1. Supplementary Material and Methods 2
   1.1 Study patients 2
   1.2 DNA extraction and genome-wide genotyping in the discovery and validation patients 2
   1.3 Imputation of genetic variants associated with SLE risk 4
   1.4 Pathway-based association analysis 5
   1.5 Differential expression analysis of VEGF pathway genes after topical immunotherapies 5

2. Supplementary Tables 7
   2.1 Table S1. Association of SLE risk genes with SLE clinical phenotypes in the discovery cohort 7
   2.2 Table S2. Genome-wide pathway associations obtained analyzing the 11 SLE clinical phenotypes in the discovery cohort 8
   2.3 Table S3. Association results of the SNPs from the VEGF pathway associated with oral ulcers in SLE 105
   2.4 Table S4. Statistical significance of the differential expression analysis performed on the VEGF pathway genes after immunotherapy 106
   2.5 Table S5. Statistical significance of the VEGF genetic pathway perturbation after topical immunotherapy 107
   2.6 Table S6. Established genetic variants for SLE risk 108
   2.7 Table S7. Reference biological pathways selected for the present study 109

3. Supplementary Figures 117
   3.1 Figure S1. Principal components of the SLE discovery cohort 117

4. References 118
1. Supplementary Material and Methods

1.1 Study patients

In the discovery stage, a total of 482 SLE patients were recruited. SLE patients were collected from the outpatient’s clinics of the rheumatology departments of 15 Spanish University Hospitals belonging to the Immune-Mediated Inflammatory Disease (IMID) Consortium [1]. The IMID Consortium is a Spanish network of researchers working on the genetic basis of IMIDs. All SLE patients were diagnosed using the 1982 revised ACR diagnosis criteria [2]. All patients included in this study were >16 years old at the time of sample collection and had >3 years of evolution from the diagnosis date. SLE patients with psoriasis, inflammatory bowel disease (Crohn’s disease or ulcerative colitis) or other rheumatic diseases like rheumatoid arthritis, or multiple sclerosis were excluded from the study. All SLE patients were Caucasian European with all four grandparents born in Spain.

In the validation stage, an independent cohort of 425 SLE patients was used to replicate the genetic pathways that were significantly associated with the SLE phenotypes in the discovery stage. All patients from the validation cohort fulfilled the ACR diagnostic criteria for SLE and were also collected from the IMID Consortium, following the same inclusion and exclusion criteria as for the discovery cohort.

1.2 DNA extraction and genome-wide genotyping in the discovery and validation patients

Whole blood samples (5 mL) were collected from all SLE patients from the discovery and replication cohorts. Genomic DNA was then isolated using the Chemagic Magnetic Separation Module I (PerkinElmer, Waltham, MA).
In the discovery stage, the genome-wide genotyping of the 482 SLE patients was performed using the Illumina Quad610 Beadchips (Illumina, San Diego, California, USA) at the Centro Nacional de Genotipado (CeGen, Madrid, Spain). Genotype calling was performed using the GenomeStudio data analysis software v2011.1 (Illumina, San Diego, California, USA). The genotyping quality control analysis was performed using PLINK software [3]. From the 598,258 SNPs available in the Illumina genotyping array, a total of 582,539 autosomal SNPs were selected for the quality control analysis. The SNPs included in the association analysis had a minor allele frequency >0.05 and <5% of missing data (94.17% SNPs). Using an additional cohort of 1,558 healthy controls from the same population, we tested the deviation of the SNPs from the Hardy-Weinberg equilibrium [4]. Those SNPs that were not in Hardy-Weinberg equilibrium in this cohort (0.03% SNPs, $P<1e^{-4}$) were subsequently removed. To evaluate the presence of potential population stratification in the SLE patient cohorts, we used the principal component analysis (PCA) implemented in EIGENSOFT (v4.2) software [5]. Using the first 10 PCs of variation over 10 iterations we identified 14 samples showing an outlier genetic background and were excluded from downstream analysis. After the quality control analysis, a final data set of 507,051 SNPs and 395 SLE patients was available for the GWPA.

The validation of the two genetic pathways associated in the discovery stage required the genotyping and analysis of a total 1,347 SNPs. Given the relatively large number of variants and the utility of genome-wide data for accurate ancestry outlier identification, the 425 SLE patients of the validation cohort were also genotyped using Illumina Quad610 microarray (Illumina, San Diego, California, USA) at the HudsonAlpha Institute for Biotechnology (Huntsville, Alabama, USA). For the pathway-based analysis, we excluded all non-autosomal SNPs, SNPs with a minor allele frequency
<0.05, >5% of missing data (85.01%) as well as those SNPs that were not in Hardy-Weinberg equilibrium (0.03% SNPs, \( P<1\times10^{-4} \)) in a cohort of 1,558 controls from the same population [4]. All 1,347 SNPs from the two genetic pathways associated in the discovery stage passed the quality control. In order to estimate the principal components (PCs) of variation, we analyzed the genome-wide genetic variation using the EIGENSOFT (v4.2) software. Based on the first 10 PCs of variation over 10 iterations, we identified 4 samples showing an outlier genetic background that were subsequently discarded from the pathway-based analysis. A total of 394 SLE patients and all 1,347 SNPs from the two genetic pathways passed the quality control and were available for the pathway-based analysis of the validation stage.

1.3 Imputation of genetic variants associated with SLE risk

From the established autosomal SLE risk SNPs (N=41 SNPs), the genetic variants that were not directly genotyped by the GWAS Quad610 genotyping array (N=17 SNPs) were imputed. SHAPEIT V2-644 (Oxford, UK) software was used to pre-phase the haplotypes of the SNPs that passed the genotyping quality control analysis [6], and these haplotypes were subsequently analyzed using IMPUTE V2 (Oxford, UK) software [7] to impute the missing SLE risk SNPs. The reference genotyping data used for imputation was obtained from the European cohort (N=379 samples) of the latest release of the 1000 Genomes Project (phase 1, version 3) [8]. In the imputation quality control analysis, we excluded those SNPs that had an IMPUTE2 info quality metric < 0.8 (N=1 SNP). After the imputation quality control, a total of 40 SLE risk SNPs were finally available for the association analysis with SLE phenotypes in the discovery cohort. In the validation cohort, the same procedure was followed to obtain the genotypes of the risk variants to be tested for replication.
1.4 Pathway-based association analysis

The set- or pathway-based association analysis implemented in the PLINK software is composed by four steps. In the first step, the raw genotype data is used to compute the linkage disequilibrium ($r^2$) between pathway SNPs in order to identify truly independent SNPs ($r^2<0.2$). In the second step, the association between each SNP and SLE clinical phenotype is tested using the allelic $\chi^2$ test. The independent SNPs that are nominally associated with the SLE phenotype are then selected for each genetic pathway. In the third step, the pathway statistic is computed as the average of the $\chi^2$ statistics of the selected SNPs. In the last step, the statistical significance of the pathway association with the SLE phenotype is computed using a permutation-based approach. In the permutation procedure, the SLE phenotype is randomly assigned to the patient cohort and the $\chi^2$ statistic is subsequently computed for each pathway. This analysis is then repeated multiple times (n=1,000,000 permutations). Finally, the empirical P-value of each pathway is computed as the proportion of permuted $\chi^2$ statistics that are higher than the observed $\chi^2$ statistic.

1.5 Differential expression analysis of VEGF pathway genes after topical immunotherapies

Cutaneous and mucocutaneous phenotypes in SLE are treated with a diverse group of immunotherapies. Given the observed genetic association between VEGF and oral ulcers, we hypothesized that the topical immunotherapies commonly prescribed for cutaneous SLE should induce significant transcriptional changes in the VEGF pathway genes. In order to test this hypothesis, we used transcriptional data from microarray experiments at the NCBI Gene Expression Omnibus microarray database (GEO, http://www.ncbi.nlm.nih.gov/geo/) [9]. In this database, we searched for whole genome expression profiling datasets from cutaneous/mucocutaneous human samples collected
from non-cancer individuals or cellular cultures (5th November 2015). From these, we looked for tissue or cell cultures treated with any of the common steroid and non-steroid topical immunotherapies most widely used in SLE. The former group was composed by 6 drugs (betamethasone valerate, clobetasol propionate, flucinolone acetonide, fluocinonide, hydrocortisone butirate and triamcinolone acetonide) [10] and the latter group included a total of 12 drug (ABT-281, anthralin, calcipotriol, diphencyprone, imiquimod, intralesional interferon, pimecrolimus, sirolimus, squartic acid dibutyl ester, tacrolimus, topical interferon and topical zinc) [11]. Given that sample size is one of the major concerns to confidently identify differentially expressed genes between two experimental groups [12], small datasets were excluded from the search. We found a total of three gene expression datasets generated after treatment with four common immunotherapies for cutaneous SLE: betamethasone valerate and pimecrolimus (GSE32473), diphencyprone (GSE52360) and imiquimod (GSE68182). For each gene expression dataset, we performed quality control analysis and subsequent normalization on the log2-scale using the quantile normalization method (Figure S3) [13]. The differential expression analysis for the VEGF pathway genes between treated and non-treated samples was performed using Student’s t-test. The statistical significance of the global perturbation of the VEGF pathway was assessed using the Binomial test. All analyses were performed using the R statistical software [14].
## 2. Supplementary Tables

### 2.1 Table S1. Association of SLE risk genes with SLE clinical phenotypes in the discovery cohort.

| SNP | CHE | POS | GENE | NUCLEOTIDE | BASE |
|-----|-----|-----|------|------------|------|
| euch29495 | 1 | 16375762 | ATG5 | 5,2E-09 | 5,2E-09 |
| euch29573 | 1 | 16379598 | PRDM1 | 7,9E-09 | 7,9E-09 |
| euch29605 | 1 | 16379604 | DISCOID RASH | 2,3E-09 | 2,3E-09 |
| euch29665 | 1 | 16379651 | IKZF3 | 1,5E-09 | 1,5E-09 |
| euch29715 | 1 | 16379717 | MHC class III | 1,3E-09 | 1,3E-09 |
| euch29763 | 1 | 16379769 | IRF5 | 1,0E-09 | 1,0E-09 |
| euch29825 | 1 | 16379829 | Nucleotide Polymorphism | | |
| euch29885 | 1 | 16379885 | OR (95% CI) | | |
| euch29935 | 1 | 16379935 | OR (95% CI) | | |

### Abbreviations:
- Chr: chromosome
- CI: confidence interval
- OR: odds ratio
- NA: odds ratio was not estimated due to the presence of zero-cell counts
- Position: SNP base pair in build GRCh37/hg19
- P: P-value obtained from the association analysis
- SNP: Single-Nucleotide Polymorphism
2.2 Genome-wide pathway associations obtained analyzing the 11 SLE clinical phenotypes in the discovery cohort.
rs12413938  | rs1144171  | rs1019033  | rs9896052  | rs708030    | rs2871444  | rs17090708  |
rs1714594   | rs1466447  | rs2041120  | rs17785945 | rs873592    | rs2194051  | rs10493211  |
rs878066    | rs2397446  | rs12207548 | rs9295464  | rs624797    | rs1468934  | rs3820028   |
rs1872568   | rs6878196  | rs6770805  | rs4702473  | rs4701780   | rs10421422 | rs13168690  |
rs7206142   | rs17360897 | rs10228945 | rs2327162  | rs2287778   | rs7623679  | rs1477031   |
rs1108386   | rs11610288 | rs11611796 | rs9458157  | rs2305913   | rs9534844  | rs10970427  |
rs11893686  | rs7600094  | rs955358   | rs1946741  | rs2970358   | rs1554668  | rs2160517   |
rs371043    | rs174532   | rs4671408  | rs1053079  | rs633742    | rs6928843  | rs9615025   |
rs306090    | rs6807740  | rs9447579  | rs4685165  | rs8081512   | rs208147   | rs4884479   |
rs1484197   | rs10153006 | rs809942   | rs1205357  | rs2039585   | rs220988   | rs12021681  |
rs9328355   | rs13133050 | rs11063954 | rs9287095  | rs4671408   | rs870777   | rs12517345  |
rs970969    | rs9534844  | rs10970427 | rs11893686 | rs7600094   | rs955358   | rs1946741   |
rs2970358   | rs1554668  | rs2160517  | rs12191179 | rs372334    | rs12901499 | rs12915039  |
rs59        | rs333968   | rs773878   | rs6681035  | rs12318072  | rs1714594  | rs1466447   |

Antinuclear Antibodies

ARGININE_AND_PROLINE_METABOLISM
VEGF_PATHWAY
CSK_PATHWAY
POST_TRANSLATIONAL_PROTEIN_MODIFICATION
MCALPAIN_PATHWAY
THROMBOXANE_SIGNALLING_THROUGH_TP_RECEPTOR
PHOSPHORYLATION_OF_THE_APC_C
COMPLEMENT_AND_COAGULATION_CASCADES
PKA_MEDIATED_PHOSPHORYLATION_OF_CREB
SIGNALING_BY_FGFR1_MUTANTS
REGULATION_OF_INSULIN_SECRETION
ETS_PATHWAY
G_BETA_GAMMA_SIGNALLING_THROUGH_PI3KGAMMA
NTHI_PATHWAY
BIOCARTA
REACTOME
REACTOME
REACTOME
REACTOME
REACTOME
REACTOME

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null
| rs6533710 | rs422437 | rs1534131 | rs885244 | rs2005219 | rs851010 | rs12652661 |
| rs16854131 | rs10841952 | rs2302600 | rs6605 | rs660489 | rs693293 | rs12608960 |
| rs7721613 | rs1499368 | rs1397829 | rs701078 | rs4817754 | rs7689213 | rs2823209 |
| rs17237251 | rs00901 | rs4554825 | rs2229032 | rs760782 | rs10818964 | rs7153386 |
| rs6503113 | rs2291782 | rs8852 | rs1369450 | rs1534131 | rs885244 | rs1396980 |
| rs583720 | rs291353 | rs7531583 | rs2224957 | rs17514846 | rs958937 | rs9323731 |
| rs12323801 | rs230632 | rs7955100 | rs4259245 | rs13190668 | rs1509844 | rs2207317 |
| rs6039211 | rs1554465 | rs42417 | rs4404878 | rs880183 | rs7169544 | rs10505528 |
| rs1468727 | rs7703433 | rs2005219 | rs490 | rs1149 | rs554 | rs1322 |
| rs1388 | rs2313 | rs1617 | rs1102 | rs435 | rs753 | rs1296 |
| rs1134 | rs691 | rs682 | rs27 | | | |

**Gene Networks**

- **Arthritis**
- **GLYCOSPHINGOLIPID_BIOSYNTHESIS_LACTO_AND_NEOLACTO_SERIES**
- **AUTODEGRADATION_OF_CDH1_BY_CDH1_APC**
- **G2_PATHWAY**
- **REGULATION_OF_INSULIN_SECRETION_BY_GLUCAGON_LIKE_PEPTIDE1**
- **RAS_PATHWAY**
- **ERK5_PATHWAY**
- **AMINO_ACID_SYNTHESIS_AND_INTERCONVERSION_TRANSAMINATION**
- **ECM_PATHWAY**
- **KEGG**
- **BIOCARTA**
- **REACTOME**

**Pathways and Related Genes**

- **rs12129768**
- **rs2287047**
- **rs12026714**
- **rs1921082**
- **rs735563**
- **rs3844279**
- **rs785512**
- **rs2302234**
- **rs121133609**
- **rs10515086**
- **rs559**
- **rs4078830**
- **rs1652583**
- **rs1959011**
- **rs3134942**
- **rs1007637**
- **rs12274970**
- **rs2906142**
- **rs1887735**
- **rs17677652**
- **rs4417522**
- **rs1514254**
- **rs891398**
| rs12045689 | rs17221851 | rs10475030 | rs2872821 | rs11630961 | rs7530853 | rs7551550 |
| rs9955719 | rs7931895 | rs12969349 | rs2301226 | rs777709 | rs2160919 | rs17554245 |
| rs1865288 | rs13209604 | rs12957142 | rs518345 | 1464459 | rs4938440 | rs17476583 |
| 1464459 | rs2805434 | rs9293478 | rs1405331 | rs7254601 | rs6700222 | 52661 |
| rs12129709 | rs9913908 | rs198182 | rs2322376 | rs3796944 | rs7721613 | rs7149441 |
| rs2005219 | rs2854028 | rs6470648 | rs10490823 | rs2938395 | rs11196146 | rs592412 |
| 3298230 | rs6460004 | rs17193211 | rs1636874 | rs12711539 | rs6438549 | rs718939 |
| 1998762 | rs2235366 | rs2168043 | rs2017750 |

**KEGG**

1326

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**BIOCARTA**

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| rs16974808 | rs10955078 | rs8055955 | rs2722639 | rs11185438 | rs2516614 | rs353639 | 723 | rs106203397101 | rs1331683 | rs9972635 | rs12606601 | rs4867023 | rs13153654 | rs4403186 | rs2963711 | 462800 | rs10017353 | rs7442627 | rs269853 | 2561944 | 01096 | rs785512 | rs10147042 | rs7986346 | rs336209 | rs230530 | rs17237251 | rs2494738 | 5089 | rs633891 | rs6463716 | rs3737147 | rs653844 | rs9540055 | rs6499137 | rs226981 |
|------------|------------|------------|------------|------------|------------|------------|-----|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis | Arthritis | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  | Arthritis  |

**Pathways:**
- NUCLEOTIDE EXCISION REPAIR
- GLYCOSAMINOGLYCAN BIOSYNTHESIS HEPARAN SULFATE
- ASPARAGINE N-LINKED GLYCOSYLATION
- POST TRANSLATIONAL MODIFICATION SYNTHESIS OF GPI ANCHORED PROTEINS
- DOWNREGULATION OF TGF BETA RECEPTOR SIGNALING
- GLYCINE SERINE AND THREONINE METABOLISM
- HISTIDINE METABOLISM
- PYK2 PATHWAY
- OXYGEN DEPENDENT PROLINE HYDROXYLATION OF HYPOXIA INDUCIBLE FACTOR ALPHA

**Database Source:**
- KEGG
- BIOCARTA
- REACTOME

**Gene IDs:**
- rs16974808
- rs10955078
- rs8055955
- rs2722639
- rs11185438
- rs2516614
- rs353639
- rs723
- rs106203397101
- rs1331683
- rs9972635
- rs12606601
- rs4867023
- rs13153654
- rs4403186
- rs2963711
- 462800
- rs10017353
- rs7442627
- rs269853
- 2561944
- 01096
- rs785512
- rs10147042
- rs7986346
- rs336209
- rs230530
- rs17237251
- rs2494738
- 5089
- rs633891
- rs6463716
- rs3737147
- rs653844
- rs9540055
- rs6499137
- rs226981

**Additional Notes:**
- Certain gene IDs are repeated, indicating multiple entries or references.
- The pathway interactions and relationships are complex and involve various biological processes.
| Gene ID | Description |
|---------|-------------|
| rs2716121 | Photosensitivity |
| rs904453 | Photosensitivity |
| rs33344 | Photosensitivity |
| rs10515068 | Photosensitivity |
| rs6452735 | Photosensitivity |
| rs7193148 | Photosensitivity |
| rs1423236 | Photosensitivity |
| rs7984951 | Photosensitivity |
| rs2357291 | Photosensitivity |
| rs17567 | Photosensitivity |
| rs17491036 | Photosensitivity |
| rs1982837 | Photosensitivity |
| rs9574595 | Photosensitivity |
| rs11604757 | Photosensitivity |
| rs2808787 | Photosensitivity |
| rs7782469 | Photosensitivity |
| rs7089663 | Photosensitivity |
| rs10952049 | Photosensitivity |
| rs6722598 | Photosensitivity |
| rs134174 | Photosensitivity |
| rs10484565 | Photosensitivity |
| rs2286670 | Photosensitivity |
| rs11687619 | Photosensitivity |
| rs5610865573 | Photosensitivity |
| rs6516498 | Photosensitivity |
| rs990309 | Photosensitivity |
| rs1977298 | Photosensitivity |
| rs267131 | Photosensitivity |
| rs7622781 | Photosensitivity |
| rs12480230 | Photosensitivity |
| rs1542568 | Photosensitivity |
| rs1415879 | Photosensitivity |
| rs918167 | Photosensitivity |
| rs2348182 | Photosensitivity |
| rs4745514 | Photosensitivity |
| rs4239343 | Photosensitivity |
| rs8044109 | Photosensitivity |
| rs7206380 | Photosensitivity |
| rs3815076 | Photosensitivity |
| rs1613070 | Photosensitivity |
| rs6817487 | Photosensitivity |
| rs1283614 | Photosensitivity |
| rs12878503 | Photosensitivity |
| rs12655172 | Photosensitivity |
| rs7429360 | Photosensitivity |
| rs6952793 | Photosensitivity |
| rs10787899 | Photosensitivity |
| rs3825073 | Photosensitivity |
| rs162202 | Photosensitivity |
| rs6059703 | Photosensitivity |
| rs1211975 | Photosensitivity |
| rs11217129 | Photosensitivity |
| rs5845 | Photosensitivity |
| rs6181 | Photosensitivity |
| rs1094 | Photosensitivity |
| rs3203 | Photosensitivity |
| rs1298 | Photosensitivity |
| rs3006 | Photosensitivity |
| rs1900 | Photosensitivity |
| rs2264 | Photosensitivity |
| rs1564 | Photosensitivity |
| rs999 | Photosensitivity |
| rs7429360 | Photosensitivity |
| rs6952793 | Photosensitivity |
| rs10787899 | Photosensitivity |
| rs3825073 | Photosensitivity |
| rs162202 | Photosensitivity |
| rs6059703 | Photosensitivity |
| rs1211975 | Photosensitivity |
| rs11217129 | Photosensitivity |
| rs5845 | Photosensitivity |
| rs6181 | Photosensitivity |
| rs1094 | Photosensitivity |
| rs3203 | Photosensitivity |
| rs1298 | Photosensitivity |
| rs3006 | Photosensitivity |
| rs1900 | Photosensitivity |
| rs2264 | Photosensitivity |
| rs1564 | Photosensitivity |
| rs999 | Photosensitivity |
null
| rs1801516 | rs1321311 | rs6989591 | rs653079 | rs4980335 | rs2597189 |
| 319 | rs10819283 | rs9036 | rs7971218 | rs4976178 | rs7530862 | rs13103835 | rs1728803 |
| 5833 | rs1045288 | rs3859192 | rs17477673 | rs11543947 | rs10868558 | rs7169989 | rs11023238 |
| 9930 | rs2178603 | rs10516713 | rs1490752 | rs1899745 | rs4147452 | rs6768674 | rs4794756 |
| 512 | rs2608654 | rs4863687 |
| 0305 | rs6118062 | rs8078231 | rs2179798 | rs9927848 | rs11646540 | rs4816089 | rs17192160 |
| 97854 | rs10500175 | rs6973683 | rs2221513 | rs6942446 | rs3135363 | rs2591454 | rs9348863 |
| 11218954 | rs2227956 | rs3115673 | rs7745906 | rs11672983 | rs7322307 | rs1242105 |
| 8062 | rs3729877 | rs2179798 | rs316689 | rs4816089 | rs7755078 | rs1983635 | rs6055748 |
| 411 | 538723 | rs494340 | rs39502 | rs17074679 | rs1884839 | rs9550565 | rs5743291 | rs3130283 |
| 71594 | rs311572 | rs4151374 | rs3789724 | rs4150667 | rs2020892 | rs4669463 | rs1467464 | rs2584624 | rs1045288 | rs133416 | rs3859192 | rs690705 | rs11543947 |
| 176 | rs12024682 | rs6142711 | rs8009527 | rs13245967 | rs5758168 | rs4150454 | rs1420426 |
| 192469 | rs17766515 | rs9345126 | rs230530 | rs5743942 | rs9345117 | rs4326648 | rs538723 | rs7019909 | rs1888363 | rs1702956 | rs765614 | rs2532100 | rs3130320 | rs10484160 | rs8003146 |

Oral Ulcers

GAP_JUNCTION_ASSEMBLY

CELL_ADHESION_MOLECULES_CAMS

CTNNB1_PHOSPHORYLATION_CASCADE

LIPOPROTEIN_METABOLISM

CHEMICAL_PATHWAY

DC_PATHWAY

NCAM1_INTERACTIONS

RNA_POL_I_TRANSCRIPTION_INITIATION

NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY

ANTIGEN_PROCESSING_AND_PRESENTATION

PYK2_PATHWAY

ARAP_PATHWAY

ATRBRCA_PATHWAY

GLUTATHIONE_CONJUGATION

CHEMOKINE_RECEPTORS_BIND_CHEMOKINES

TYPE_I_DIABETES_MELLITUS

REACTOME

BIOCARTA

KEGG

REACTOME

BIOCARTA

REACTOME

REACTOME

REACTOME

REACTOME

REACTOME

REACTOME

KEGG

BIOCARTA

REACTOME
| Gene ID   | Name                                      | NUM  |
|----------|-------------------------------------------|------|
| rs7594007| rs2958522| 2.79E-03| 0.001 | 0.001 |
| rs7719763| rs12896325| 2.96E-03| 0.001 | 0.001 |
| rs6985681| rs12594750| 2.96E-03| 0.001 | 0.001 |
| rs10070379| rs4554825| 2.96E-03| 0.001 | 0.001 |
| rs10940145| rs7255657| 2.96E-03| 0.001 | 0.001 |
| rs6987802| rs3810168| 2.96E-03| 0.001 | 0.001 |
| rs10225279| rs4558175| 2.96E-03| 0.001 | 0.001 |

**Hematopoietic Cell Lineage**

**IGF1-MTOR Pathway**

**GSK3 Pathway**

**EIF4 Pathway**

**IL-1 Receptor-SHC Signaling**

**HER2 Pathway**

**Natural Killer Cell-Mediated Cytotoxicity**

**Reactome**

**KEGG**

**BIOCARTA**

**Discoid Rash**
rs569647 | rs221725 | rs4964005 | rs2192724 | rs715305 | rs7972342 | rs7629595
rs6593011 | rs7045845 | rs8891 | rs10521121 | rs1038378 | rs7280485 | rs4878805
rs696 | rs2501657 | rs7163945 | rs3773650 | rs9342261 | rs7169592 | rs968088
rs10889011 | rs9291117 | rs4425665 | rs4668631 | rs7893330 | rs3019260 | rs6678588
rs4310569 | rs2051920 | rs669669 | rs12580394 | rs3739809 | rs12911091 | rs6804202 | rs2720662

Malar Rash

TGF_BETA_SIGNALING_PATHWAY
G_PROTEIN_ACTIVATION
KINESINS
AMINO_ACID_AND_OLIGOPEPTIDE_SLC_TRANSPORTERS
VALINE_LEUCINE_AND_ISOLEUCINE_DEGRADATION
SMALL_CELL_LUNG_CANCER
NTHI_PATHWAY
ANTIVIRAL_MECHANISM_BY_IFN_STIMULATED_GENES
PANCREATIC_CANCER
PLATELET_HOMEOSTASIS

KEGG
REACTOME
BIOCARTA

2,25E-01
9,17E-09
2,06E-01
1,95E-01
1,87E-01
1,74E-01
1,60E-01
1,58E-01
1,45E-01

9,17E-09
9,17E-09
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9,17E-09
9,17E-09
9,17E-09
9,17E-09
9,17E-09
9,17E-09

1,74E-01
1,60E-01
1,58E-01
1,45E-01
1,32E-01
1,29E-01
1,25E-01
1,21E-01
1,17E-01

null
| rs4641872 | rs6550146 | rs10512889 | rs730424 | rs8049212 | rs1432295 | rs17630822 |
|-----------|-----------|------------|--------|-----------|-----------|------------|
| rs6871452 | rs178255  | rs12251654 | rs2017750 | rs17822304 | rs4234512 | rs383542   |
| rs16897109 | rs16897180 | rs17350527 | rs2867316 | rs4673260 | rs4976028 | rs7618747  |
| rs12153515 | rs2013573 | rs11135312 | rs6738678 | rs17608022 | rs316144  | rs10874814 |
| 21        | rs4834779 | rs703505  | rs934803  | rs10898864 | rs6443558 | rs7077665  |
| 2          | 101       | 20         | 15       | 20         | 11         | 20         |
| 20        | 20        | 20         | 20       | 20         | 20         | 20         |

**Serositis**

**NA_CL_DEPENDENT_NEUROTRANSMITTER_TRANSPORTERS**

**REGULATION_OF_SIGNALING_BY_CBL**

**SIGNALLING_TO_RAS**

**PLATELET_HOMEOSTASIS**

**RNA_POL_III_TRANSCRIPTION**

**DESTABILIZATION_OF_MRNA_BY_BRF1**

**REACTOME**

**BIOCARTA**

**KEGG**

**737**

**1,09E-01**
| rs17464037 | rs11465990 | rs1366315 | rs6871452 | rs1531846 | rs178255 | rs9895159 |
| rs4952147 | rs1900448 | rs895344 | rs16878220 | rs1921874 | rs4819329 | rs2269423 |
| rs1930762 | rs1558909 | rs1594485 | rs4952147 | rs1900448 | rs895344 | rs16878220 |
| rs714158 | rs7973701 | rs2026628 | rs12671372 | rs7536180 | rs747020 | rs10872893 |
| rs2049051 | rs7751192 | rs8190645 | rs701492 | rs2815736 |
| rs12342878 | rs9298935 | rs17470048 | rs7024321 | rs6015032 | rs2647168 | rs1536002 |
| rs54809 | rs747020 | rs6885261 | rs383542 | rs12142335 | rs1636808 | rs764605 |
| rs10232489 | rs541425 | rs2302984 | rs2020902 | rs12544147 | rs4859540 | rs10209471 |
| rs3783754 | rs7290191 | rs6018627 | rs12495548 | rs3744550 | rs1734852 | rs4689001 |

**Serositis**

**ANTIGEN_PROCESSING_AND_PRESENTATION**

**TGF_BETA_RECEPTOR_SIGNALING_IN_EMT_EPITHELIAL_TO_MESENCHYMAL_TRANSITION**

**BIOSYNTHESIS_OF_UNSATURATED_FATTY_ACIDS**

**TELOMERE_MAINTENANCE**

**DARPP_32_EVENTS**

**FATTY_ACID_METABOLISM**

**CITRATE_CYCLE_TCA_CYCLE**

**RESOLUTION_OF_AP_SITES_VIA_THE_MULTIPLE_NUCLEOTIDE_PATCH_REPLACEMENT_PATHWAY**

**CELL_SURFACE_INTERACTIONS_AT_THE_VASCULAR_WALL**

**INTRINSIC_PATHWAY_FOR_APOPTOSIS**

**ACTINY_PATHWAY**

**REACTOME**

**BIOCARTA**

**KEGG**

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null
INTEGRATION_OF_ENERGY_METABOLISM

CELLCYCLE_PATHWAY

RESPONSE_TO_ELEVATED_PLATELET_CYTOSOLIC_CA2+

FOCAL_ADHESION

SIGNALING_BY_RHO_GTPASES

RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY

ALPHA_LINOLENIC_ACID_METABOLISM

MRNA_SPLICING_MINOR_PATHWAY

GLUCAGON_SIGNALING_IN_METABOLIC_REGULATION

DNA_REPLICATION

EXTRACELLULAR_MATRIX_ORGANIZATION

NCAM1_INTERACTIONS

NONSENSE_MEDIATED_DECAY_ENHANCED_BY_THE_EXON_JUNCTION_COMPLEX

XENOBIOTICS

G_ALPHA1213_SIGNALLING EVENTS

GROWTH_HORMONE_RECEPTOR_SIGNALING

INITIAL_TRIGGERING_OF_COMPLEMENT

EIF_PATHWAY

REACTOME

KEGG

BIOCARTA

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| rs4432229 | rs4726499 | rs10857733 | rs2181874 | rs98866628 | rs1128864 | rs6743777 | rs4672803 | rs2917779 | rs4599669 | rs137602 | rs1406334 |
|-----------|-----------|-------------|-----------|-------------|-----------|-----------|-----------|---------|-----------|----------|-----------|
| rs1251465 | rs3928852 | rs2945770 | rs538977 | rs10784585 | rs7814358 | rs29128 | rs996009 | rs6796803 | rs698951 | rs2283333 | 996009 |
| rs1422884 | rs11859534 | 12201680 | rs6543716 | rs7177101 | rs1782808 | rs1010650 | rs13031237 | rs10788819 | rs2141484 | rs1572507 | rs6108237 |
| rs2239093 | rs2239041 | rs11048455 | rs7008202 | rs7651990 | rs6766238 | rs757911 | rs6965030 | rs6955791 | rs895479 | rs12155027 |

| POST_TRANSLATIONAL_PROTEIN_MODIFICATION | GLUCOSE_TRANSPORT | MUSCLE_CONTRACTION | DOWNSTREAM_SIGNALING_EVENTS_OF_B_CELL_RECEPTOR_BCR | REGULATION_OF_ORNITHINE_DECARBOXYLASE_ODC | ENOS_ACTIVATION_AND_REGULATION | CDT1_ASSOCIATION_WITH_THE_CDC6_ORC_ORIGIN_COMPLEX | ASSEMBLY_OF_THE_PRE_REPLICATIVE_COMPLEX | SMOOTHE_MUSCLE_CONTRACTION | RENAL_TRANSPORT | INTESTINAL_CELLULAR_TRANSPORT | INTERACTIONS_OF_VPR_WITH_HOST_CELLULAR_PROTEINS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | FORMATION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS |
|--------------------------------------|------------------|------------------|-----------------------------------------------|-----------------------------------------------|------------------|-----------------------------------------------|-----------------------------------------------|------------------|------------------|------------------|-----------------------------------------------|------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|------------------|-----------------------------------------------|------------------|-----------------------------------------------|
| POST_TRANSLATIONAL_PROTEIN_MODIFICATION | GLUCOSE_TRANSPORT | MUSCLE_CONTRACTION | DOWNSTREAM_SIGNALING_EVENTS_OF_B_CELL_RECEPTOR_BCR | REGULATION_OF_ORNITHINE_DECARBOXYLASE_ODC | ENOS_ACTIVATION_AND_REGULATION | CDT1_ASSOCIATION_WITH_THE_CDC6_ORC_ORIGIN_COMPLEX | ASSEMBLY_OF_THE_PRE_REPLICATIVE_COMPLEX | SMOOTHE_MUSCLE_CONTRACTION | RENAL_TRANSPORT | INTESTINAL_CELLULAR_TRANSPORT | INTERACTIONS_OF_VPR_WITH_HOST_CELLULAR_PROTEINS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | FORMATION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS |
| POST_TRANSLATIONAL_PROTEIN_MODIFICATION | GLUCOSE_TRANSPORT | MUSCLE_CONTRACTION | DOWNSTREAM_SIGNALING_EVENTS_OF_B_CELL_RECEPTOR_BCR | REGULATION_OF_ORNITHINE_DECARBOXYLASE_ODC | ENOS_ACTIVATION_AND_REGULATION | CDT1_ASSOCIATION_WITH_THE_CDC6_ORC_ORIGIN_COMPLEX | ASSEMBLY_OF_THE_PRE_REPLICATIVE_COMPLEX | SMOOTHE_MUSCLE_CONTRACTION | RENAL_TRANSPORT | INTESTINAL_CELLULAR_TRANSPORT | INTERACTIONS_OF_VPR_WITH_HOST_CELLULAR_PROTEINS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | FORMATION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS |
| POST_TRANSLATIONAL_PROTEIN_MODIFICATION | GLUCOSE_TRANSPORT | MUSCLE_CONTRACTION | DOWNSTREAM_SIGNALING_EVENTS_OF_B_CELL_RECEPTOR_BCR | REGULATION_OF_ORNITHINE_DECARBOXYLASE_ODC | ENOS_ACTIVATION_AND_REGULATION | CDT1_ASSOCIATION_WITH_THE_CDC6_ORC_ORIGIN_COMPLEX | ASSEMBLY_OF_THE_PRE_REPLICATIVE_COMPLEX | SMOOTHE_MUSCLE_CONTRACTION | RENAL_TRANSPORT | INTESTINAL_CELLULAR_TRANSPORT | INTERACTIONS_OF_VPR_WITH_HOST_CELLULAR_PROTEINS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | FORMATION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS | TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS | INTERACTIONS_OF_VPN_WITH_HOST_CELLULAR_PROTEINS |
null
rs419588 | rs785437 | rs3731828 | rs35684 | rs1555772 | rs7213960 | rs4075688 | rs770082
rs24079 | rs11251588 | rs9268911 | rs10907192 | rs10243170 | rs13243079 | rs5439
rs61116 | rs2830076 | rs8132767 | rs2906766 | rs1510470 | rs12419174 | rs9294511 | rs204991
rs281389 | rs3815341 | rs9276711 | rs181997
rs6541017 | rs2684806 | rs541682 | rs2110290 | rs17392492 | rs6586116 | rs534182 | rs3806929
rs618956 | rs11658645 | rs7691016 | rs2167239 | rs7069860 | rs10148024 | rs2303147 | rs7018784
rs73704 | rs2235360 | rs9805578 | rs12220387 | rs11953134 | rs1924210 | rs10477181 | rs140504
rs90 | rs3802727 | rs491675 | rs11599360 | rs7126210 | rs2448343 | rs13209654 | rs3027267
rs79158 | rs12454712 | rs12901358 | rs4637783 | rs6995630 | rs4791032 | rs2395851 | rs7162314
rs934967 | rs2269429 | rs3823717 | rs2299893 | rs11126361 | rs3742377 | rs2899472 | rs9309462

Hematologic Disorder

GAP_JUNCTION_ASSEMBLY
ELONGATION_ARREST_AND_RECOVERY
YAP1_AND_WWTR1_TAZ_STIMULATED_GENE_EXPRESSION
SEMA4D_INDUCED_CELL_MIGRATION_AND_GROWTH_CONE_COLLAPSE
VEGF_SIGNALING_PATHWAY
SIGNALING_BY_FGFR
MPR_PATHWAY
DRUG_METABOLISM_OTHER_ENZYMES
EICOSANOID_LIGAND_BINDING_RECEPTORS
SPHINGOLIPID_METABOLISM
ERK_PATHWAY
SYNTHESIS_OF_BILE_ACIDS_AND_BILE_SALTS
SCFSKP2_MEDIATED_DEGRADATION_OF_P27_P21
CHONDROITIN_SULFATE_DERMATAN_SULFATE_METABOLISM

REACTOME

KEGG

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rs17631340|rs1427988|rs9295312|rs13320527|rs12554375|rs954241|rs1155876|rs7307700|rs12503593|rs316738|rs2107232|rs221725|rs11945064|rs12789511|rs1805775|rs8049025|rs4544229|9627|rs3829078|rs902130|rs370476|rs4312645|rs10215237|rs340|rs10790921|rs7972214|rs12318072|rs6537883|rs10846670|rs1110904|rs870844|rs764190|rs706725|rs10781329|rs10000770|rs11078772|rs228271|rs2667096|rs3756121|rs706725|rs3765141|rs6449947|rs12536419|rs3829078|rs2161529|rs11153318|rs7025162|rs7582020|rs12294732|rs1075405|57742|rs5996534|rs9642880|rs3009935|rs1125467|rs2834906|rs266335|rs13320527|51|rs639622|rs236504|rs13264567|rs4832505|rs17230421|rs7552646|rs1883767|1398|rs3135363|rs9469310|45045|rs1678002|rs730830|rs2094405|rs10506210|rs17152433|rs9299346|rs1997696|6|rs1007482|rs6434036|rs457372|rs8078165|rs11902670|rs773546|rs1115882

Immunologic Disorder

ENERGY_DEPENDENT_REGULATION_OF_MTOR_BY_LKB1_AMPK
ERK_MAPK_TARGETS
WNT_SIGNALING_PATHWAY
SIGNALING_BY_FGFR1_FUSION_MUTANTS
GLUCOSE_TRANSPORT
TRAFFICKING_OF_AMPA_RECEPTORS
METAL_ION_SLC_TRANSPORTERS
HYPERTROPHIC_CARDIOMYOPATHY_HCM
RENAL_CELL_CARCINOMA
ION_CHANNEL_TRANSPORT
SIGNALLING_TO_ERKS
EIF4_PATHWAY
BASE_EXCISION_REPAIR
APOPTOSIS
PI3K_AKT_ACTIVATION
TGFB_PATHWAY
NUCLEAR_RECEPTOR_TRANSCRIPTION_PATHWAY
POTASSIUM_CHANNELS
PROTEIN_FOLDING
ERK_PATHWAY
PI_METABOLISM

KEGG
REACTOME
BIOCARTA
| rs16902328 | rs920293 | rs7351039 | rs4464148 | rs7652697 |
|---------|--------|---------|----------|---------|
| 0.0004  | 0.0030 | 0.0053  | 0.0058   | 0.0036  |

| rs1322487 | rs9933029 | rs11670126 | rs981257 | rs1376091 | rs470168 | rs17782215 | rs2475193 |
|---------|--------|---------|---------|---------|---------|---------|---------|
| 0.0033  | 0.0015 | 0.0019  | 0.0060  | 0.0016  | 0.0012  | 0.0061  |

| rs2038712 | rs10870911 | rs10908200 | rs10495929 | rs9922362 | rs10743591 | rs3782309 | rs3787011 |
|---------|-----------|-----------|-----------|---------|-----------|---------|---------|
| 0.0002  | 0.0003    | 0.0001    | 0.0001    | 0.0001  | 0.0001    | 0.0001  |

| rs6981247 | rs2282128 | rs12602230 | rs4943189 | rs3786136 | rs2033098 | rs764190 | rs1832265 |
|---------|---------|-----------|---------|---------|---------|---------|---------|
| 0.0071  | 0.0024  | 0.0001    | 0.0001   | 0.0001  | 0.0001   | 0.0001   |

| rs2362 | rs10743591 | rs3782309 | rs10794486 | rs4629562 | rs13190668 | rs6736093 | rs2177640 |
|---------|-----------|---------|-----------|---------|-----------|---------|---------|
| 0.0012  | 0.0001    | 0.0001   | 0.0001    | 0.0001   | 0.0001    | 0.0001   |

| rs64190 | rs16963394 | rs4148412 | rs1235805 |
|---------|------------|---------|---------|
| 0.0001  | 0.0001     | 0.0001  |

| rs7707082 | rs4544229 |
|----------|----------|
| 0.0001   |

| rs64190 | rs13173003 | rs31309 | rs4150196 | rs11731252 | rs706725 | rs3804357 | rs10781329 |
|---------|-----------|-------|---------|-----------|--------|---------|---------|
| 0.0001  | 0.0001    | 0.0001 | 0.0001  | 0.0001    | 0.0001 | 0.0001  |

| rs560718 | rs16972457 | rs22827151 | rs4401921 | rs752503 | rs1105168 | rs7311469 | rs3770705 |
|---------|------------|------------|---------|---------|-----------|---------|---------|
| 0.0001  | 0.0001     | 0.0001     | 0.0001  |

| rs11644646 | rs13173003 | rs17793122 | rs2261612 | rs1064825 | rs10798106 | rs706725 | rs3804357 |
|------------|------------|------------|---------|----------|-----------|--------|---------|
| 0.0001     | 0.0001     | 0.0001     | 0.0001  | 0.0001   | 0.0001    | 0.0001 | 0.0001  |

| rs10258834 | rs2025448 | rs1124275 | rs2051547 | rs7357092 | rs886420 | rs17195683 | rs21671 |
|------------|-----------|---------|---------|---------|--------|------------|---------|
| 0.0001     | 0.0001    | 0.0001  | 0.0001  | 0.0001  | 0.0001 | 0.0001     | 0.0001  |

| rs11083384 | rs428340 |
|------------|--------|
| 0.0001     |

| Immunologic Disorder | GLYCOSPHINGOLIPID_METABOLISM | AT1R_PATHWAY | FORMATION_OF_INCISION_COMPLEX_IN_GG_NER | RNA_POL_II_TRANSCRIPTION_PRE_INITIATION_AND_PROMOTER_OPENING | IL2_PATHWAY | CREB_PATHWAY | RNA_POL_I_TRANSCRIPTION_INITIATION | MEF2D_PATHWAY | CELL_CYCLE | TRANSCRIPTION | STATHMIN_PATHWAY | PROCESSING_OF_CAPPED_INTRON_CONTAINING_PRE_MRNA | TRANSCRIPTION_COUPLED_NER_TC_NER | PLATELET_SENSITIZATION_BY_LDL | TPO_PATHWAY |
|---------------------|-----------------------------|-------------|----------------------------------------|----------------------------------------------------------|-------------|-------------|----------------------------------|------------|-----------|----------------|---------------------|-------------------------------|---------------------------|-----------------------------|------------|
| 0.0001               | 0.0001                      | 0.0001      | 0.0001                                 | 0.0001                                                   | 0.0001      | 0.0001      | 0.0001                           | 0.0001     | 0.0001   | 0.0001         | 0.0001                       | 0.0001                         | 0.0001                     | 0.0001                      | 0.0001     |
| Gene ID | Gene Symbol | Description |
|---------|-------------|-------------|
| rs2583194 | | |
| rs965078 | | |
| rs174556 | | |
| rs2293464 | | |
| rs2686187 | | |
| rs1462529 | | |
| rs3809335 | | |
| rs8006358 | | |
| rs2882359 | | |
| rs12407294 | | |
| rs4585434 | | |
| rs1012178 | | |
| rs1548687 | | |
| rs4513489 | | |
| rs1341458 | | |
| rs1557399 | | |
| rs78040 | | |
| rs2602218 | | |
| rs3738043 | | |
| rs9474314 | | |
| rs7497607 | | |
| rs12580698 | | |
| rs2514051 | | |
| rs2287396 | | |
| rs3268 | | |
| rs7536947 | | |
| rs446304 | | |
| s3025643 | | |
| rs16837945 | | |
| rs9906150 | | |
| rs6674438 | | |
| rs7221237 | | |
| rs1999498 | | |
| rs9983351 | | |
| rs978708 | | |
| rs3010681 | | |
| rs10493889 | | |
| rs4775749 | | |
| rs290826 | | |
| rs1253795 | | |
| rs517483 | | |
| rs1934272 | | |
| rs2669429 | | |
| rs7916268 | | |
| rs40760903 | | |
| rs2006564 | | |
| rs910534 | | |
| rs920293 | | |
| rs469999 | | |
| rs319264 | | |
| rs1605888 | | |
| rs1165641 | | |
| rs4515788 | | |
| rs9841706 | | |
| rs280737 | | |
| rs1005805 | | |
| rs10381 | | |
| rs1982473 | | |
| rs1462529 | | |
| rs3809335 | | |
| rs8006358 | | |
| rs2882359 | | |
| rs12407294 | | |
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| rs1548687 | | |
| rs4513489 | | |
| rs1341458 | | |
| rs1557399 | | |
| rs78040 | | |
| rs2602218 | | |
| rs3738043 | | |
| rs9474314 | | |
| rs7497607 | | |
| rs12580698 | | |
| rs2514051 | | |
| rs2287396 | | |
| rs3268 | | |
| rs7536947 | | |
| rs446304 | | |
| s3025643 | | |
| rs16837945 | | |
| rs9906150 | | |
| rs6674438 | | |
| rs7221237 | | |
| rs1999498 | | |
| rs9983351 | | |
| rs978708 | | |
| rs3010681 | | |
| rs10493889 | | |
| rs4775749 | | |
| rs290826 | | |
| rs1253795 | | |
| rs517483 | | |
| rs1934272 | | |
| rs2669429 | | |
| rs7916268 | | |
| rs40760903 | | |
| rs2006564 | | |
| rs910534 | | |
| rs920293 | | |
| rs469999 | | |
| rs319264 | | |
| rs1605888 | | |
| rs1165641 | | |
| rs4515788 | | |
| rs9841706 | | |
| rs280737 | | |
| rs1005805 | | |
| rs10381 | | |
| rs1982473 | | |
| rs1462529 | | |
| rs3809335 | | |
| rs8006358 | | |
| rs2882359 | | |
| rs12407294 | | |
| rs4585434 | | |
| rs1012178 | | |
| rs1548687 | | |
| rs4513489 | | |
| rs1341458 | | |
| rs1557399 | | |
| rs78040 | | |
| rs2602218 | | |
| rs3738043 | | |
| rs9474314 | | |
| rs7497607 | | |
| rs12580698 | | |
| rs2514051 | | |
| rs2287396 | | |
| rs3268 | | |
| rs7536947 | | |
| rs446304 | | |
| s3025643 | | |
| rs16837945 | | |
| rs9906150 | | |
| rs6674438 | | |
| rs7221237 | | |
| rs1999498 | | |
| rs9983351 | | |
| rs978708 | | |
| rs3010681 | | |
| rs10493889 | | |
| rs4775749 | | |
| rs290826 | | |
| rs1253795 | | |
| rs517483 | | |
| rs1934272 | | |
| rs2669429 | | |
| rs7916268 | | |
| rs40760903 | | |
| rs2006564 | | |
| rs910534 | | |
| rs920293 | | |
| rs469999 | | |
| rs319264 | | |
| rs1605888 | | |
| rs1165641 | | |
| rs4515788 | | |
| rs9841706 | | |
| rs280737 | | |
| rs1005805 | | |
| rs10381 | | |
| rs1982473 | | |
| rs1462529 | | |
| rs3809335 | | |
| rs8006358 | | |
| rs2882359 | | |
| rs12407294 | | |
| rs4585434 | | |
| rs1012178 | | |
| rs1548687 | | |
| rs4513489 | | |
| rs1341458 | | |
| rs1557399 | | |
| rs78040 | | |
| rs2602218 | | |
| rs3738043 | | |
| rs9474314 | | |
| rs7497607 | | |
| rs12580698 | | |
| rs2514051 | | |
| rs2287396 | | |
| rs3268 | | |
| rs7536947 | | |
| rs446304 | | |
| rs7281786 | rs6443552 | rs7303830 | rs1879417 | rs10505867 | rs3819902 | rs1143960 |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| 5169      | rs2184778 | rs1459590 | rs10490697 | rs2025880 | rs2292867 | rs16975294 | rs12602314 |
| 59169     | rs13023787 | rs1962515 | rs843346 | rs11204910 | rs7204987 | rs660442 | rs1947372 |
| 58        | rs9506807 | rs516391 | rs1368406 | rs13312770 | rs9318729 | rs4435493 | rs10796853 |
| 72935     | rs563649 | 9153 | rs11226342 | rs771941 | rs2128650 | rs1962515 | rs3741403 |
| 381755    | rs1340343 | rs4331688 | rs3774051 | rs7611269 | rs6083725 | rs17022214 | rs4489814 |

### Genomic Variants

| rs2938769 | rs2219556 | rs3779972 | rs518558 | rs4751955 | rs4747345 | rs4842157 | rs4963857 |
|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| rs2761367 | rs16942 | rs4435493 | rs9634672 | rs11157432 | rs3934711 | rs17049508 | rs3761034 |
| rs4698855 | rs566416 | rs461970 | rs4963857 | rs10907192 | rs465531 | rs2423356 | rs3753242 |
| rs6918969 | rs11130040 | rs650229 | rs4382556 | rs1613070 | rs3740526 | rs3890801 | rs1229568 |
| rs4839797 | rs11612284 | rs363512 | rs170290 | rs8066734 | rs11938486 | rs4747345 | rs10907192 |
| rs11650230 | rs218378 | rs2300267 | rs2924149 | rs20 | rs34719083 | rs3771254 | rs10495717 |
| rs312049 | rs1373656 | rs7605009 | rs2242062 | rs1363518 | rs12708616 | rs6854637 | rs1352062 |
| rs5022631 | rs3922855 | rs6892782 | rs4695 | 92 |

### Gene Enrichment Analysis

- **Neurologic Disorder**
- **MEIOTIC RECOMBINATION**
- **CHEMOKINE_SIGNALING_PATHWAY**
- **TRANSMISSION_ACROSS_CHEMICAL_SYNAPSES**
- **SIGNALING_BY_RHO_GTPASES**
- **TNFR1_PATHWAY**
- **HUNTINGTONS_DISEASE**

### Reactome and KEGG Pathways

- **Reactome**
- **KEGG**

| Pathway Description | Pathway ID | Gene Count |
|---------------------|------------|------------|
| 1261                |            | 14         |
| 1529                |            | 38         |
| 1605                |            | 39         |
| 522                 |            | 32         |
| 5407                |            | 44         |
| 699                 |            | 31         |
| 9089                |            | 26         |
| 6096                |            | 2          |

### Additional Gene Information

- **rs01**
- **01**
- **9,90E**
- **-**

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**Note:** The table above represents a selection of genomic variants and their associated gene enrichment analysis results. Further details and context are provided in the integrated pathways and pathways with overlapping genes.
| rs228935 | rs10993754 | rs651933 | rs308195 | rs6916861 | rs3846211 | rs17043569 | rs2488809 | rs1534166 | rs9561932 | rs10490815 | rs1545033 | rs6503691 | rs13023787 | rs1962515 | rs6003709 | rs445775 | rs11048776 | rs2268833 | rs4573621 | rs1800627 | rs10486056 | rs776686 | rs1337988 | rs36631 | rs11046483 |
|---------|-----------|---------|---------|---------|---------|---------|----------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| 72986   |           |         |         |         |         |         |           |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |         |

**Neurologic Disorder**

- SPHINGOLIPID_METABOLISM
- INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION
- UNFOLDED_PROTEIN_RESPONSE
- GLYCOSPHINGOLIPID_METABOLISM
- CK1_PATHWAY
- GABA_B_RECEPTOR_ACTIVATION
- SPLICEOSOME
- GLUCONEOGENESIS

**REACTOME**

- 1153
- 752
- 3710
- 742
- 788
- 2702
- 195
- 1072
- 874
- 1557
- 3434

**KEGG**

- 30
- 18
- 38
- 21
- 38
- 35
- 20
- 20
- 20
- 14
- 20
- 20
- 20
- 20
- 20
- 20

**93**
| Gene ID | Symbol | Description |
|---------|--------|-------------|
| rs3770387 | rs2183124 | rs4732025 | rs4485425 | rs2388268 | rs12257705 | rs7089499 |
| rs2282735 | rs958766 | rs525007 | rs7274475 | rs6958081 | rs12962644 | rs11167020 |
| rs2254883 | rs12544882 | rs9880553 | rs2075355 | rs9561932 | rs10480450 |
| rs2207067 | rs1430004 | rs10510302 | rs16830230 | rs4821901 | rs1707113 | rs3784730 |
| rs1119864 | rs6114527 | rs4981468 | rs11749500 | rs178323 | rs11606866 | rs9695993 |
| rs2075555 | rs306962 | rs12419365 | rs17749288 | rs1160798 | rs265454 |
| rs10748834 | rs2439321 | rs306962 | rs12611955 | rs9390184 |
| rs262498 | rs10970923 | rs752409 | rs9526420 | rs6025639 |
| rs7070744 | rs17593512 | rs12577790 | rs1229976 | rs9378878 |
| rs6692958 | rs10973770 | 018228 | rs7099767 | rs2580 |
| rs1119864 | rs6114527 | rs4981468 | rs11749500 | rs178323 | rs11606866 | rs9695993 |
| rs2075555 | rs306962 | rs12419365 | rs17749288 | rs1160798 | rs265454 |
| rs10748834 | rs2439321 | rs306962 | rs12611955 | rs9390184 |
| rs262498 | rs10970923 | rs752409 | rs9526420 | rs6025639 |
| rs7070744 | rs17593512 | rs12577790 | rs1229976 | rs9378878 |
| rs6692958 | rs10973770 | 018228 | rs7099767 | rs2580 |
| rs1119864 | rs6114527 | rs4981468 | rs11749500 | rs178323 | rs11606866 | rs9695993 |
| rs2075555 | rs306962 | rs12419365 | rs17749288 | rs1160798 | rs265454 |
| Gene ID  | Description                                                      |
|---------|------------------------------------------------------------------|
| rs6667880 | FGFR2 Ligand Binding Pathway                                      |
| rs4790838 | FGFR2 Ligand Binding Pathway                                      |
| rs236106  | FGFR2 Ligand Binding Pathway                                      |
| rs2303744 | FGFR2 Ligand Binding Pathway                                      |
| rs3004318 | FGFR2 Ligand Binding Pathway                                      |
| rs9898519 | FGFR2 Ligand Binding Pathway                                      |
| rs1995785 | FGFR2 Ligand Binding Pathway                                      |
| rs918842  | FGFR2 Ligand Binding Pathway                                      |
| rs2877260 | FGFR2 Ligand Binding Pathway                                      |
| rs6018257 | FGFR2 Ligand Binding Pathway                                      |
| rs11760524| FGFR2 Ligand Binding Pathway                                      |
| rs7009399 | FGFR2 Ligand Binding Pathway                                      |
| rs4603211 | FGFR2 Ligand Binding Pathway                                      |
| rs10023724| FGFR2 Ligand Binding Pathway                                      |
| rs9362786 | FGFR2 Ligand Binding Pathway                                      |
| rs484754  | FGFR2 Ligand Binding Pathway                                      |
| rs12173146| FGFR2 Ligand Binding Pathway                                      |
| rs5166    | FGFR2 Ligand Binding Pathway                                      |
| rs11877878| FGFR2 Ligand Binding Pathway                                      |
| rs16972457| FGFR2 Ligand Binding Pathway                                      |
| rs16960774| FGFR2 Ligand Binding Pathway                                      |
| rs2716605 | FGFR2 Ligand Binding Pathway                                      |
| rs2230571 | FGFR2 Ligand Binding Pathway                                      |
| rs425594  | FGFR2 Ligand Binding Pathway                                      |
| rs6950715 | FGFR2 Ligand Binding Pathway                                      |
| rs2311552 | FGFR2 Ligand Binding Pathway                                      |
| rs1064576 | FGFR2 Ligand Binding Pathway                                      |
| rs1002170 | FGFR2 Ligand Binding Pathway                                      |
| rs133431  | FGFR2 Ligand Binding Pathway                                      |
| rs7332652 | FGFR2 Ligand Binding Pathway                                      |
| rs1994189 | FGFR2 Ligand Binding Pathway                                      |
| rs576040  | FGFR2 Ligand Binding Pathway                                      |
| rs918842  | FGFR2 Ligand Binding Pathway                                      |
| rs6539125 | FGFR2 Ligand Binding Pathway                                      |
| rs1015166 | FGFR2 Ligand Binding Pathway                                      |
| rs9275582 | FGFR2 Ligand Binding Pathway                                      |
| rs938486  | FGFR2 Ligand Binding Pathway                                      |
| rs28009721| FGFR2 Ligand Binding Pathway                                      |
| rs13164947| FGFR2 Ligand Binding Pathway                                      |
| rs3785690 | FGFR2 Ligand Binding Pathway                                      |
| rs17666787| FGFR2 Ligand Binding Pathway                                      |
| rs11248060| FGFR2 Ligand Binding Pathway                                      |
| rs9643302 | FGFR2 Ligand Binding Pathway                                      |
| rs8039131 | FGFR2 Ligand Binding Pathway                                      |
| rs6713082 | FGFR2 Ligand Binding Pathway                                      |
| rs104103| FGFR2 Ligand Binding Pathway                                      |
| rs7142869 | FGFR2 Ligand Binding Pathway                                      |
| rs2120823 | FGFR2 Ligand Binding Pathway                                      |
| rs12208181| FGFR2 Ligand Binding Pathway                                      |
| rs4678200 | FGFR2 Ligand Binding Pathway                                      |
| rs10490578| FGFR2 Ligand Binding Pathway                                      |
| rs1994174 | FGFR2 Ligand Binding Pathway                                      |
| rs2552346 | FGFR2 Ligand Binding Pathway                                      |
| rs10112596| FGFR2 Ligand Binding Pathway                                      |
| rs4338396 | FGFR2 Ligand Binding Pathway                                      |
| rs849430  | FGFR2 Ligand Binding Pathway                                      |
| rs17153698| FGFR2 Ligand Binding Pathway                                      |
| rs1881735 | FGFR2 Ligand Binding Pathway                                      |
| rs13173003| FGFR2 Ligand Binding Pathway                                      |
| rs853812  | FGFR2 Ligand Binding Pathway                                      |
| rs3327    | FGFR2 Ligand Binding Pathway                                      |
| rs12832680| FGFR2 Ligand Binding Pathway                                      |
| rs10495431| FGFR2 Ligand Binding Pathway                                      |
| rs946637  | FGFR2 Ligand Binding Pathway                                      |
| rs6731427 | FGFR2 Ligand Binding Pathway                                      |
| rs8016905 | FGFR2 Ligand Binding Pathway                                      |
| rs2357960 | FGFR2 Ligand Binding Pathway                                      |

Abbreviations: Database, database from the Molecular Signatures Databases (MSigDB) containing the indicated genetic pathway; FDR, False Discovery Rate; P, empirical set-based P-value; Pathway, genetic pathways tested for association with the 11 SLE clinical phenotypes of systemic lupus erythematosus; SNPs\_PATH, number of SNPs mapping to a particular pathway; SLE phenotype, clinical phenotypes of systemic lupus erythematosus tested for association with each pathway; SNPs\_PASS, list of SNPs passing the pathway analysis thresholds; SNPs\_TOTAL, total number of SNPs below the P-value threshold; SNPs\_SIGNIF, number of significant SNPs also passing the LD criteria.
### 2.3 Table S3. Association results of the SNPs from the VEGF pathway associated with oral ulcers in SLE.

| POPULATION    | SNP          | CHR | POSITION       | A1 | A2 | OR  | P     | GENE  |
|---------------|-------------|-----|----------------|----|----|-----|-------|-------|
| Discovery     | rs2373929   | 7   | 150714812      | A  | G  | 1.91| 2.64E-5| NOS3  |
| Discovery     | rs1709898   | 4   | 55957723       | G  | A  | 0.53| 1.50E-4| KDR   |
| Discovery     | rs743507    | 7   | 150707488      | G  | A  | 0.53| 2.61E-4| NOS3  |
| Discovery     | rs10940145  | 5   | 67290972       | G  | A  | 0.55| 3.26E-4| PIK3R1|
| Discovery     | rs1396875   | 11  | 551405         | G  | A  | 2.01| 7.16E-4| HRAS  |
| Discovery     | rs7726943   | 5   | 67815851       | G  | A  | 1.68| 7.80E-4| PIK3R1|
| Discovery     | rs10461535  | 5   | 67218216       | G  | A  | 2.17| 1.30E-3| PIK3R1|
| Discovery     | rs227913    | 17  | 64607394       | C  | A  | 0.62| 2.67E-3| PRKCA |
| Discovery     | rs2372183   | 5   | 67197955       | A  | G  | 2.06| 2.98E-3| PIK3R1|
| Discovery     | rs4976028   | 5   | 67290733       | G  | A  | 1.70| 3.46E-3| PIK3R1|
| Discovery     | rs904132    | 4   | 55802108       | G  | A  | 0.40| 5.78E-3| KDR   |
| Discovery     | rs11133360  | 4   | 55982752       | G  | A  | 0.67| 7.40E-3| KDR   |
| Discovery     | rs9892886   | 17  | 64382588       | G  | A  | 1.73| 8.06E-3| PRKCA |
| Discovery     | rs11860367  | 16  | 24011167       | G  | A  | 0.66| 8.25E-3| PRKCB |
| Discovery     | rs10515068  | 5   | 67450499       | C  | A  | 1.61| 1.02E-2| PIK3R1|
| Discovery     | rs7719763   | 5   | 67681425       | A  | G  | 1.47| 1.38E-2| PIK3R1|
| Discovery     | rs8051034   | 16  | 23925134       | C  | G  | 0.40| 1.53E-2| PRKCB |
| Discovery     | rs863818    | 5   | 67554023       | A  | G  | 0.69| 1.65E-2| PIK3R1|
| Discovery     | rs10515059  | 5   | 67241677       | A  | C  | 0.65| 2.22E-3| PIK3R1|
| Discovery     | rs6504424   | 17  | 64387328       | G  | A  | 1.49| 2.27E-2| PRKCA |
| Replication   | rs1762553   | 13  | 28968770       | G  | A  | 0.43| 2.35E-4| FLT1  |
| Replication   | rs1324057   | 13  | 28925435       | G  | A  | 0.52| 2.56E-4| FLT1  |
| Replication   | rs11959164  | 5   | 180096972      | G  | A  | 1.61| 1.44E-3| FLT4  |
| Replication   | rs10515077  | 5   | 67613801       | C  | A  | 2.26| 2.86E-3| PIK3R1|
| Replication   | rs6129760   | 20  | 39746403       | G  | A  | 1.61| 3.29E-3| PLCG1 |
| Replication   | rs1744801   | 5   | 67301383       | C  | A  | 0.56| 3.56E-3| PIK3R1|
| Replication   | rs7202459   | 16  | 24039013       | G  | A  | 0.64| 4.25E-3| PRKCB |
| Replication   | rs6842830   | 4   | 55873926       | G  | A  | 0.65| 4.31E-3| KDR   |
| Replication   | rs3844278   | 3   | 10211918       | A  | G  | 0.52| 5.15E-3| VHL   |
| Replication   | rs9550377   | 13  | 29101681       | A  | G  | 2.03| 8.17E-3| FLT1  |
| Replication   | rs2228246   | 20  | 39792063       | G  | A  | 0.59| 8.75E-3| PLCG1 |
| Replication   | rs1708609   | 13  | 28929711       | G  | A  | 1.50| 1.02E-2| FLT1  |
| Replication   | rs10067755  | 5   | 67307462       | G  | A  | 1.46| 1.15E-2| PIK3R1|
| Replication   | rs6947821   | 7   | 150729212      | G  | A  | 1.48| 1.21E-2| NOS3  |
| Replication   | rs4290512   | 17  | 64395039       | A  | C  | 0.43| 1.39E-3| PRKCA |
| Replication   | rs2283540   | 16  | 24130770       | A  | G  | 0.68| 1.53E-2| PRKCB |
| Replication   | rs708030    | 3   | 10212494       | G  | A  | 1.43| 1.83E-2| VHL   |
| Replication   | rs10283368  | 8   | 141679817      | A  | G  | 0.70| 2.00E-2| PTK2  |
| Replication   | rs4791036   | 17  | 64797135       | G  | A  | 0.62| 2.29E-2| PRKCA |
| Replication   | rs2125489   | 4   | 55953483       | A  | G  | 0.55| 2.39E-2| KDR   |

Abbreviations: A1, minor allele; A2, major allele; Chr, chromosome; Position, SNP base pair in build GRCh37/hg19; OR, Odds Ratio; P, P-value obtained from the single-marker association analysis; SNP, Single-Nucleotide Polymorphism.
2.4 Table S4. Statistical significance of the differential expression analysis performed on the VEGF pathway genes after immunotherapy.

| GENE  | \( P_{\text{BETAMETHASONE VALERATE}} \) | \( P_{\text{IMIQUIMOD}} \) | \( P_{\text{DIPHENCYPRONE}} \) | \( P_{\text{PIMECROLIMUS}} \) |
|-------|-----------------------------------------|-----------------|-----------------|-----------------|
| ARNT  | 1.10E-02                                | 5.26E-03        | 1.22E-01        | 2.63E-02        |
| EIF1  | 4.93E-02                                | 2.65E-06        | 6.68E-04        | 3.31E-01        |
| EIF1AX| 6.93E-02                                | 2.88E-03        | 1.33E-01        | 5.56E-01        |
| EIF2B1| 6.82E-01                                | 6.49E-03        | 9.26E-01        | 7.20E-01        |
| EIF2B2| 1.87E-02                                | 2.99E-01        | 4.66E-01        | 1.86E-01        |
| EIF2B3| 3.57E-01                                | 5.91E-01        | 4.15E-02        | 8.83E-01        |
| EIF2B4| 8.87E-03                                | 7.67E-01        | 1.25E-01        | 3.33E-01        |
| EIF2B5| 8.20E-01                                | 4.92E-01        | 3.61E-01        | 8.41E-01        |
| EIF2S1| 2.37E-03                                | 7.54E-03        | 1.20E-01        | 1.16E-02        |
| EIF2S2| 1.20E-01                                | 7.64E-06        | 2.18E-03        | 2.63E-01        |
| EIF2S3| 2.57E-01                                | 1.69E-02        | 1.64E-01        | 5.93E-01        |
| ELAVL1| 5.34E-03                                | 6.83E-03        | 4.95E-02        | 1.61E-01        |
| FLT1  | 4.86E-03                                | 1.70E-02        | 6.32E-02        | 5.89E-02        |
| FLT4  | 3.05E-01                                | 2.73E-01        | 2.11E-01        | 2.91E-01        |
| HIF1A | 1.76E-01                                | 2.46E-02        | 9.17E-02        | 6.53E-01        |
| HRAS  | 1.04E-03                                | 1.21E-08        | 5.19E-01        | 2.78E-02        |
| KDR   | 1.80E-01                                | 6.39E-02        | 3.55E-01        | 2.94E-01        |
| NOS3  | 6.31E-01                                | 6.32E-01        | 3.96E-01        | 3.21E-01        |
| PIK3CA| 9.54E-02                                | 1.42E-08        | 1.09E-01        | 1.62E-01        |
| PIK3CG| 2.08E-01                                | 1.95E-01        | 1.85E-01        | 5.18E-01        |
| PIK3R1| 1.12E-04                                | 4.70E-06        | 2.76E-04        | 1.66E-01        |
| PLCG1 | 2.44E-01                                | 2.06E-01        | 1.74E-02        | 1.91E-01        |
| PRKCA | 1.84E-01                                | 2.50E-01        | 1.75E-01        | 1.82E-01        |
| PRKCB | 3.19E-01                                | 5.34E-02        | 1.56E-01        | 3.53E-01        |
| PTK2  | 3.01E-04                                | 6.72E-09        | 7.51E-02        | 1.44E-01        |
| PXN   | 2.18E-01                                | 8.53E-02        | 4.97E-01        | 1.08E-01        |
| SHC1  | 4.17E-04                                | 9.64E-03        | 2.94E-01        | 9.82E-02        |
| VEGFA | 2.24E-04                                | 2.20E-11        | 3.34E-02        | 2.88E-02        |
| VHL   | 6.66E-02                                | 7.61E-02        | 2.64E-01        | 5.51E-01        |

Abbreviations: Gene, gene from the VEGF genetic pathway (only the most significant probe was considered for those genes mapped by more than one probe); \( P_{\text{BETAMETHASONE VALERATE}} \), P-value obtained from the differential expression analysis comparing samples before (N=10) and after (N=10) betamethasone valerate treatment; \( P_{\text{DIPHENCYPRONE}} \), P-value obtained from the differential expression analysis comparing samples before (N=22) and after (N=22) diphencyprone treatment; \( P_{\text{IMIQUIMOD}} \), P-value obtained from the differential expression analysis comparing samples before (N=6) and after (N=54) imiquimod treatment; \( P_{\text{PIMECROLIMUS}} \), P-value obtained from the differential expression analysis comparing samples before (N=10) and after (N=10) pimecrolimus treatment.
Table S5. Statistical significance of the VEGF genetic pathway perturbation after topical immunotherapy.

| VEGF PATHWAY | BETAMETHASONE VALERATE | IMIQUIMOD | DIPHENCYPRONE | PIMECROLIMUS |
|--------------|-------------------------|-----------|---------------|--------------|
| DEG (n)      | 12                      | 16        | 7             | 4            |
| NDEG (n)     | 17                      | 13        | 22            | 25           |
| Total Genes (n) | 29                  | 29        | 29            | 29           |
| P-value      | 5.69E-9                 | 5.38E-14  | 4.59E-4       | 5.50E-2      |

Abbreviations: DEG, number of VEGF pathway genes that were differentially expressed comparing untreated and treated samples (P<0.05); NDEG, number of VEGF pathway genes that were not differentially expressed comparing untreated and treated samples (P>0.05); P-value, statistical significance of the VEGF genetic pathway perturbation (Binomial test); Total Genes, total number of genes mapping to the VEGF genetic pathway; VEGF pathway, features of the VEGF genetic pathway related with the differential gene expression analysis.
### 2.6 Table S6. Established genetic variants for SLE risk.

| SNP       | CHR | POSITION   | LOCUS | RISK ALLELE |
|-----------|-----|------------|-------|-------------|
| rs2476601 | 1   | 14437588   | PTPN22| A           |
| rs1801274 | 1   | 161479745  | FCGR2A| C           |
| rs704840  | 1   | 173226195  | TNFSF4| G           |
| rs17849501| 1   | 183542323  | SMG7-NCF2| T         |
| rs3024505 | 1   | 206939904  | IL10 | T           |
| rs9782955 | 1   | 236039877  | LYST  | C           |
| rs2111485 | 2   | 163110536  | IFIH1 | G           |
| rs3768792 | 2   | 213871709  | IKZF2 | C           |
| rs6740462 | 2   | 65667272   | SPRED2| A           |
| rs11889341| 2   | 191943742  | STAT4 | T           |
| rs9311676 | 3   | 58470351   | ABHD6-PXK | C        |
| rs564799  | 3   | 159728987  | IL12A | C           |
| rs10028805| 4   | 102737250  | BANK1 | G           |
| rs7726414 | 5   | 133431834  | TCF7-SKP1| T         |
| rs10036748| 5   | 150458146  | TNIP1 | T           |
| rs2431697 | 5   | 159879978  | MIR146A| T          |
| rs9462027 | 6   | 34797241   | UHRF1BP1| A         |
| rs6568431 | 6   | 106588006  | PRDM1-ATG5| A       |
| rs6932056 | 6   | 138242437  | TNFAIP3| C          |
| rs1270942 | 6   | 31918860   | MHC class III| C          |
| rs849142  | 7   | 28185891   | JA2F1 | A           |
| rs4917014 | 7   | 50305863   | IKZF1 | T           |
| rs10488631| 7   | 128594183  | IRF5  | C           |
| rs2736340 | 8   | 11343973   | BLK   | T           |
| rs2663052 | 10  | 50069395   | WDFY4 | C           |
| rs4948496 | 10  | 63005617   | ARID5B| C           |
| rs3794060 | 11  | 71187679   | DHR7-NADSYN1| C  |
| rs2732549 | 11  | 35083999   | CD44  | T           |
| rs7941765 | 11  | 128499000  | ETS1-FLH1| C          |
| rs12802200| 11  | 566936     | IRF7  | C           |
| rs10774625| 12  | 111910219  | SH2B3 | A           |
| rs1059312 | 12  | 129278864  | SLC15A4| C          |
| rs4902562 | 14  | 68731458   | RAD51B| A           |
| rs2289583 | 15  | 75311036   | CSK   | A           |
| rs0652601 | 16  | 11174365   | CHIA-SOCS1| G        |
| rs34572943| 16  | 31272353   | ITGAM | A           |
| rs11644034| 16  | 85972612   | IRF8  | G           |
| rs2286672 | 17  | 4712617    | PLD2  | T           |
| rs2941509 | 17  | 37921194   | IKZF3 | A           |
| rs2304256 | 19  | 10475652   | TYK2  | C           |
| rs7444    | 22  | 21976934   | UBE2L3| C           |
| rs887369  | X   | 30577846   | CXorf21| C          |
| rs1734787 | X   | 153325446  | IRAK1-MECP2| C         |

**Abbreviations:** Chr, chromosome; Position, SNP base pair in build GRCh37/hg19; SNP, Single-Nucleotide Polymorphism.
### 2.7 Table S7. Reference biological pathways selected for the present study.

| PATHWAY          | DATABASE | GENES |
|------------------|----------|-------|
| RELA_PATHWAY     | BIOCARTA | 16    |
| BCELLSURVIVAL_PATHWAY | BIOCARTA | 16    |
| CAGAME_PATHWAY   | BIOCARTA | 16    |
| COMA2_PATHWAY    | BIOCARTA | 16    |
| CST13_PATHWAY    | BIOCARTA | 16    |
| IL23BP_PATHWAY   | BIOCARTA | 16    |
| LPS_PATHWAY      | BIOCARTA | 16    |
| MHC_CLASSI_PATHWAY | BIOCARTA | 16    |
| NFKB_PATHWAY     | BIOCARTA | 16    |
| P53_PATHWAY      | BIOCARTA | 16    |
| ACH_PATHWAY      | BIOCARTA | 16    |
| CDC42RAC_PATHWAY | BIOCARTA | 16    |
| SHH_PATHWAY      | BIOCARTA | 16    |
| LRRK2_PATHWAY    | BIOCARTA | 17    |
| BCELLSURVIVAL_PATHWAY | BIOCARTA | 17    |
| CACAM_PATHWAY    | BIOCARTA | 16    |
| CDMAC_PATHWAY    | BIOCARTA | 16    |
| EIF_PATHWAY      | BIOCARTA | 16    |
| GATA3_PATHWAY    | BIOCARTA | 17    |
| IL22BP_PATHWAY   | BIOCARTA | 16    |
| P53_PATHWAY      | BIOCARTA | 16    |
| ACH_PATHWAY      | BIOCARTA | 16    |
| CDC42RAC_PATHWAY | BIOCARTA | 16    |
| SHH_PATHWAY      | BIOCARTA | 16    |
| LAIR_PATHWAY     | BIOCARTA | 17    |
| HCMV_PATHWAY     | BIOCARTA | 17    |
| IL17_PATHWAY     | BIOCARTA | 17    |
| IL10_PATHWAY     | BIOCARTA | 17    |
| IL7_PATHWAY      | BIOCARTA | 17    |
| NO2IL12_PATHWAY  | BIOCARTA | 17    |
| PHI_PATHWAY      | BIOCARTA | 17    |
| IFN_PATHWAY      | BIOCARTA | 17    |
| IFN_PATHWAY      | BIOCARTA | 17    |
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| IFN_PATHWAY      | BIOCARTA | 17    |
| IFN_PATHWAY      | BIOCARTA | 17    |

109
| Term                                           | KEGG   |
|-----------------------------------------------|--------|
| AMINOACYL_TRNA_BIOSYNTHESIS                   | 41     |
| FATTY_ACS_METABOLISM                          | 42     |
| TYROSINE_METABOLISM                           | 42     |
| ALDOSTERONE_REGULATED_SODIUM_REABSORPTION     | 42     |
| BLADDER_CANCER                                | 42     |
| GRAFT_VERSUSHOST_DISEASE                      | 42     |
| VALINE_LEUCINE_AND_Isoleucine_DEGRADATION     | 44     |
| LYSINE_DEGRADATION                            | 44     |
| AMINO_SUGAR_AND_NUCLEOTIDE_SUGAR_METABOLISM   | 44     |
| ABC_TRANSPORTERS                              | 44     |
| NUCLEOTIDE_EXCISION_REPAIR                    | 44     |
| TYPE_1_DIABETES_MELLITUS                      | 44     |
| TYPE_2_DIABETES_MELLITUS                      | 45     |
| FERMENTATION_IMMUNE_NETWORK_FOR_IGA_PRODUCTION| 48     |
| GLYCEROLOID_METABOLISM                        | 49     |
| GLUTAMATE_METABOLISM                          | 50     |
| DRUG_METABOLISM_OTHER_ENZYMES                 | 51     |
| STARCH_AND_SUCROSE_METABOLISM                 | 52     |
| TASTE_TRANSDUCTION                            | 52     |
| ENDOMETRIAL_CANCER                            | 52     |
| AMYOTROPHIC_LATERAL_SCLEROSIS_ALS             | 53     |
| AUTOMUNE_THYROID_DISEASE                      | 53     |
| ARGinine_AND_PROLINE_METABOLISM               | 54     |
| INOSITOL_PHOSPHATE_METABOLISM                 | 54     |
| NON_SMALL_CELL_LUNG_CANCER                    | 54     |
| STEROID_HORMONE_BIOSYNTHESIS                  | 55     |
| BASAL_CELL_CARCINOMA                          | 55     |
| CYTOKININ_SIGNALING_PATHWAY                   | 56     |
| CYTOSOLIC_CNA_SENSING_PATHWAY                 | 56     |
| DIMERO_CHLORIDE_INFECTION                     | 56     |
| ARACHIDONIC_ACIDS_METABOLISM                  | 58     |
| PROTEASOME                                     | 59     |
| PATHOGENIC_ESCHERICHIA_COLI_INFECTION         | 59     |
| ACUTE_MYLIOID_LEUKAEMIA                       | 60     |
| GLYCEROLYSIS_GLUONGLUCONEogenesis             | 62     |
| NOC1_LIKE_RECEPTOR_SIGNALING_PATHWAY           | 62     |
| COLORECTAL_CANCER                             | 62     |
| METABOLISM                                    | 64     |
| GLOMMA                                        | 65     |
| ADIPOCYTOKINE_SIGNALING_PATHWAY                | 67     |
| EPITHELIAL_CELL_SIGNALING_IN_Helicobacter_PYLORI_INFECTION | 68     |
| IP3AR_SIGNALING_PATHWAY                        | 69     |
| P2Y1_SIGNALING_PATHWAY                        | 69     |
| COMPLEMENT_AND_COAGULATION_CASCADES           | 69     |
| METABOLISM_OF_BENZENES BY_CYTOCHROME_P450     | 70     |
| LONG_TERM_POTENTIATION                        | 70     |
| LONG_TERM_DEPRESSION                          | 70     |
| RENAL_CELL_CARCINOMA                          | 70     |
| PANCREATIC_CANCER                              | 70     |
| B_R1_LIKE_RECEPTOR_SIGNALING_PATHWAY           | 71     |
| MELANOMA                                      | 71     |
| DRUG_METABOLISM_CYTOCHROME_P450               | 72     |
| LEISHMANIA_INFECTION                          | 72     |
| CHRONIC_MYELOID_LEUKAEMIA                     | 73     |
| VIRAL_MYOCARDITIS                             | 73     |
| ADHESION_JUNCTION                             | 75     |
| B_CELL_RECEPTOR_SIGNALING_PATHWAY             | 75     |
| PHOSPHOAMINOGLYCOSIT_SIGNALING_SYSTEM         | 75     |
| ALKALOID_BIOSYNTHESIS                         | 76     |
| ARRHENOGENIC_RIGHT_VENTRICULAR_CAR Diomyopath_AVC | 76     |
| GLYCEROPHOSPHOLIPID_METABOLISM                | 77     |
| PEROXISOME                                    | 78     |
| PC_EPSILON_III_SIGNALING_PATHWAY               | 79     |
| CARDIO_MUSCLE_CONTRACTION                     | 80     |
| ECM_RECEPTOR_INTERACTION                      | 84     |
| SMALL_CELL_LUNG_CANCER                        | 84     |
| HYPERTRHOSIC_CARDiomyopathy_HCM               | 85     |
| TGF_BETA_SIGNALING_PATHWAY                    | 86     |
| PROGESTERONE_MEDIATED_GYOCYTE_MATURATION      | 86     |
| ERBB SIGNALING_PATHWAY                         | 87     |
| HIBOSOME                                      | 88     |
| APOPTOSIS                                     | 88     |
| HEMATOPOIETIC_CELL_LINEAGE                    | 88     |
| ANTIGEN_PROCESSING_AND_PRESENTATION           | 89     |
| PROSTATE_CANCER                               | 89     |
| GAP_JUNCTION                                  | 90     |
| DELATED_CARDiomyopathy                        | 92     |
| PC_GAMMA_MEDIATED_PHAGOCYTOSIS                | 97     |
| PYRIMIDINE_METABOLISM                         | 98     |
| CMP SIGNALING_PATHWAY                          | 101    |
| TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY           | 102    |
| MELOGENESIS                                   | 102    |
| T_CELL_RECEPTOR_SIGNALING_PATHWAY             | 108    |
| CYTOSOME_MISOSIS                              | 114    |
| VASCULAR_SMOOTH_MUSCLE_CONTRACTION            | 115    |
| LEUKOCYTE_TRANSENDOTHELIAL_MIGRATION          | 115    |
| LYSOSOME                                      | 121    |
| NEUROTROPHIN_SIGNALING_PATHWAY                | 125    |
| GPCR_JUNCTION                                 | 128    |
| CELL_CYCLE                                    | 128    |
| ALEN_SUGARANCE                                | 129    |
| PARKINSONS_DISEASE                            | 133    |
| CELL_ACHESION_MOLECULES_CAMS                  | 134    |
| TIGHT_JUNCTION                                | 134    |
| DIDGEITIVE_PHOSPHORYLATION                    | 135    |
| NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY     | 137    |

111
| Biochemical Pathway                                                                 | Reactome ID |
|-----------------------------------------------------------------------------------|-------------|
| Formation of RNA POL II elongation complex                                         | 45          |
| G2/M checkpoint                                                                   | 45          |
| NOTCH1 intracellular domain regulated transcription                                  | 46          |
| Activation of CHAPERONE GENES BY NPXR                                               | 46          |
| Lipid digestion, mobilization and transport                                        | 46          |
| Nucleotide binding domain, leucine rich repeat containing, receptor NLR signaling pathways | 46          |
| Pyruvate metabolism and citric acid cycle                                           | 48          |
| Cross-presentation of soluble exogenous antigens, endosomes                         | 48          |
| P.53 metabolism                                                                    | 48          |
| CDK mediated phosphorylation and removal of CDKs                                    | 48          |
| Muscle contraction                                                                  | 48          |
| Senescence dependent, MPA decay                                                    | 48          |
| Packaging of telomere ends                                                          | 48          |
| Metabolism of non-coding RNA                                                        | 49          |
| D-chondroitin sulfate, dermatan sulfate, metabolism                                 | 49          |
| Regulation of ornithine decarboxylase, ODC                                          | 49          |
| Nuclear receptor, transcription pathway                                             | 49          |
| AMPK, ACO1, and diaphorase SLC, transportants                                       | 49          |
| MAPK kinase activation, mTOR, cascade                                               | 50          |
| Metabolism of vitamins and cofactors                                               | 51          |
| Defensins                                                                          | 51          |
| P53-independent, G1-S DNA damage checkpoint                                         | 51          |
| Cytochrome P450, cytochrome by substrate type                                       | 51          |
| Nucleotide excision, repair                                                         | 51          |
| Autodegradation of the E3 ubiquitin ligase cop1                                     | 51          |
| Aquaporin mediated, transport                                                      | 51          |
| SCF, beta, Trcp, mediated degradation of EMI                                         | 51          |
| Heparin sulfate, heparin HS, GAG metabolism                                         | 52          |
| SARK, receptor activation                                                           | 52          |
| DFR, mediated degradation of APOPCSG                                                  | 52          |
| Protein folding                                                                    | 53          |
| Golgi-associated, vesicle, biogenesis                                               | 53          |
| Carcinoembryonic antigen                                                            | 53          |
| Activation of IkB alpha by ACP1, IKK, NF-kB                                       | 53          |
| Transport of mature, transcribed to cytoplasm                                       | 54          |
| Phosphatidylserine, C-mediated cascade                                              | 54          |
| Apoptotic execution, phase                                                          | 54          |
| Ion channel transport                                                               | 55          |
| Cell cycle, cell organization                                                      | 56          |
| CDK1 association, with the CDK1, ORC, ORC, complex                                   | 56          |
| P53, CASPASE                                                                      | 56          |
| SCF, beta, mediated degradation of P3, P5                                           | 56          |
| Chk2, kinase, receptors, BIM, CHK2, CHK1                                             | 57          |
| P53 dependent, G1-S DNA damage response                                             | 57          |
| Mitochondrial protein, import                                                      | 58          |
| Collagen formation                                                                 | 58          |
| Regulation of apoptosis                                                             | 58          |
| D-linked, glycosylation, of mucins                                                  | 58          |
| Loss of NF-κB, from mitotic, centrosomes                                            | 59          |
| Tran, doug, network, vesicle, budding                                               | 59          |
| Cell death, signaling, VIA, NAG, MRP, and NAC                                       | 60          |
| BR, phosphoglucomutase                                                              | 61          |
| RNA POL II, pre-transcription events                                               | 61          |
| RNA POL II promoter, opening                                                        | 62          |
| Costimulation, by the COX2, family                                                 | 63          |
| Interferon, gamma, signaling                                                        | 63          |
| Signaling, by TGF, beta, receptor, receptor complex                                  | 63          |
| Activation of NF-kB, KAP2, in B, cells                                             | 64          |
| NCAM signaling, for neutroph, out growth                                            | 64          |
| Disposition of new, chima, containing nucleosides, at the centrosome               | 64          |
| Interferon, alpha, beta, signaling                                                  | 64          |
| Autodegradation of CDK1, by CDK1, APC-2                                             | 64          |
| Signaling, by UNI                                                                    | 65          |
| Cyclin E, associated, events, during G1-S transition,                               | 65          |
| Assembly of the pre, replicative, complex                                           | 65          |
| Antiviral, mechanism, by IFN, stimulated, genes                                     | 66          |
| Recruitment of mitotic, centrosome, proteins, and complexes                         | 66          |
| Orc1, removal, from chromatin                                                       | 67          |
| Senapin, interactions                                                               | 68          |
| Rhinoglycolipid, metabolism                                                        | 69          |
| Glucose metabolism                                                                 | 69          |
| Immunoregulatory, interactions, between A, lymphoid and A, non-lymphoid cell       | 70          |
| Signaling, by Ndt-1                                                                  | 70          |
| Phagosome, functionalization, of compounds                                          | 70          |
| Phage, c, conjugation                                                               | 70          |
| Phagosome, c, conjugation                                                           | 70          |
| Pum, cascade                                                                        | 71          |
| Metabolism, of nucleotides                                                          | 72          |
| NFκB and MAP kinases, activation, mediated by TLR signaling, receptor repertoire    | 72          |
| Transcriptional, regulation of white adipocyte, differentiation                     | 72          |
| APC C, CDH1, mediated, degradation of CD28 and other, APC C, CDH1, targeted, proteins in, late, mitosis, early G1 | 72          |
| H2a, I, NEAS, mediated, induction of, IFN, alpha, beta, pathway                      | 72          |
| APC C, CD26, mediated, degradation of mitotic, proteins                             | 73          |
| NER, stimulation                                                                    | 73          |
| Formation of the tetrapyr, complex and subsequently, the 43S complex                | 74          |
| Tnf, mediated, tumor signaling                                                      | 74          |
| G, alpha,h2a,132, signaling events                                                  | 74          |
| Telomere, maintenance                                                               | 75          |
| Antigen, processing, droves, presentation                                            | 76          |
| TNF, mediated, induction of, NFκB, and MAP kinases, upon, tumor, I, or, II, activation | 77          |
| Signaling, by SCF, kit                                                              | 78          |
| Vector, signaling                                                                   | 78          |
| Cell junction, organization                                                         | 78          |
| Platelet, homeostasis                                                               | 78          |
| Integrin, cell, surface, interactions                                               | 79          |
| Respiratory, election, transport                                                    | 79          |
| Unfolded, protein, response                                                         | 80          |
| P53, NTR, receptor, mediated, signaling                                             | 81          |
| M, G1, transition                                                                  | 81          |
| NITRIC, G2-M, PHAGES                                                                | 81          |
| ASPARAGINE, N, LINKED, GLYCOSYLATION                                                | 81          |
3. Supplementary Figures

3.1 Figure S1. Principal components of the SLE discovery cohort.

Figure S1. Principal components of the SLE discovery cohort. The SLE patients (blue dots) and control patients (red dots) are plotted according to their first (PC1) and second (PC2) principal components estimated in EIGENSTRAT using the genome-wide data. In the present figure, samples showing an outlier genetic background (i.e. samples with >6 standard deviations in any of the 10 principal components of variation) were excluded.
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