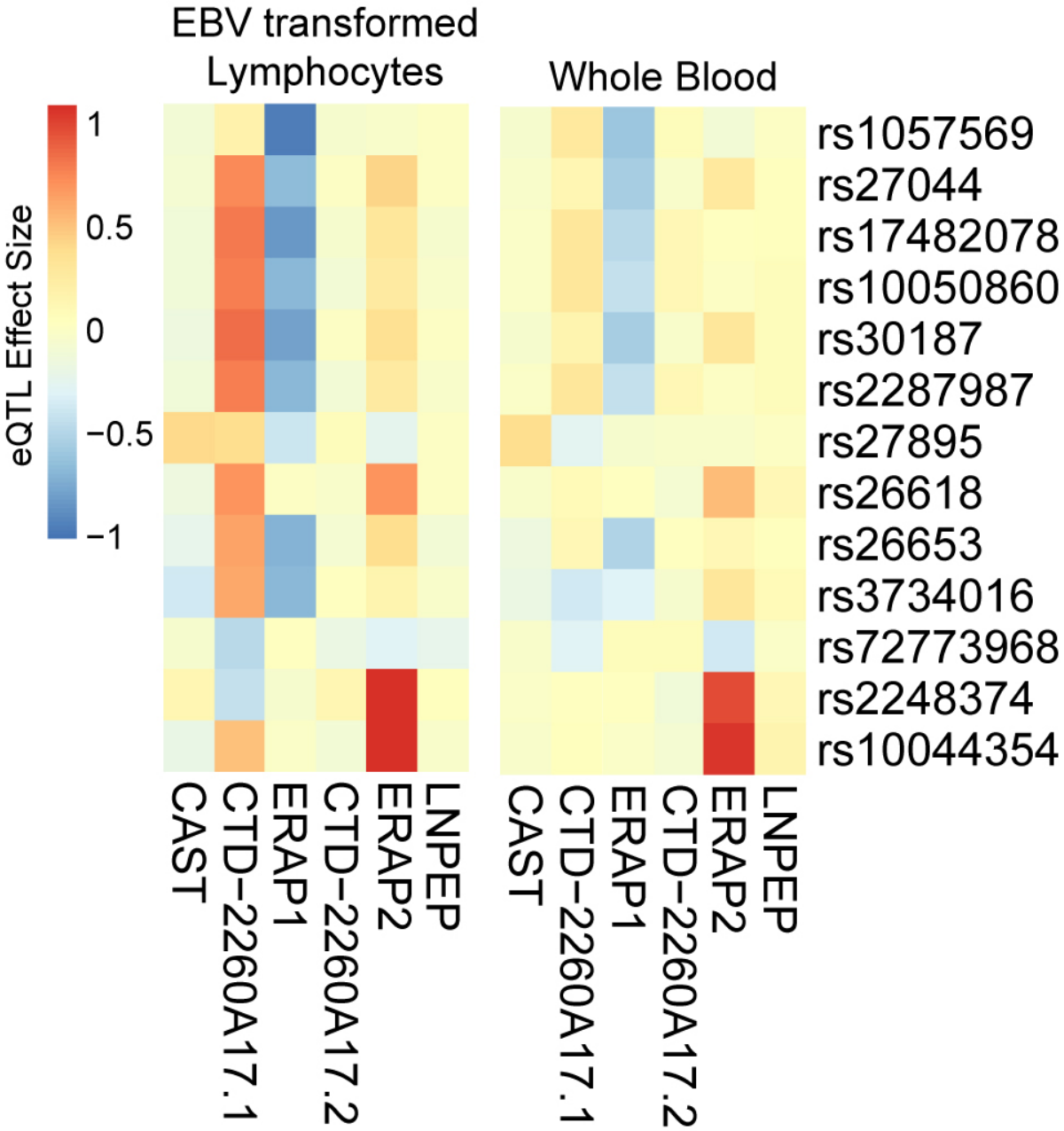
**Supplementary Figure 4 | ERAP1 and ERAP2 expression in B cell lines of Birdshot uveitis and HLA-A29-positive controls.** We assessed ERAP1 and ERAP2 protein levels in EBV transformed B cells (EBV-LCL), from twelve HLA-A*2902-positive individuals (except NA11994) from the 1000 Genomes project and EBV-LCLs generated from peripheral blood mononuclear cells of four BU patients genotyped in this study, by western blotting. Protein lysates (10µg/lane) from cells were separated on a 4-20% Mini-PROTEAN TGX gel (Bio-Rad Laboratories) and transferred to a PVDF membrane. Proteins were detected using a 1:5000 dilution of primary antibodies; goat anti-ERAP2 polyclonal antibody (AF3830, R&D Systems), goat anti-ERAP1 polyclonal antibody (AF2334, R&D Systems) and anti-α-tubulin monoclonal prepared in mouse (T6199, Sigma). Anti-mouse secondary antibody conjugated to Horseradish Peroxidase (HRP) (Jackson ImmunoResearch; 1:5000) and anti-goat secondary antibody conjugated to HRP (DAKO; 1:5000) were used to probe primary antibodies. Protein bands were detected with Amersham Prima Western Blotting (RPN22361, GE Healthcare) on the ChemiDoc Gel Imaging System (Bio-Rad Laboratories). Independent experiments are individually outlined below for ERAP1. The ratio of the intensity of the ERAP1 over α-tubulin band was calculated using Image Lab 5.1 (Bio-Rad Laboratories) for each experiment. All ratios of the intensities were grouped according to the distribution of *Hap10* (red = homozygous for rs2287987-C, orange = heterozygous for rs2287987-C, green is non-carrier) for quantitative analysis as outlined in **Figure 2F**.



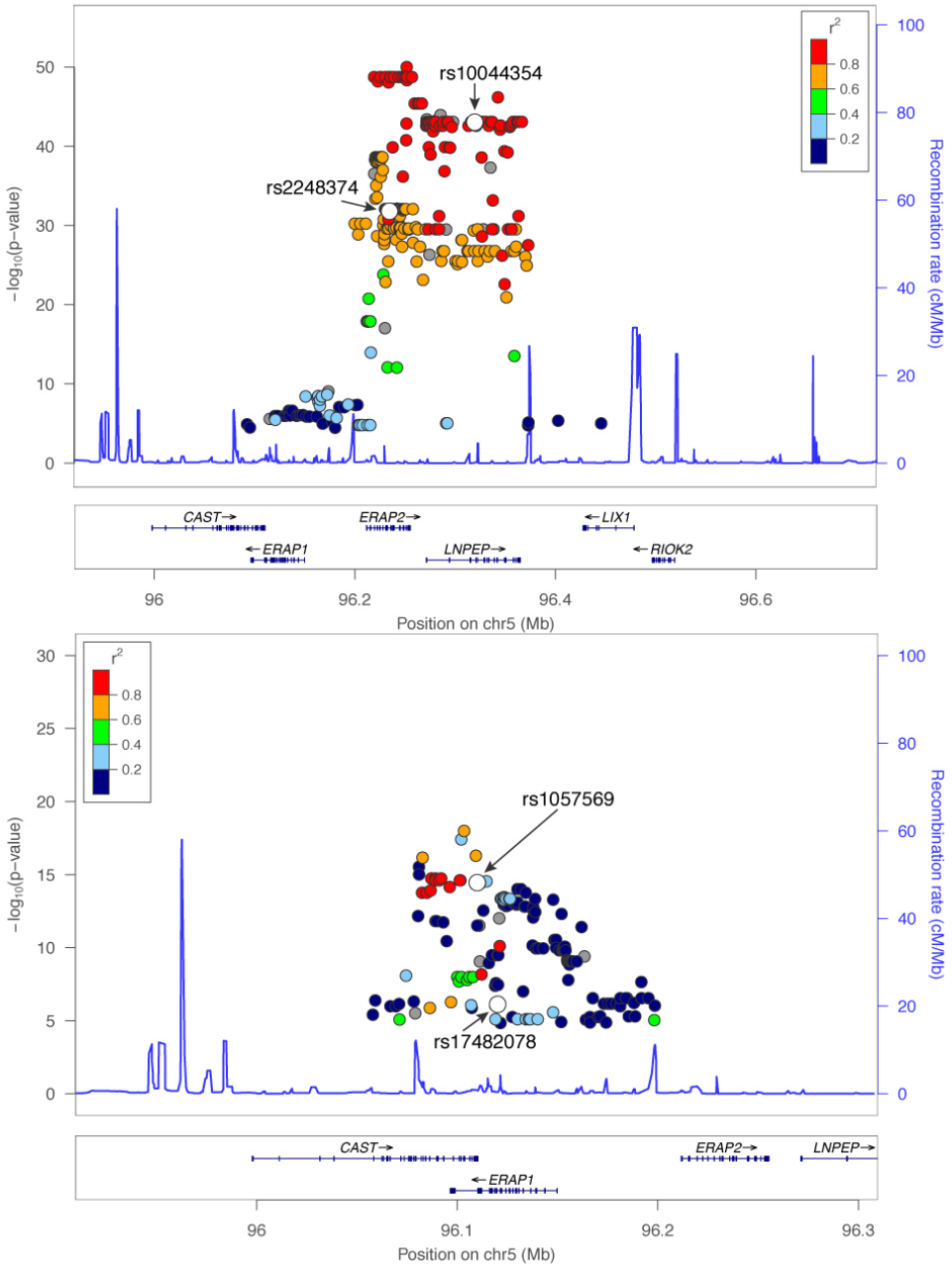
**Supplementary Figure 5 | rs10044354 is in tight LD with a splice region variant in *LNPEP*.** We searched the 5 European populations (British [GBR], Iberian [IBS], Finnish [FIN], Utah residents with Northern and Western European Ancestry [CEU], and Tuscany [TSI]) of the *1000 Genomes Project* [43] for missense or splice region variants of *LNPEP* in high LD ($r^2$ >0.75) with rs10044354; The rs10044354 variant is in tight LD ($r^2$ >0.96-1.0) with rs3836862 located in the splice region of intron 6-7 of *LNPEP*. These exons encode the key Zn-binding motif of the enzyme. The *Human splicing finder* software (http://www.umd.be/HSF3/) predicted a potential impact of the rs3836862 on splicing of this region. To explore if rs3836862 altered splicing of intron-6-7, we tested if the presence of rs10044354/rs3836862 affects the sequence of the predominant mature transcripts near this splice region. We selected four lymphoid cell lines that were homozygous null and four homozygous carries of the C allele of rs3836862 (as determined by Sanger sequencing). For each cell line, a total of 1 × $10^6$ cells were cultured in 2 mL RPMI 1640 (Life Technologies), supplemented with 10% (v/v) heat-inactivated FCS (Biowest) and 1% (v/v) penicillin and streptomycin (Life Technologies) in a six wells plate for 24 hours and stimulated with TLR agonists resiquimod (*R848*; 1 µg/ml), or CpG-B (*ODN684*; 5 µM, both from *InvivoGen*), or left untreated. Total RNA was extracted using QiaCube and RNeasy mini kit (*Qiagen*) and a 443 bp cDNA fragment from exon 5 to exon 8 of *LNPEP* was generated by SuperScript ® cDNA synthesis kit (Invitrogen, UK) using 5'-3' (forward) TATGCCTTGGAAACAACTGTGA and 5'-3'(reverse) TGTTCTGAAGACTGAACAGA TGAT. A 438 bp cDNA fragment was amplified using proof reading Pfu DNA polymerase-PCR reaction (Agilent Technologies, Santa Clara, CA, USA) with 5'-3'(forward) TGCCTTGGAAA CAACTGTGAAG and 5'-3' (reverse) TCTGAAGACTGAACAGATGATGA. A single band was detected in all conditions by agarose gel and sequenced at Macrogen Europe (Netherland) with 5'-3'(forward) GGAAACAACTGTGAAGCTTCTTGA and 5'-3'(reverse) CTTTCTTCATGGTTTT AAATCGAGC. Chromatograms from representative donors (unstimulated) from each group are indicated below. These analyses detected a sequence identical to the canonical transcript of *LNPEP* (Ensemble ID *ENST00000231368*) in all samples. We concluded that rs3836862 does not affect the sequence of the predominant (detectable) mature LNPEP transcripts in lymphoid cell lines under the described conditions.



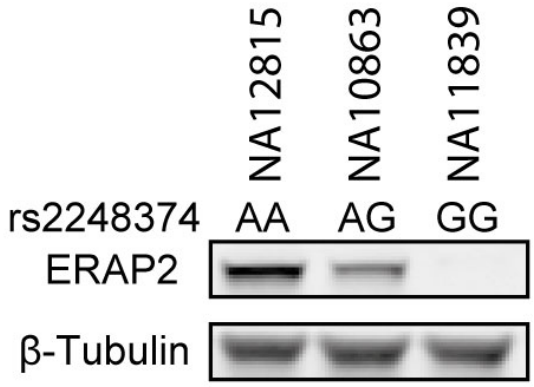
**Supplementary Figure 6 | The normalized effect size from the eQTL analysis for variants at 5q15 derived from the Genotype-Tissue Expression (GTEx) Project.** Data for 117 lymphoid cell lines and 369 whole blood samples were obtained from the GTExportal (GTEx Analysis Release V7, reference 51) as described in the method section.



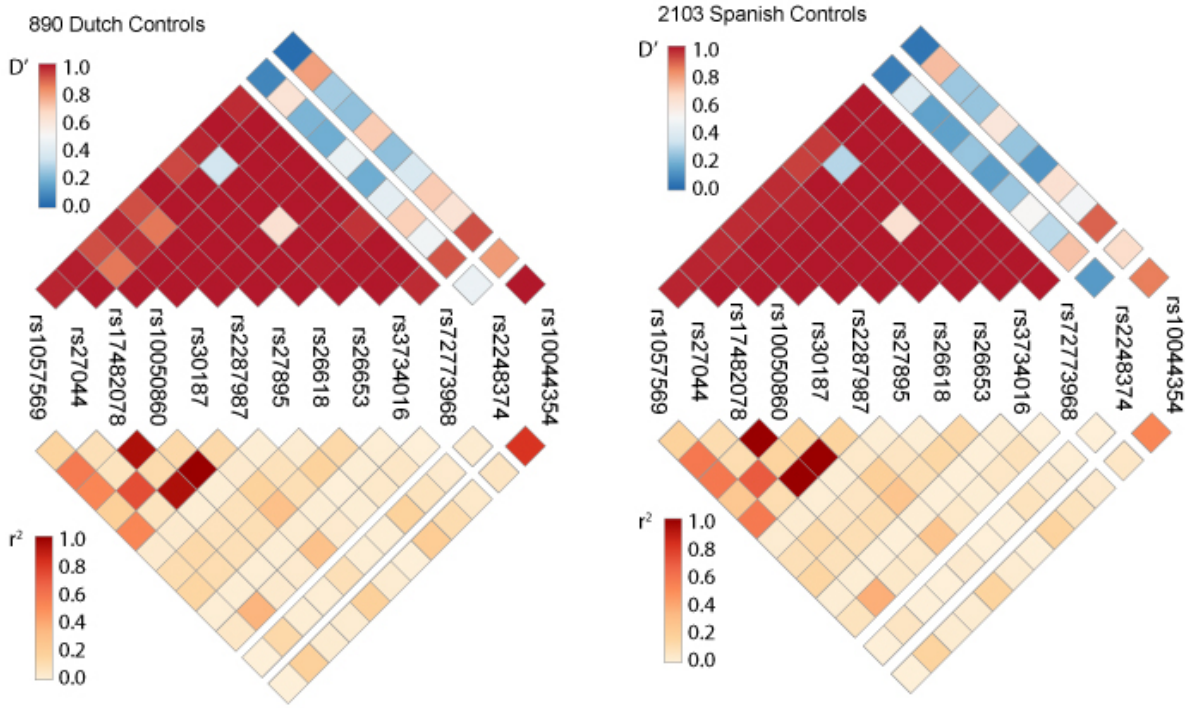
**Supplementary Figure 7 | eQTL data for variants in *ERAP1* and *ERAP2* in lymphoid cell lines of 117 individuals from the Genotype-Tissue Expression (GTEx) Project.** P-values from eQTL analysis for *ERAP1* and *ERAP2* were obtained from the Genotype-Tissue Expression (GTEx) [51] Project (GTEx Analysis Release V7). Gene expression for *ERAP1* is based on ERAP1~202 (ENST00000443439, average TPM unit of transcript expression = 29.2) in EBV-LCLs and ERAP1~201 (ENST00000296754 average TPM = 2.16, other transcript TPM<2). Gene expression for ERAP2 based on ERAP2~202 (ENST00000437043, average TPM = 18.1) in EBV-LCLs (other transcripts with >18 exons show TPM<2). The eQTLs rs1057569 for *ERAP1* and rs10044354 for *ERAP2*, and rs2248374 and rs17482078 are indicated in white. The hg19 European [EUR] 2014 1000 Genomes LD structure ($r^2$) is color coded. Plots were generated in LocusZoom [53].



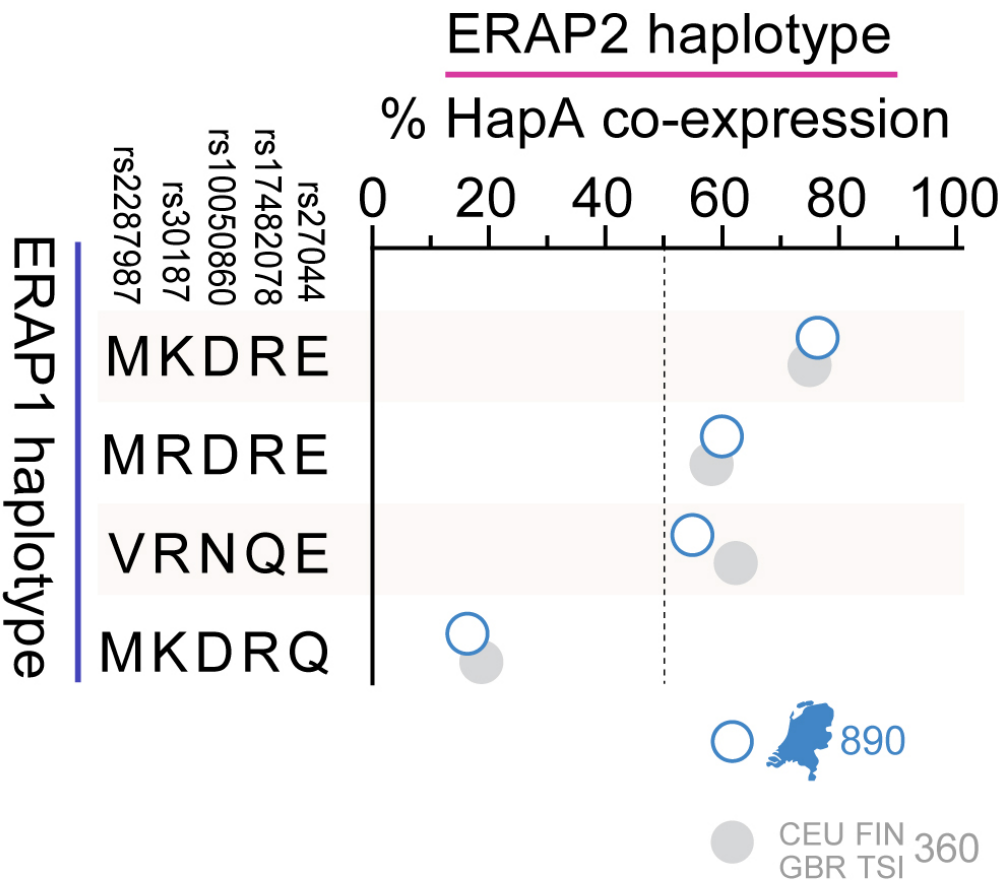
**Supplementary Figure 8 | The common splice region variant of *ERAP2* tags the bimodal distribution of protein expression.** *ERAP2* encodes at least two common haplotypes that are tagged by rs2248374. The A allele tags the protein-coding haplotype (HapA), while the G allele tags a haplotype that encodes a transcript that is usually prone to none-sense mediated decay [9] and loss strongly reduced protein expression. Expression of ERAP2 in CEPH controls according to rs2248374 genotype is provided for three B-cell lines from individuals from the CEPH panel (*Dausset J. et al. Centre d'etude du polymorphisme humain (CEPH): collaborative genetic mapping of the human genome. Genomics. 1990;6:575–577*). Genotype information was obtained from the *Ensembl Genome Browser* (rs2248374 or rs2549797 that is in full LD [$r^2$ =1] with rs2248374). Cells were lysed and ERAP2 expression was assessed after SDS–PAGE and western blotting with antibodies to ERAP2. The endogenous levels of β-tubulin protein were analyzed as a loading control.



**Supplementary Figure 9 | Linkage disequilibrium across the 13 polymorphisms in *ERAP1* and *ERAP2* in cases and controls**. The linkage disequilibrium across the functional variants at 5q15. The heatmaps show the D'prime and $r^2$ values calculated for SNPs in the Dutch and Spanish controls.



**Supplementary Figure 10 | Non-random distribution of the ERAP2-protein coding haplotype across common ERAP1 haplotypes based on 5 SNPs.** Five missense variants in *ERAP1* encode four discrete and common (>1% freq) haplotypes [12], while *ERAP2* encodes 1 common protein-coding haplotype (*HapA* tagged by the A allele of rs2248374) and non-coding haplotypes (tagged by the G allele). Each chromosome harbors 1 ERAP1 haplotype and 1 ERAP2 haplotype. We outlined the percentage of *HapA* per ERAP1 haplotype on the same chromosome using phased ERAP1-ERAP2 haplotype data of 890 Dutch controls (blue) and ERAP1-ERAP2 haplotype data for the 360 samples from the CEU, FIN, GBR, and TSI populations (grey) from the 1000 Genomes sample collection used for functional investigation in this study [48].



# Supplementary Tables

**Supplementary Table 1.** Association results for common functional variants at 5q15 in *ERAP1*, *ERAP2* and *LNPEP* genes in Dutch and Spanish populations.

| CHR | Gene | Function | SNP | Position | Allele (minus strand) | *Netherlands* | | | | *Spain* | | | | *Meta -analysis* | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Freq | | OR (95% CI) | *P* | Freq | | OR (95% CI) | *P* | | |
| | | | | | | Case (n=84) | Control (n=890) | | | Case (n=46) | Control (n=2103) | | | *OR* | *P* |
| 5 | *ERAP1* | eQTL of *ERAP1* | rs1057569 | 96109610 | A | 0.42 | 0.29 | 1.69(1.19-2.40) | $3.25 \times 10^{-3}$ | 0.35 | 0.28 | 1.37(0.89-2.11) | 0.15 | 1.56 | $1.41 \times 10^{-3}$ |
| 5 | *ERAP1* | 730Q | rs27044 | 96118852 | G | 0.15 | 0.29 | 0.45(0.29-0.71) | $5.84 \times 10^{-4}$ | 0.24 | 0.32 | 0.67(0.42-1.08) | 0.10 | 0.55 | $2.89 \times 10^{-4}$ |
| 5 | *ERAP1* | 725Q | rs17482078 | 96118866 | T | 0.36 | 0.19 | 2.20(1.51-3.20) | $3.53 \times 10^{-5}$ | 0.29 | 0.19 | 1.73(1.10-2.71) | 0.017 | 1.99 | $2.58 \times 10^{-6}$ |
| 5 | *ERAP1* | 575N | rs10050860 | 96122210 | T | 0.38 | 0.21 | 2.24(1.56-3.24) | $1.51 \times 10^{-5}$ | 0.29 | 0.19 | 1.70(1.08-2.67) | 0.021 | 2.01 | $1.46 \times 10^{-6}$ |
| 5 | *ERAP1* | 528K | rs30187 | 96124330 | T | 0.16 | 0.34 | 0.37(0.24-0.58) | $1.20 \times 10^{-5}$ | 0.35 | 0.40 | 0.80(0.52-1.23) | 0.31 | 0.55 | $1.53 \times 10^{-4}$ |
| 5 | *ERAP1* | 349V | rs2287987 | 96129535 | C | 0.38 | 0.20 | 2.25(1.56-3.24) | $1.49 \times 10^{-5}$ | 0.29 | 0.19 | 1.70(1.09-2.67) | 0.020 | 2.01 | $1.41 \times 10^{-6}$ |
| 5 | *ERAP1* | 346D | rs27895 | 96129543 | T | 0.07 | 0.07 | 0.92(0.47-1.81) | 0.82 | 0.05 | 0.06 | 0.86(0.35-2.11) | 0.75 | 0.90 | 0.70 |
| 5 | *ERAP1* | 276M | rs26618 | 96130836 | C | 0.29 | 0.25 | 1.32(0.90-1.92) | 0.16 | 0.20 | 0.22 | 0.85(0.51-1.42) | 0.53 | 1.13 | 0.45 |
| 5 | *ERAP1* | 127R | rs26653 | 96139250 | C | 0.17 | 0.28 | 0.50(0.33-0.78) | $1.87 \times 10^{-3}$ | 0.25 | 0.31 | 0.74(0.46-1.18) | 0.20 | 0.60 | $2.00 \times 10^{-3}$ |
| 5 | *ERAP1* | 56K | rs3734016 | 96139464 | T | 0.05 | 0.04 | 1.42(0.68-2.95) | 0.35 | 0.04 | 0.03 | 1.69(0.62-4.58) | 0.31 | 1.51 | 0.18 |
| 5 | *ERAP1* | 12I | rs72773968 | 96139595 | A | 0.06 | 0.13 | 0.48(0.24-0.94) | 0.03 | 0.14 | 0.15 | 0.90(0.50-1.61) | 0.72 | 0.69 | 0.09 |
| 5 | *ERAP2* | Splice-variant | rs2248374 | 96235896 | A | 0.67 | 0.47 | 2.26(1.59-3.22) | $6.11 \times 10^{-6}$ | 0.56 | 0.48 | 1.40(0.92-2.12) | 0.12 | 1.85 | $7.96 \times 10^{-6}$ |
| 5 | *LNPEP* | eQTL of *ERAP2* | rs10044354 | 96320495 | T | 0.63 | 0.42 | 2.42(1.69-3.45) | $1.21 \times 10^{-6}$ | 0.53 | 0.40 | 1.68(1.11-2.55) | 0.014 | 2.07 | $1.24 \times 10^{-7}$ |

**Supplementary Table 2 | Results of test for association of the haplotype rs2287987 (risk allele C) and rs10044354 (risk allele T) with Birdshot Uveitis in 130 cases and 2993 controls using a logistic regression model.**

| Cohort | rs2287987 | rs10044354 | Haplotype Frequency | | OR [95%CI] | P value |
|---|---|---|---|---|---|---|
| | | | Cases | Controls | | |
| Netherlands | C | T | 0.24 | 0.12 | 3.1 [1.96-4.90] | $1.4 \times 10^{-6}$ |
| | T | T | 0.39 | 0.31 | 1.44 [0.99-2.08] | 0.05 |
| | C | C | 0.14 | 0.08 | 1.34 [0.75-2.40] | 0.33 |
| | T | C | 0.23 | 0.49 | 0.30 [0.20-0.46] | $3.5 \times 10^{-8}$ |
| | | | | | | |
| Spain | C | T | 0.19 | 0.11 | 2.29 [1.31-4.02] | $3.9 \times 10^{-3}$ |
| | T | T | 0.34 | 0.30 | 1.23 [0.79-1.92] | 0.36 |
| | C | C | 0.10 | 0.08 | 1.2 [0.57-2.53] | 0.63 |
| | T | C | 0.37 | 0.51 | 0.53 [0.34-0.84] | $6.2 \times 10^{-3}$ |
| | | | | | | |
| Meta-analysis | C | T | | | 2.75 [1.92-3.92] | $2.6 \times 10^{-8}$ |
| | T | T | | | 1.35 [1.02-1.80] | 0.04 |
| | C | C | | | 1.291 [0.81-2.03] | 0.28 |
| | T | C | | | 0.39 [0.30-0.55] | $3.9 \times 10^{-9}$ |

**Supplementary Table 3 | Distribution of Hap10 in the Dutch and Spanish cases and controls.** The frequency of the rs2287987-C (i.e. Hap10+ individuals) or rs2287987-CC (i.e. Hap10 homozygous individuals) genotypes in cases and controls was tested by Fischer's exact test. OR; odds ratio. 95%CI; 95% confidence interval.

| Cohort | % of individuals with rs2287987 CT+CC genotype | | OR (95%CI) | *P* value | % of individuals with rs2287987 CC genotype | | OR (95%CI) | *P* value Fischer's Exact test |
|---|---|---|---|---|---|---|---|---|
| | Case | Control | | | Case | Control | | |
| | CT+CC | CT+CC | | | CC | CC | | |
| Netherlands | 63.1 | 37.2 | 2.88(1.78-4.75) | $6.34 \times 10^{-6}$ | 13.1 | 3.7 | 3.90(1.71-8.33) | $7.36 \times 10^{-4}$ |
| Spain | 45.7 | 34.7 | 1.58(0.83-2.96) | 0.16 | 13.0 | 4.1 | 3.55(1.20-8.74) | 0.0118 |

**Supplementary Table 4 | Birdshot-associated SNPs are eQTLs for *ERAP1* and *ERAP2* isoforms.** We tested the association between the risk alleles rs2287987 (correcting for rs1057569) and rs10044354 (correcting for rs2248374) with 4 detected transcripts at 5q15 in 360 lymphoid cell lines from European ancestry of the 1000 genomes project [48]. The incidence rate ratio (IRR) is calculated as the exponentiated genotype coefficient from the generalized linear mixed model and represents the change in transcript expression (scaled counts) associated with each sequential increase in risk allele count [23]. The $IRR^2$ is conceptually similar to the change in expression in homozygous risk individuals relative to those homozygous for the protective allele (e.g. 1.542 ~ 54% increase) as previously described [23]. The mean count per transcript is indicated for individuals homozygous for the protective and risk allele. The *P* values are corrected for multiple testing using Bonferroni's correction. Observations of $IRR^2$ <0.60 or >1.30 (i.e. >30% change in expression) are considered biologically relevant and are highlighted in orange (increase) and blue (decrease).

| | Risk allele | IRR (95%CI) | $IRR^2$ (95%CI) | % change expression AA x BB | P value | Mean count in homozygous Protective allele | Mean count in homozygous Protective allele | Ratio Risk/Protective AA x BB |
|---|---|---|---|---|---|---|---|---|
| **ERAP1~201 ENST00000296754.7** | | | | | | | | |
| rs1057569 | A | 4.13(3.63 -4.7) | 17.05(13.15-22.1) | 1605% | $1.66 \times 10^{-100}$ | 1.17 | 15.78 | 13.49 |
| rs2287987 | C | 2.59(2.17 -3.09) | 6.7(4.7-9.56) | 570% | $1.56 \times 10^{-24}$ | 3.18 | 14.86 | 4.67 |
| rs2287987 corrected for rs1057569 | C | 1.03(0.87 -1.21) | 1.05(0.76-1.47) | 5% | 1 | | | |
| rs10044354 corrected for rs1057569 | T | 1.01(0.9 -1.13) | 1.02(0.82-1.27) | 2% | 1 | 5.29 | 7.22 | 1.36 |
| **ERAP1~202 ENST00000443439.6** | | | | | | | | |
| rs1057569 | A | 0.62(0.59 -0.64) | 0.38(0.35-0.42) | -62% | $1.93 \times 10^{-105}$ | 74.37 | 25.36 | 0.34 |
| rs2287987 | C | 0.66(0.62 -0.7) | 0.44(0.39-0.49) | -56% | $1.77 \times 10^{-44}$ | 68.01 | 27.54 | 0.40 |
| rs2287987 corrected for rs1057569 | C | 0.98(0.91 -1.05) | 0.96(0.83-1.11) | -4% | 1 | | | |
| rs10044354 corrected for rs1057569 | T | 0.93(0.9 -0.97) | 0.87(0.8-0.94) | -13% | $8.06 \times 10^{-3}$ | 64.10 | 49.61 | 0.77 |
| **ERAP2~202 ENST00000437043.7** | | | | | | | | |
| rs1057569 corrected for rs2248374 | A | 1.07(1 -1.14) | 1.14(1.01-1.3) | 14% | 0.54 | 57.05 | 69.31 | 1.21 |
| rs2287987 corrected for rs2248374 | C | 1.06(0.99 -1.14) | 1.13(0.99-1.29) | 13% | 1 | 57.05 | 72.10 | 1.26 |
| rs10044354 corrected for rs2248374 | T | 1.83(1.66 -2.02) | 3.35(2.76-4.06) | 235% | $3.48 \times 10^{-33}$ | 23.75 | 89.61 | 3.77 |
| **LNPEP~201 ENST00000231368.9** | | | | | | | | |
| rs1057569 | A | 0.99(0.95 -1.03) | 0.98(0.9-1.06) | -2% | 1 | 92.22 | 89.60 | 0.97 |
| rs2287987 | C | 0.99(0.94 -1.03) | 0.97(0.89-1.06) | -3% | 1 | 91.06 | 87.86 | 0.96 |
| rs10044354 | T | 0.97(0.93 -1.01) | 0.94(0.87-1.01) | -6% | 1 | 92.00 | 87.49 | 0.95 |

**Supplementary Table 5 | ERAP1 amino acids positions for Haplotype 10 (Hap10).** Using molecular cloning, full-length *ERAP1* was sequenced from a patient homozygous for *Hap10 and a patient heterozygous for Hap10 (based on common genotyped SNPs)*. Previously reported amino acid positions in *ERAP1* are adapted from *Reeves et al.*[24] and *Ombrello et al.* [21]

| | ***Amino Acid position in ERAP1*** | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Allotype* | **12** [a] | **56** [a,b] | **82** [b] | **102** [b] | **115** [b] | **127** [a,b] | **199** [b] | **276** [a,b] | **346** [a,b] | **349** [a,b] | **528** [a,b] | **575** [a,b] | **725** [a,b] | **727** [b] | **730** [a,b] | **737** [b] | **752** [b] | **847** [b] |
| Hap10[c] | T | E | V | I | L | P | F | I | G | V | R | N | Q | L | E | V | R | M |
| **001*[d] | | | V | I | L | P | F | | | V | R | N | Q | L | E | V | R | M |
| *Hap10*[e] | | E | | | | P | | I | G | V | R | N | Q | | E | | | |

[a]Amino acid identified by genotyping/imputation
[b]Amino acid identified by sanger sequencing of full-length cDNA of *ERAP1*
[c] Full-length cDNA (Allotype) amino acid sequence obtained from two Birdshot uveitis patients heterozygous and homozygous for *Hap10* in this study.
[d]Allotype name and amino acid positions adapted from [24]
[e]Allotype name and amino acid positions adapted from [21]

**Supplementary Table 6 | The frequency of the rs2248374 A allele in *ERAP2* co-occurring with each of the 8 common ERAP1 haplotypes is non-random in phased haplotype data of 890 Dutch and 2103 Spanish controls.** The *ERAP2* protein-coding haplotype [9] is tagged by the A allele of rs2248374 in *ERAP2*. We used a two-sided exact binominal test to assess if the observed frequencies were non-random (deviation from a test probability of 0.5 or the hypothesis that ERAP2 co-occurs in 50% of any particular ERAP1 haplotype). Frequency distribution of ERAP2 for each of the ERAP1 haplotypes was considered non-random if the frequency deviated at a significant level of [A or G rs2248374 for 8 ERAP1 haplotypes = 0.05/16] $p<2.5 \times 10^{-3}$ in both the Dutch and Spanish populations (with consistent direction of deviation from 50%). ERAP1 haplotypes that fulfilled these criteria are highlighted (in orange haplotypes that more frequently co-occur with rs2248374-A allele and in blue haplotypes that less frequently co-occur with rs2248374-A allele).

| ERAP1 haplotype | Number of Dutch haplotypes (n=1780) | % Co-occurring A-rs2248374 (95% CI) | P value | Number of Spanish haplotypes (n=4206) | % Co-occurring A-rs2248374 (95% CI) | P value |
|---|---|---|---|---|---|---|
| *Hap1** | 225 | 24(18-30) | $7.35 \times 10^{-16}$ | 641 | 43(39-47) | $3.71 \times 10^{-4}$ |
| *Hap2** | 268 | 7(4-11) | $2.66 \times 10^{-52}$ | 683 | 34(30-37) | $1.02 \times 10^{-17}$ |
| *Hap3* | 101 | 76(67-84) | $1.18 \times 10^{-7}$ | 340 | 55(49-60) | 0.093 |
| *Hap5* | 117 | 30(22-39) | $1.65 \times 10^{-5}$ | 259 | 42(36-49) | 0.018 |
| *Hap6** | 165 | 8(4-13) | $3.10\times 10^{-31}$ | 348 | 35(30-40) | $1.42 \times 10^{-8}$ |
| *Hap7** | 71 | 96(88-99) | $5.06 \times 10^{-17}$ | 110 | 72(62-80) | $5.34 \times 10^{-6}$ |
| *Hap8** | 442 | 83(79-86) | $1.41 \times 10^{-46}$ | 935 | 61(58-64) | $5.33 \times 10^{-12}$ |
| *Hap10* | 345 | 55(49-60) | 0.085 | 808 | 51(47-54) | 0.65 |
| **Total (% of ERAP1 haplotypes)** | **1734 (97%)** | | | **4124 (98%)** | | |