

# **SUPPLEMENTARY MATERIAL**

## **INDEX**

<b>1. Supplementary Material and Methods</b>	<b>2</b>
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
<b>2. Supplementary Tables</b>	<b>7</b>
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
<b>3. Supplementary Figures</b>	<b>117</b>
3.1 Figure S1. Principal components of the SLE discovery cohort	117
<b>4. References</b>	<b>118</b>

# **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,  $P < 1e-4$ ) 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, flucocinolone 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, squaric 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 log<sub>2</sub>-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	CHR	POS	GENE	MALAR RASH		DISCOID RASH		PHOTOSENSITIVITY		ORAL ULCERS		ARTHRITIS		SEROISITIS		RENAL DISORDER		NEUROLOGIC DISORDER		HEMATOLOGIC DISORDER		IMMUNOLOGIC DISORDER		ANTINUCLEAR ANTIBODIES	
				P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)
rs2476601	1	11477368	PPP2R2	5.28E-01	0.86(0.53-1.37)	9.45E-01	0.97(0.48-1.97)	5.41E-01	0.86(0.54-1.38)	9.37E-01	1.02(0.61-1.64)	2.44E-01	0.77(0.47-1.26)	3.12E-01	0.77(0.47-1.26)	6.47E-01	0.89(0.54-1.45)	4.92E-01	0.73(0.32-1.69)	3.92E-01	NA(NA-NA)	9.41E-01	0.98(0.54-1.77)	1.64E-02	NA(NA-NA)
rs1001274	1	16419745	FCGR2A	7.99E-01	0.86(0.72-1.29)	4.49E-01	1.10(0.75-1.85)	1.69E-01	1.22(0.91-1.68)	1.25E-01	1.25(0.91-1.69)	2.86E-01	1.2(0.85-1.7)	9.09E-01	0.98(0.71-1.35)	1.51E-01	0.83(0.59-1.09)	1.57E-01	0.67(0.38-1.19)	1.66E-01	1.58(0.81-3.11)	1.37E-01	0.76(0.52-1.11)	3.62E-01	1.72(0.78-3.8)
rs702610	1	173256195	TNFSF4	1.95E-01	1.23(0.89-1.7)	1.03E-01	0.87(0.39-1.13)	4.27E-01	1.13(0.82-1.57)	3.04E-01	0.83(0.41-1.48)	9.64E-01	1.01(0.69-1.48)	6.15E-02	1.37(0.97-1.93)	4.07E-02	1.41(0.1-1.96)	1.15E-01	0.59(0.28-1.23)	8.56E-01	1.07(0.51-2.26)	2.14E-01	1.29(0.84-1.96)	8.12E-01	0.77(0.34-1.75)
rs2024505	1	206939984	IL10	1.77E-01	0.77(0.52-1.14)	6.47E-01	0.87(0.48-1.46)	1.79E-01	0.85(0.57-1.25)	1.70E-01	0.77(0.51-1.14)	3.25E-02	1.68(1.01-2.81)	1.71E-01	1.32(0.88-1.99)	7.98E-01	0.95(0.63-1.43)	3.45E-01	1.4(0.69-2.81)	8.95E-02	0.52(0.24-1.1)	1.31E-01	0.79(0.49-1.26)	4.16E-01	0.68(0.27-1.73)
rs978255	1	236039877	LYST	9.19E-01	1.02(0.71-1.46)	2.38E-01	1.4(0.78-2.52)	7.55E-01	1.06(0.74-1.51)	8.56E-01	1.03(0.72-1.49)	5.45E-01	1.14(0.78-1.72)	8.87E-01	1.03(0.71-1.52)	8.36E-01	0.96(0.66-1.4)	5.48E-01	1.25(0.59-2.62)	7.82E-01	0.89(0.38-2.07)	9.48E-01	1.01(0.65-1.59)	8.13E-01	1.12(0.44-2.83)
rs740462	2	65662722	SPRED2	1.67E-01	0.79(0.56-1.11)	6.73E-01	1.11(0.66-1.88)	4.46E-01	0.88(0.63-1.24)	1.64E-01	0.79(0.56-1.11)	3.08E-02	1.51(1.03-2.21)	5.89E-01	0.91(0.63-1.3)	5.36E-01	1.12(0.78-1.6)	8.56E-01	1.06(0.54-2.08)	1.18E-01	1.74(0.86-3.51)	8.42E-01	1.04(0.68-1.59)	7.96E-01	1.12(0.46-2.7)
rs211485	2	163110536	ITIH1	2.68E-01	0.84(0.62-1.14)	9.43E-01	1.02(0.64-1.61)	5.67E-01	1.09(0.81-1.48)	6.64E-01	0.94(0.69-1.27)	6.35E-01	1.09(0.76-1.56)	3.45E-01	0.86(0.62-1.19)	4.89E-01	0.99(0.65-1.23)	2.87E-01	0.73(0.41-1.31)	5.51E-01	1.23(0.62-2.43)	5.30E-01	1.13(0.77-1.65)	7.93E-01	0.9(0.39-2.04)
rs1188941	2	191943742	STAT4	5.20E-02	0.73(0.54-1.01)	5.74E-01	1.14(0.72-1.82)	3.48E-01	0.88(0.65-1.21)	3.23E-01	0.83(0.62-1.17)	7.71E-01	0.95(0.65-1.37)	9.00E-01	0.98(0.7-1.38)	8.05E-01	0.99(0.69-1.34)	4.04E-01	0.77(0.41-1.46)	8.53E-02	1.98(0.86-4.59)	7.52E-01	1.07(0.71-1.59)	7.31E-01	1.57(0.62-3.96)
rs3708792	2	213871709	ICZF2	2.76E-01	1.25(0.84-1.86)	6.03E-01	1.18(0.63-2.2)	4.37E-02	1.51(1.02-2.25)	5.44E-01	1.13(0.76-1.7)	3.66E-01	1.24(0.79-1.95)	1.96E-01	0.76(0.51-1.1)	7.97E-01	1.06(0.69-1.61)	3.78E-01	1.47(0.61-3.53)	3.19E-02	2.38(1.14-4.99)	9.75E-01	1.01(0.61-1.66)	1.71E-01	1.94(0.84-7.3)
rs9311676	3	58470351	ABHD5,PKX	5.99E-01	0.91(0.68-1.23)	3.22E-01	1.26(0.81-1.96)	5.60E-01	1.09(0.81-1.47)	3.38E-02	0.72(0.53-0.97)	5.30E-01	1.12(0.79-1.6)	4.40E-01	0.88(0.64-1.21)	8.06E-01	1.04(0.76-1.42)	1.10E-01	0.67(0.33-1.12)	6.02E-01	1.21(0.61-2.4)	3.01E-01	0.82(0.56-1.18)	1.09E-01	2.05(0.85-4.86)
rs564799	3	159728687	IL12A	9.22E-01	1.02(0.73-1.41)	4.11E-02	1.63(1.03-2.58)	3.81E-01	0.86(0.62-1.2)	3.30E-01	1.18(0.85-1.63)	7.39E-01	0.94(0.64-1.37)	9.52E-01	1.01(0.71-1.44)	9.44E-01	0.99(0.71-1.39)	1.30E-01	1.6(0.88-2.9)	9.22E-01	1.04(0.49-2.19)	2.13E-01	1.31(0.85-2.0)	1.09E-01	2.25(0.76-6.6)
rs1028205	4	102737250	BANK1	4.64E-01	0.89(0.65-1.21)	6.43E-01	1.11(0.71-1.76)	4.21E-01	0.88(0.65-1.2)	8.19E-01	1.04(0.76-1.42)	7.98E-02	1.39(0.96-2.03)	3.84E-01	1.16(0.83-1.61)	7.12E-01	1.06(0.77-1.47)	8.17E-01	1.07(0.59-1.95)	9.83E-02	1.9(0.85-23)	7.38E-01	0.94(0.64-1.38)	6.80E-01	1.19(0.51-2.78)
rs7726414	5	133418184	TCF7,SKPI	6.94E-01	1.12(0.66-1.91)	5.46E-01	1.28(0.61-2.7)	7.33E-01	0.91(0.53-1.55)	4.66E-01	1.23(0.72-2.1)	2.41E-01	1.53(0.76-3.08)	1.79E-01	1.49(0.86-2.58)	5.25E-01	1.4(0.81-2.41)	5.50E-01	0.7(0.21-2.31)	1.78E-01	3.26(0.44-24.26)	8.78E-02	0.57(0.31-1.03)	5.73E-01	0.68(0.22-33)
rs1036748	5	15048146	TNIP1	8.21E-01	0.96(0.69-1.33)	3.97E-01	0.8(0.48-1.34)	3.94E-01	0.87(0.63-1.2)	6.60E-01	1.08(0.78-1.5)	8.72E-01	1.03(0.71-1.52)	6.05E-01	1.1(0.77-1.56)	2.52E-01	0.89(0.63-1.26)	3.08E-01	0.7(0.35-1.4)	2.99E-01	0.68(0.34-1.37)	6.05E-01	1.12(0.74-1.7)	8.83E-01	1.07(0.44-2.58)
rs2431697	5	159879978	MIR146A	5.74E-01	0.92(0.68-1.24)	2.49E-01	0.76(0.48-1.22)	6.96E-01	0.94(0.71-1.27)	7.79E-01	0.96(0.71-1.3)	2.39E-01	1.24(0.86-1.78)	9.23E-01	1.02(0.73-1.41)	3.46E-01	1.16(0.85-1.6)	8.60E-01	1.05(0.59-1.9)	2.94E-01	0.7(0.36-1.36)	9.65E-02	0.73(0.5-1.06)	4.39E-01	0.73(0.33-1.61)
rs1318860	6	34797241	MHC class III	6.72E-01	0.9(0.55-1.46)	1.75E-01	1.59(0.83-3.04)	4.21E-01	1.22(0.75-1.99)	5.35E-02	1.62(0.99-2.63)	1.38E-02	2.3(1.12-4.72)	7.01E-01	0.9(0.53-1.54)	1.46E-01	0.67(0.39-1.16)	9.62E-01	0.98(0.38-2.55)	8.06E-02	4.14(0.56-30.71)	1.56E-01	0.66(0.38-1.15)	1.56E-01	1.38(0.32-5.95)
rs9462027	6	rs1979421	UHRF1BP1	2.63E-02	0.7(0.51-0.95)	2.63E-01	1.31(0.83-2.06)	8.90E-01	1.02(0.75-1.39)	2.51E-02	0.69(0.5-0.95)	6.25E-01	0.91(0.63-1.31)	2.45E-01	1.23(0.88-1.71)	1.14E-01	0.76(0.54-1.06)	6.09E-01	1.18(0.65-2.13)	8.41E-01	0.93(0.46-1.87)	9.55E-01	1.01(0.69-1.49)	6.79E-01	0.84(0.37-1.87)
rs658431	6	106588806	PRDM1,ATG5	7.35E-01	1.05(0.78-1.42)	4.46E-01	1.2(0.76-1.9)	1.20E-01	1.27(0.94-1.71)	6.53E-01	0.93(0.67-1.37)	1.10E-01	1.07(0.76-1.5)	1.10E-01	1.09(0.79-1.5)	4.77E-01	0.81(0.45-1.45)	6.39E-02	0.5(0.23-1.08)	5.21E-02	0.68(0.46-1.01)	9.33E-01	0.97(0.43-2.16)		
rs6932056	6	138242437	TNFAIP3	2.88E-01	1.48(0.7-3.13)	4.91E-01	0.66(0.18-2.39)	4.82E-01	1.3(0.62-2.73)	4.85E-01	0.77(0.36-1.64)	4.16E-01	1.45(0.56-3.8)	1.93E-02	2.37(1.14-4.95)	6.58E-02	1.97(0.95-4.1)	5.86E-01	1.43(0.41-5.01)	6.67E-01	0.72(0.17-3.13)	1.15E-01	2.37(0.69-8.12)	1.29E-01	53.54(0.0-29660.0)
rs484942	7	28189391	JAZF1	9.52E-01	0.99(0.74-1.33)	9.88E-01	1.0(0.64-1.56)	6.19E-01	1.08(0.81-1.45)	5.49E-01	1.09(0.81-1.47)	9.09E-01	1.02(0.72-1.45)	1.72E-01	1.26(0.91-1.75)	2.74E-01	0.84(0.61-1.14)	7.11E-01	1.12(0.66-2.0)	5.52E-01	0.72(0.36-1.43)	8.83E-02	0.72(0.49-1.04)	4.07E-01	0.71(0.32-1.58)
rs4917014	7	9038865	JAZF1	4.88E-01	1.14(0.83-1.57)	9.54E-01	1.01(0.63-1.64)	1.31E-01	0.85(0.62-1.17)	2.80E-02	1.42(1.03-1.96)	5.03E-01	1.14(0.77-1.67)	1.22E-01	0.76(0.55-1.09)	1.29E-01	1.29(0.92-1.8)	7.13E-01	1.12(0.62-2.08)	9.11E-01	0.96(0.46-1.99)	1.01E-01	1.41(0.92-2.15)	7.46E-01	1.16(0.88-1.79)
rs1088631	7	128594183	IRF7	8.62E-01	0.96(0.64-1.45)	5.46E-02	0.5(0.24-1.07)	9.37E-01	0.98(0.65-1.48)	2.98E-01	0.76(0.51-1.16)	1.96E-01	1.45(0.85-2.4)	8.50E-01	0.86(0.62-1.15)	2.67E-01	1.27(0.84-1.94)	3.65E-01	1.42(0.69-2.92)	8.08E-01	1.13(0.43-3.96)	5.09E-01	1.19(0.72-2.0)	2.06E-01	0.59(0.23-1.51)
rs2176340	8	11343973	BLK	1.23E-01	1.31(0.94-1.84)	2.55E-01	0.73(0.43-1.25)	5.92E-01	0.91(0.65-1.27)	6.08E-01	1.1(0.78-1.53)	6.44E-01	1.1(0.74-1.64)	6.51E-01	1.09(0.76-1.56)	9.56E-01	1.01(0.71-1.44)	7.30E-01	0.89(0.45-1.73)	5.54E-01	0.79(0.38-1.65)	1.09E-01	1.45(0.92-2.26)	4.15E-01	1.5(0.65-4.05)
rs263652	10	9060936	WDR5A	5.38E-01	0.91(0.68-1.23)	6.61E-01	0.91(0.58-1.41)	8.24E-01	0.97(0.72-1.3)	6.70E-01	1.07(0.79-1.43)	5.63E-01	1.11(0.78-1.57)	3.59E-01	0.86(0.63-1.19)	6.98E-01	0.94(0.69-1.29)	3.70E-02	1.86(1.01-3.44)	3.89E-01	0.75(0.38-1.48)	4.46E-01	0.87(0.61-1.26)	9.59E-01	1.02(0.47-2.28)
rs4948496	10	6386517	ARID1B	3.31E-02	0.75(0.54-0.97)	1.66E-01	0.73(0.47-1.13)	2.02E-02	0.7(0.52-0.95)	6.80E-01	0.94(0.71-1.26)	6.18E-01	0.91(0.65-1.3)	6.84E-01	0.94(0.68-1.29)	2.68E-01	0.84(0.61-1.14)	8.28E-01	1.07(0.61-1.9)	9.74E-01	0.99(0.51-1.94)	5.14E-01	0.88(0.61-1.28)	3.12E-01	1.3(0.59-2.86)
rs1280200	11	566936	IRF7	4.38E-01	1.15(0.78-1.7)	1.07E-01	1.52(0.89-2.59)	2.64E-01	0.81(0.55-1.21)	7.65E-01	1.06(0.75-1.58)	8.32E-01	0.96(0.61-1.5)	9.09E-01	0.98(0.64-1.4)	7.38E-01	0.94(0.62-1.41)	1.38E-01	0.55(0.22-1.37)	9.06E-01	0.95(0.42-2.28)	7.65E-01	0.93(0.58-1.51)	4.86E-01	1.45(0.45-4.65)
rs2732549	11	35088399	CD4A	8.62E-01	0.97(0.72-1.31)	4.26E-01	0.83(0.53-1.29)	3.82E-01	1.02(0.76-1.38)	3.83E-01	0.87(0.65-1.18)	1.59E-01	1.29(0.91-1.83)	5.71E-01	0.91(0.66-1.25)	6.13E-01	0.92(0.67-1.26)	4.06E-01	1.29(0.71-2.35)	7.40E-01	0.89(0.45-1.77)	1.63E-02	1.59(1.09-2.3)	1.21E-01	5.55(2.5-6.66)
rs3794060	11	7118679	DONKNAOSYNI	6.56E-01	0.93(0.68-1.27)	2.44E-01	1.33(0.82-2.17)	9.45E-01	0.99(0.73-1.35)	9.33E-01	1.0(0.73-1.37)	4.69E-01	1.15(0.81-1.65)	3.65E-01	0.86(0.61-1.19)	9.25E-01	0.99(0.71-1.37)	5.83E-01	0.84(0.47-1.53)	8.96E-01	0.95(0.47-1.94)	5.43E-01	0.88(0.6-1.31)	2.14E-01	1.67(0.76-3.67)



























































































Discoid Rash	HISTIDINE METABOLISM	KEGG	674	25	18	5.88E-01	9.96E-01	rs17024981	rs1788224	rs4836277	rs854121	rs12605520	rs16375090	rs2107116	rs6569455	rs730870	rs480245	rs1968736	rs1768267	rs675631	rs13809524	rs1465936	rs16840472
Discoid Rash	NUCLEOTIDE LIKE PURINERGIC RECEPTORS	REACTOME	272	16		5.91E-01	9.96E-01	rs8112063	rs1123571	rs4814728	rs7208308	rs6440739	rs1202765	rs236481	rs5104295	rs382936	rs1089906						
Discoid Rash	G PROTEIN ACTIVATION	REACTOME	703	21		5.91E-01	9.96E-01	rs2159917	rs91646	rs3959759	rs1181073	rs1270672	rs442611	rs1106673	rs3232987	rs65042	rs1468242	rs287340	rs955457	rs121495	rs1775118		
Discoid Rash	GLYCOYLATION	REACTOME	790	42		5.92E-01	9.96E-01	rs4927432	rs107994	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632	rs1283632
Discoid Rash	PIP3 ACTIVATES AKT SIGNALING	REACTOME	587	21		5.92E-01	9.96E-01	rs8734181	rs7223396	rs7810457	rs1850409	rs4943769	rs8176205	rs1189254	rs312681	rs1268160	rs66821	rs1202235	rs1049228	rs2954023			
Discoid Rash	SIGNALING_BY_ROBO_RECEPTOR	REACTOME	1030	32		5.93E-01	9.96E-01	rs17031463	rs6057009	rs6797725	rs10114970	rs7612183	rs2634771	rs1843786	rs98821	rs2623769	rs11697698	rs1480689	rs1719738	rs692301	rs1685896	rs30438	rs761026
Discoid Rash	INSULIN PATHWAY	BIOCARTA	725	36		5.96E-01	9.96E-01	rs4976132	rs1490801	rs6759915	rs28118769	rs7507911	rs12150519	rs4970288	rs10739966	rs1784488	rs801305	rs3719763	rs1079379	rs6775899	rs1784842	rs10940145	rs1066323
Discoid Rash	INSULIN PATHWAY	BIOCARTA	1253	29		5.96E-01	9.96E-01	rs8096920	rs23785383	rs1245316	rs1453342	rs2179948	rs392715	rs958835	rs17288929	rs1180262	rs140561	rs6792241	rs8015153	rs11646540	rs686525	rs17557659	rs7811655
Discoid Rash	PHOSPHORYLATION_OF_THE_APC_C	REACTOME	219	15		5.96E-01	9.96E-01	rs653414	rs4688520	rs11248087	rs16941635	rs9867568	rs1775614										
Discoid Rash	REGULATORY_RNA_PATHWAYS	REACTOME	345	29		5.96E-01	9.96E-01	rs7160403	rs1083293	rs12186785	rs1781885	rs100711108	rs17408227	rs3746162	rs17146052	rs2997025							
Discoid Rash	DIABETES_PATHWAYS	REACTOME	395	28		5.97E-01	9.96E-01	rs1074311	rs1362988	rs6077718	rs2172225	rs1165607	rs2136703	rs294654	rs6478233	rs1199980	rs2409403	rs3415142	rs1024175	rs1737483	rs703487	rs1545229	rs6893892
Discoid Rash	TERMINATION_OF_O_GLYCAN BIOSYNTHESIS	REACTOME	960	47		5.97E-01	9.96E-01	rs2829241	rs2404399	rs6620381	rs1804258	rs8446209	rs9811923	rs10467147	rs1804313	rs1084566	rs125287	rs1049538	rs1049538	rs293346	rs68301	rs808430	rs1001828
Discoid Rash	GLYOXYLATE AND DICARBOXYLATE METABOLISM	KEGG	704	33		6.00E-01	9.96E-01	rs15551790	rs2346892	rs117669	rs2073069	rs2423222	rs1223881	rs5466793	rs8003379	rs611598	rs243322	rs150831	rs680023	rs1037510	rs122014	rs727392	rs4813
Discoid Rash	NONSENSE MEDIATED DECAY ENHANCED BY THE EXON JUNCTION COMPLEX	REACTOME	1261	33		6.01E-01	9.96E-01	rs285822	rs1298632	rs1059398	rs7751261	rs108168	rs55125	rs128167	rs64231	rs46643	rs37645	rs1784209	rs201558	rs93429	rs480323	rs56631	rs247315
Discoid Rash	MITOCHONDRIAL_TRNA_AMINOACYLATION	REACTOME	500	39		6.02E-01	9.96E-01	rs2713834	rs4699172	rs2603838	rs751261	rs2326613	rs411422	rs409225	rs6779394	rs69277	rs4466764	rs2729085	rs264108	rs959186	rs313664	rs242931	rs32139
Discoid Rash	ADP_SIGNALING_THROUGH_PRR1	REACTOME	863	31		6.02E-01	9.96E-01	rs2159917	rs1049405	rs931646	rs695723	rs4463623	rs1811073	rs1474779	rs980444	rs148757	rs669755	rs376504	rs10686	rs7786	rs7825	rs682744	rs2873409
Discoid Rash	XENOBIOTICS	REACTOME	231	5		6.06E-01	9.96E-01	rs1772597	rs1950078	rs1157212	rs2970265												
Discoid Rash	DEADENYLATION_OF_MRNA	REACTOME	331	31		6.07E-01	9.96E-01	rs438406	rs1089606	rs1112955	rs3311602	rs100251	rs2361696	rs1007831	rs10740768								
Discoid Rash	DOWNSTREAM_TCR_SIGNALING	REACTOME	1573	45		6.07E-01	9.96E-01	rs4976132	rs1490801	rs8734181	rs1084353	rs1845451	rs1044404	rs1710327	rs7747353	rs9276724	rs270712	rs4976208	rs1004923	rs1073996	rs595025	rs10485405	rs283334
Discoid Rash	FORMATION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC	REACTOME	227	9		6.08E-01	9.96E-01	rs818299	rs108794	rs3852166													
Discoid Rash	ACTV_CHAIN_REMODELING_OF_PE	REACTOME	696	30		6.09E-01	9.96E-01	rs1049405	rs959732	rs443808	rs792406	rs1471978	rs90444	rs148757	rs766133	rs672585	rs7051	rs105999	rs76698	rs76691	rs973936	rs682744	rs129706
Discoid Rash	AMINO_ACID_SYNTHESIS_AND_INTERCONVERSION_TRANSMINATION	REACTOME	580	21		6.11E-01	9.96E-01	rs215703	rs1229564	rs1137606	rs1087689	rs1499531	rs6291921	rs1915	rs1244537	rs19492	rs94443	rs141026	rs97978	rs76801	rs66655	rs40005	rs702179
Discoid Rash	DEATH_PATHWAY	BIOCARTA	505	22		6.14E-01	9.96E-01	rs1048345	rs1710327	rs4605938	rs365238	rs4719793	rs1693964	rs9868605	rs954945	rs3850170	rs1199732	rs3783953	rs716796	rs724402	rs2844930	rs1437212	rs120681
Discoid Rash	PORPHYRIA_AND_CHLOROPHYLL_METABOLISM	KEGG	1163	58		6.14E-01	9.96E-01	rs1002849	rs117031	rs10521	rs2586795	rs76194	rs48226	rs699512	rs1007090	rs6178404	rs1661637	rs686633	rs294755	rs1605975	rs385339	rs7650232	rs18704
Discoid Rash	NOTCH_SIGNALING_PATHWAY	KEGG	1387	29		6.16E-01	9.96E-01	rs2179688	rs1160821	rs6843495	rs4923889	rs1051952	rs387681	rs1264059	rs33857	rs708797	rs1241734	rs783948	rs378051	rs7650232	rs18704	rs684306	rs57581
Discoid Rash	VIP_PATHWAY	KEGG	1393	38		6.16E-01	9.96E-01	rs2264888	rs1272061	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917	rs12159917
Discoid Rash	GLYCEROPHOSPHOLIPID BIOSYNTHESIS	REACTOME	2483	38		6.17E-01	9.96E-01	rs2087179	rs2292545	rs655915	rs4823104	rs1214147	rs1049405	rs659732	rs11127284	rs446323	rs6680326	rs6072343	rs341422	rs792406	rs474797	rs2012024	rs1559746
Discoid Rash	RNA_POLYMERASE	KEGG	351	21		6.17E-01	9.96E-01	rs124537	rs1712322	rs378016	rs763417	rs7594007	rs2423506	rs3746162	rs411207	rs754950							
Discoid Rash	PROTEIN EXPORT	KEGG	750	22		6.18E-01	9.96E-01	rs3829406	rs7811230	rs12267330	rs1551368	rs1024511	rs1390245	rs109364	rs108453	rs1528035	rs37642	rs2065134	rs801351	rs694611	rs1233432	rs1156868	rs1156334
Discoid Rash	CELL_DEATH_SIGNALING_VIA_NG2_NG2	REACTOME	1000	37		6.22E-01	9.96E-01	rs2264888	rs1275868	rs1048539	rs1719952	rs1125745	rs1710327	rs1024511	rs138599	rs1700808	rs2664537	rs1050507	rs1747549	rs1141048	rs491	rs69856	rs1786729
Discoid Rash	RAP1_SIGNALING	REACTOME	855	32		6.23E-01	9.96E-01	rs613071	rs304077	rs92001	rs1217111	rs1000160	rs402981	rs293131	rs1024289	rs1107339	rs199169	rs6968005	rs1802	rs2860493	rs197683	rs1058982	rs480375
Discoid Rash	BETA_ALANINE_METABOLISM	KEGG	711	40		6.23E-01	9.96E-01	rs379357	rs117882	rs4363277	rs1625597	rs58148	rs822607	rs290826	rs1293056	rs2605520	rs2786529	rs2401542	rs1723422	rs28107	rs1634	rs4085458	rs1408353
Discoid Rash	DRUG_METABOLISM_OTHER_ENZYMES	KEGG	1609	52		6.25E-01	9.96E-01	rs1002849	rs1493793	rs1202869	rs1177597	rs1625597	rs290826	rs290826	rs145226	rs1086508	rs294755	rs2811219	rs1487302	rs308830	rs648997	rs768364	rs1804383
Discoid Rash	CYCLOCHROME_P450_ARRANGED_BY_SUBSTRATE_TYPE	REACTOME	1163	41		6.25E-01	9.96E-01	rs2824205	rs1746674	rs9788636	rs1773597	rs658359	rs292781	rs1314026	rs3720213	rs1314633	rs2277600	rs1907609	rs1590760	rs695541	rs4809958	rs6546738	rs1800440
Discoid Rash	CELL_DEATH_SIGNALING_VIA_NG2_NG2	REACTOME	2069	29		6.26E-01	9.96E-01	rs2633293	rs6679759	rs1540656	rs647067	rs738957	rs1074294	rs1762622	rs695938	rs1167849	rs800042	rs214666	rs1877330	rs1023823	rs3929121	rs212496	rs7280929
Discoid Rash	REGULATION_OF_KIT_SIGNALING	REACTOME	587	21		6.27E-01	9.96E-01	rs1544241	rs1217175	rs4358284	rs371321	rs1201022	rs114146	rs995970	rs7229909	rs605577	rs1011614	rs1456	rs21202				
Discoid Rash	NA_CL_DEPENDENT_NEUROTRANSMITTER_TRANSPORT	REACTOME	718	27		6.29E-01	9.96E-01	rs1083369	rs224169	rs92601	rs1108878	rs290798	rs3779723	rs350658	rs1046624	rs237651	rs1194100	rs269713	rs297159	rs170885	rs684213		
Discoid Rash	CELL_CELL_COMMUNICATION	REACTOME	9225	33		6.29E-01	9.96E-01	rs2140825	rs6766201	rs4976132	rs1142065	rs17031463	rs1330878	rs7548909	rs490801	rs944248	rs1296272	rs108921	rs4812668	rs2068066	rs157805	rs189219	rs682242
Discoid Rash	ACTIVATED AMP STIMULATES FATTY ACID OXIDATION IN MUSCLE	REACTOME	212	13		6.29E-01	9.96E-01	rs997032	rs69830	rs2025272	rs27238	rs187609	rs201704	rs127463	rs226387	rs1027823	rs148316	rs674295	rs1497709	rs40943	rs246155		
Discoid Rash	AMINOACYL TRNA BIOSYNTHESIS	KEGG	730	32		6.31E-01	9.96E-01	rs675144	rs20338	rs3879938	rs469986	rs7751261	rs1232661	rs1441024	rs49225	rs6779394	rs26744	rs676674	rs29085	rs2064	rs1088582	rs313664	rs282293
Discoid Rash	PEROXISOMAL_LIPID_METABOLISM	REACTOME	435	11		6.32E-01	9.96E-01	rs500800	rs7788404	rs485415	rs994414	rs1754418	rs380257	rs1675216									
Discoid Rash	ACETYLCHOLINE_BINDING_AND_DOWNSTREAM_EVENTS	REACTOME	242	12		6.33E-01	9.96E-01	rs445226	rs701741	rs935865	rs1051971	rs2741343	rs1290458	rs4072398	rs107150								
Discoid Rash	IRON_UPTAKE_AND_TRANSPORT	REACTOME	1163	41		6.33E-01	9.96E-01	rs2041689	rs1098200	rs868177	rs19118	rs1739259	rs3580243	rs1790943	rs6861637	rs1267009	rs7423230	rs1095421	rs1997942	rs2454039	rs3786645	rs1309526	rs1266504
Discoid Rash	GAB1_SIGNALING	REACTOME	1077	37		6.33E-01	9.96E-01	rs4376132	rs1221	rs98081	rs8734181	rs7325969	rs798104	rs1850409	rs494796	rs98182	rs1497628	rs1073996	rs18925	rs1189254	rs371023	rs1007379	rs1094145
Discoid Rash	BASE_EXCISION_REPAIR	KEGG	500	27		6.34E-01	9.96E-01	rs3805169	rs100907	rs9580991	rs1088366	rs423068	rs39460	rs11402	rs2950565	rs2153608	rs439493	rs1236181	rs3730463	rs123561	rs4840583	rs6564980	rs345803
Discoid Rash	AMINO_SUGAR_AND_NUCLEOTIDE_SUGAR_METABOLISM	KEGG	956	34		6.35E-01	9.96E-01	rs9391934	rs11848	rs1004779	rs1102193	rs7501212	rs1001323	rs100251	rs4095050	rs690932	rs2173685	rs163918	rs1756100	rs684732	rs14736	rs380064	rs1394531
Discoid Rash	COSTAMULATION_BY_THE_CD28_FAMILY	REACTOME	3679	52		6.38E-01	9.96E-01	rs4976132	rs1490801	rs217260	rs3720213	rs104405	rs1544241	rs497628	rs1693964	rs4347980	rs1011						

Discoid Rash	EGFR_DOWNREGULATION	REACTOME	1037	29	20
Discoid Rash	HOMOLOGOUS_RECOMBINATION	KEGG	730	24	14
Discoid Rash	UNFOLDED_PROTEIN_RESPONSE	REACTOME	1176	32	20
Discoid Rash	GLYCOGEN_METABOLISM_PATHWAY	KEGG	1290	39	20
Discoid Rash	CGMP_EFFECTS	REACTOME	1120	44	20
Discoid Rash	RNA_POL_III_TRANSCRIPTION	REACTOME	875	45	20
Discoid Rash	TAK1_ACTIVATES_NFKB_BY_PHOSPHORYLATION_AND_ACTIVATION_OF_IKKS_COMPLEX	REACTOME	777	37	20
Discoid Rash	AD_PATHWAY	BIOCARTA	927	37	20
Discoid Rash	GLUCAGON_TYRE_LIGAND_RECEPTORS	REACTOME	786	29	20
Discoid Rash	CD28_CO_STIMULATION	REACTOME	797	31	19
Discoid Rash	SYNTHESIS_OF_BILE_ACIDS_AND_BILE_SALTS	REACTOME	546	6	5
Discoid Rash	TRAF3_MEDIATED_IRF7_ACTIVATION	REACTOME	433	34	10
Discoid Rash	SIGNALING_BY_NODAL	REACTOME	927	37	20
Discoid Rash	SIGNALING_BY_BMP	REACTOME	918	35	15
Discoid Rash	FATTY_ACYL_COA_BIOSYNTHESIS	REACTOME	404	26	14
Discoid Rash	CONVERSION_FROM_APC_C_CDC20_TO_APC_C_CDH1_IN_LATE_ANAPHASE	REACTOME	188	17	7
Discoid Rash	GATA3_PATHWAY	BIOCARTA	41	20	20
Discoid Rash	APPTOSIS	KEGG	1226	33	20
Discoid Rash	ACTIVATED_TAK1_MEDIATES_P38_MAPK_ACTIVATION	REACTOME	649	32	16
Discoid Rash	M_G_TRANSITION	REACTOME	1315	34	20
Discoid Rash	METABOLISM_OF_MIRNA	REACTOME	2017	31	20
Discoid Rash	FATTY_ACID_TRIACYLGLYCEROL_AND_KETONE_BODY_METABOLISM	REACTOME	5526	32	20
Discoid Rash	NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY	KEGG	1406	37	20
Discoid Rash	OXIDATIVE_PHOSPHORYLATION	KEGG	2486	35	20
Discoid Rash	STRESS_PATHWAY	BIOCARTA	633	30	17
Discoid Rash	REGULATION_OF_APOPTOSIS	REACTOME	1432	42	20
Discoid Rash	CHONDROITIN_SULFATE_BIOSYNTHESIS	REACTOME	846	24	18
Discoid Rash	IGF1_PATHWAY	BIOCARTA	813	34	20
Discoid Rash	TGF_BETA_SIGNALING_PATHWAY	KEGG	3535	35	20
Discoid Rash	GLUCOSE_METABOLISM	REACTOME	544	32	20
Discoid Rash	UCALPAIN_PATHWAY	BIOCARTA	424	26	16
Discoid Rash	CHONDROITIN_SULFATE_DERMATAN_SULFATE_METABOLISM	REACTOME	278	25	16
Discoid Rash	METABOLISM_OF_XENOBIOTICS_BY_CYTOCHROME_P450	KEGG	1474	53	20
Discoid Rash	COMPLEMENT_AND_COAGULATION_CASCADES	KEGG	174	28	20
Discoid Rash	TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	KEGG	2339	34	20
Discoid Rash	BIOPETIDES_PATHWAY	BIOCARTA	1081	32	20
Discoid Rash	NOTCH1_INTRACELLULAR_DOMAIN_REGULATES_TRANSCRIPTION	REACTOME	2852	25	16
Discoid Rash	SPHINGOLIPID_DE_NOVO_BIOSYNTHESIS	REACTOME	1020	33	20
Discoid Rash	MCM_PATHWAY	BIOCARTA	234	6	5
Discoid Rash	RIBOFLAVIN_METABOLISM	KEGG	295	24	10
Discoid Rash	INITIAL_TRIGGERING_OF_COMPLEMENT	REACTOME	434	19	14
Discoid Rash	CALCIUMININ_PATHWAY	BIOCARTA	895	33	20
Discoid Rash	SYNTHESIS_SECRETION_AND_INACTIVATION_OF_GLIPI	REACTOME	174	28	20
Discoid Rash	THROMBOXANE_SIGNALING_THROUGH_TG_RECEPTOR	REACTOME	492	15	11
Discoid Rash	PROGESTERONE_MEDIATED_OOCYTE_MATURATION	KEGG	2535	45	20
Discoid Rash	TCR_SIGNALING	REACTOME	2048	24	19
Discoid Rash	TCR_PATHWAY	BIOCARTA	218	24	19
Discoid Rash	CDK_MEDIATED_PHOSPHORYLATION_AND_REMOVAL_OF_CDC6	REACTOME	698	29	20
Discoid Rash	SHH_PATHWAY	KEGG	679	20	14
Discoid Rash	GLYCOSPHINGOLIPID_BIOSYNTHESIS_LACTO_AND_NEOLACTO_SERIES	BIOCARTA	10	14	13
Discoid Rash	MITOTIC_PROMETAPHASE	REACTOME	1814	37	20
Discoid Rash	CYCLIN_E_ASSOCIATED_EVENTS_DURING_G1_S_TRANSITION	REACTOME	1212	36	20
Discoid Rash	PARKINSONS_DISEASE	KEGG	2833	31	20
Discoid Rash	AMYOTROPIC_LATERAL_SCLEROSIS_ALS	KEGG	1813	25	16
Discoid Rash	FDI_SIGNALING	REACTOME	988	30	17
Discoid Rash	MEIOSIS	BIOCARTA	1674	39	20
Discoid Rash	GENERATION_OF_SECOND_MESSENGER_MOLECULES	REACTOME	616	34	18
Discoid Rash	NEFAT_PATHWAY	BIOCARTA	1626	40	20
Discoid Rash	TOLL_RECEPTOR_CASCADES	REACTOME	3778	25	20
Discoid Rash	VEF_MEDIATED_DEGRADATION_OF_APOBEC3	REACTOME	1154	38	20
Discoid Rash	TRANSPORT_OF_VITAMINS_NUCLEOSIDES_AND_RELATED_MOLECULES	REACTOME	1154	38	20
Discoid Rash	LONG_TERM_POTENTIATION	KEGG	3260	37	20
Discoid Rash	MITOTIC_M_M_G1_PHASES	REACTOME	3176	36	20
Discoid Rash	INTEGRATION_OF_ENERGY_METABOLISM	REACTOME	4501	34	20
Discoid Rash	MIRNA_PROCESSING	REACTOME	1942	28	20
Discoid Rash	PK2_PATHWAY	BIOCARTA	752	40	20
Discoid Rash	CYTOKINE_PATHWAY	BIOCARTA	491	21	14
Discoid Rash	IL10_PATHWAY	BIOCARTA	2301	36	20
Discoid Rash	CELL_JUNCTION_ORGANIZATION	REACTOME	6981	34	20
Discoid Rash	MEIOTIC_RECOMBINATION	REACTOME	983	33	16
Discoid Rash	PPARA_ACTIVATES_GENE_EXPRESSION	REACTOME	3675	34	20
Discoid Rash	CACAE_PATHWAY	BIOCARTA	385	13	7
Discoid Rash	MIRNA_CAPPING	REACTOME	8	5	5
Discoid Rash	LIGAND_GATED_ION_CHANNEL_TRANSPORT	REACTOME	7	9	5
Discoid Rash	CHREBP2_PATHWAY	BIOCARTA	1059	52	20
Discoid Rash	P53_PATHWAY	BIOCARTA	347	12	7
Discoid Rash	FORMATION_OF_TRANSCRIPTION_COUPLED_NER_TC_NER_REPAIR_COMPLEX	REACTOME	389	9	5
Discoid Rash	REGULATION_OF_INSULIN_SECRETION	REACTOME	571	32	20
Discoid Rash	AUTODEGRADATION_OF_THE_E3_UBIQUITIN_LIGASE_COPI	REACTOME	766	26	16
Discoid Rash	TRANSMISSION_ACROSS_CHEMICAL_SYNAPSES	REACTOME	989	28	20
Discoid Rash	PI_METABOLISM	REACTOME	691	31	20
Discoid Rash	THROMBIN_SIGNALING_THROUGH_PROTEINASE_ACTIVATED_RECEPTORS_PARS	REACTOME	17	13	7
Discoid Rash	APC_C_CDH1_MEDIATED_DEGRADATION_OF_CDC20_AND_OTHER_APC_C_CDH1_TARGETS	REACTOME	959	35	20
Discoid Rash	TE MITOSIS_EARLY_G1	REACTOME	18	12	8
Discoid Rash	ENDOSOMAL_SORTING_COMPLEX_REQUIRED_FOR_TRANSPORT_ESCRT	REACTOME	1808	38	20
Discoid Rash	MITOCHONDRIA_PATHWAY	BIOCARTA	317	4	20
Discoid Rash	PYRIDIMINE_METABOLISM	REACTOME	792	44	20
Discoid Rash	JNK_C_JUN_KINASE_PHOSPHORYLATION_AND_ACTIVATION_MEDIATED_BY_ACTIVATED_RECEPTORS	REACTOME	172	37	17
Discoid Rash	KERATINOCTYTE_PATHWAY	BIOCARTA	958	30	20





























































































































### 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	<i>NOS3</i>
Discovery	rs17709898	4	55957723	G	A	0.53	1.50E-4	<i>KDR</i>
Discovery	rs743507	7	150707488	G	A	0.53	2.61E-4	<i>NOS3</i>
Discovery	rs10940145	5	67290972	G	A	0.55	3.26E-4	<i>PIK3R1</i>
Discovery	rs7396875	11	551405	G	A	2.01	7.16E-4	<i>HRAS</i>
Discovery	rs7726943	5	67818581	G	A	1.68	7.80E-4	<i>PIK3R1</i>
Discovery	rs10461535	5	67218216	G	A	2.17	1.30E-3	<i>PIK3R1</i>
Discovery	rs227913	17	64607394	C	A	0.62	2.67E-3	<i>PRKCA</i>
Discovery	rs2372183	5	67197955	A	G	2.06	2.98E-3	<i>PIK3R1</i>
Discovery	rs4976028	5	67290733	G	A	1.70	3.46E-3	<i>PIK3R1</i>
Discovery	rs904132	4	55802108	G	A	0.40	5.78E-3	<i>KDR</i>
Discovery	rs11133360	4	55982752	G	A	0.67	7.40E-3	<i>KDR</i>
Discovery	rs9892886	17	64382588	G	A	1.73	8.06E-3	<i>PRKCA</i>
Discovery	rs11860367	16	24011167	G	A	0.66	8.25E-3	<i>PRKCB</i>
Discovery	rs10515068	5	67450499	C	A	1.61	1.02E-2	<i>PIK3R1</i>
Discovery	rs7719763	5	67681425	A	G	1.47	1.38E-2	<i>PIK3R1</i>
Discovery	rs8051034	16	23925134	C	A	0.40	1.53E-2	<i>PRKCB</i>
Discovery	rs863818	5	67554023	G	A	0.69	1.65E-2	<i>PIK3R1</i>
Discovery	rs10515059	5	67241677	A	C	0.65	2.22E-2	<i>PIK3R1</i>
Discovery	rs6504424	17	64387328	G	A	1.49	2.27E-2	<i>PRKCA</i>
Replication	rs17626553	13	28968770	G	A	0.43	2.35E-4	<i>FLT1</i>
Replication	rs1324057	13	28925435	A	G	0.52	2.56E-4	<i>FLT1</i>
Replication	rs11959164	5	180096972	G	A	1.61	1.44E-3	<i>FLT4</i>
Replication	rs10515077	5	67613801	C	A	2.26	2.86E-3	<i>PIK3R1</i>
Replication	rs6129760	20	39746403	G	A	1.61	3.29E-3	<i>PLCG1</i>
Replication	rs11744801	5	67301383	C	A	0.56	3.56E-3	<i>PIK3R1</i>
Replication	rs7202459	16	24039013	G	A	0.64	4.25E-3	<i>PRKCB</i>
Replication	rs6842830	4	55873926	G	A	0.65	4.31E-3	<i>KDR</i>
Replication	rs3844278	3	10211918	A	G	0.52	5.15E-3	<i>VHL</i>
Replication	rs9550377	13	29101681	A	G	2.03	8.17E-3	<i>FLT1</i>
Replication	rs2228246	20	39792063	G	A	0.59	8.75E-3	<i>PLCG1</i>
Replication	rs17086609	13	28929711	G	A	1.50	1.02E-2	<i>FLT1</i>
Replication	rs10067755	5	67307462	G	A	1.46	1.15E-2	<i>PIK3R1</i>
Replication	rs6947821	7	150729212	G	A	1.48	1.21E-2	<i>NOS3</i>
Replication	rs4290512	17	64395039	A	C	0.43	1.39E-2	<i>PRKCA</i>
Replication	rs2283540	16	24130770	A	G	0.68	1.53E-2	<i>PRKCB</i>
Replication	rs708030	3	10212494	G	A	1.43	1.83E-2	<i>VHL</i>
Replication	rs10283368	8	141679817	A	G	0.70	2.00E-2	<i>PTK2</i>
Replication	rs4791036	17	64797135	G	A	0.62	2.29E-2	<i>PRKCA</i>
Replication	rs2125489	4	55953483	A	G	0.55	2.39E-2	<i>KDR</i>

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 <sub>BETAMETHASONE VALERATE</sub>	P <sub>IMIQUIMOD</sub>	P <sub>DIPHENCYPRONE</sub>	P <sub>PIMECROLIMUS</sub>
<i>ARNT</i>	1,10E-02	5,26E-03	1,22E-01	2,63E-02
<i>EIF1</i>	4,93E-02	2,65E-06	6,68E-04	3,31E-01
<i>EIF1AX</i>	6,93E-02	2,88E-03	1,33E-01	5,56E-01
<i>EIF2B1</i>	6,82E-01	6,49E-03	9,26E-01	7,20E-01
<i>EIF2B2</i>	1,87E-02	2,99E-01	4,66E-01	1,86E-01
<i>EIF2B3</i>	3,57E-01	5,91E-01	4,15E-02	8,83E-01
<i>EIF2B4</i>	8,87E-03	7,67E-01	1,25E-01	3,33E-01
<i>EIF2B5</i>	8,20E-01	4,92E-01	3,61E-01	8,41E-01
<i>EIF2S1</i>	2,37E-03	7,54E-03	1,20E-01	1,16E-02
<i>EIF2S2</i>	1,20E-01	7,64E-06	2,18E-03	2,63E-01
<i>EIF2S3</i>	2,57E-01	1,69E-02	1,64E-01	5,93E-01
<i>ELAVL1</i>	5,34E-03	6,83E-03	4,95E-02	1,61E-01
<i>FLT1</i>	4,86E-03	1,70E-02	6,32E-02	5,89E-02
<i>FLT4</i>	3,05E-01	2,73E-01	2,11E-01	2,91E-01
<i>HIF1A</i>	1,76E-01	2,46E-02	9,17E-02	6,53E-01
<i>HRAS</i>	1,04E-03	1,21E-08	5,19E-01	2,78E-02
<i>KDR</i>	1,80E-01	6,39E-02	3,55E-01	2,94E-01
<i>NOS3</i>	6,31E-01	6,32E-01	3,96E-01	3,21E-01
<i>PIK3CA</i>	9,54E-02	1,42E-08	1,09E-01	1,62E-01
<i>PIK3CG</i>	2,08E-01	1,95E-01	1,85E-01	5,18E-01
<i>PIK3R1</i>	1,12E-04	4,70E-06	2,76E-04	1,66E-01
<i>PLCG1</i>	2,44E-01	2,06E-01	1,74E-02	1,91E-01
<i>PRKCA</i>	1,84E-01	2,50E-01	1,75E-01	1,82E-01
<i>PRKCB</i>	3,19E-01	5,34E-02	1,56E-01	3,53E-01
<i>PTK2</i>	3,01E-04	6,72E-09	7,51E-02	1,44E-01
<i>PXN</i>	2,18E-01	8,53E-02	4,97E-01	1,08E-01
<i>SHC1</i>	4,17E-04	9,64E-03	2,94E-01	9,82E-02
<i>VEGFA</i>	2,24E-04	2,20E-11	3,34E-02	2,88E-02
<i>VHL</i>	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<sub>BETAMETHASONE VALERATE</sub>, P-value obtained from the differential expression analysis comparing samples before (N=10) and after (N=10) betamethasone valerate treatment; P<sub>DIPHENCYPRONE</sub>, P-value obtained from the differential expression analysis comparing samples before (N=22) and after (N=22) diphencyprone treatment; P<sub>IMIQUIMOD</sub>, P-value obtained from the differential expression analysis comparing samples before (N=6) and after (N=54) imiquimod treatment; P<sub>PIMECROLIMUS</sub>, P-value obtained from the differential expression analysis comparing samples before (N=10) and after (N=10) pimecrolimus treatment.

**2.5 Table S5. Statistical significance of the VEGF genetic pathway perturbation after topical immunotherapy.**

<b>VEGF PATHWAY</b>	<b>BETAMETHASONE VALERATE</b>	<b>IMIQUIMOD</b>	<b>DIPHENCYPRONE</b>	<b>PIMECROLIMUS</b>
<b>DEG (n)</b>	12	16	7	4
<b>NDEG (n)</b>	17	13	22	25
<b>Total Genes (n)</b>	29	29	29	29
<b>P-value</b>	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	114377568	<i>PTPN22</i>	A
rs1801274	1	161479745	<i>FCGR2A</i>	C
rs704840	1	173226195	<i>TNFSF4</i>	G
rs17849501	1	183542323	<i>SMG7-NCF2</i>	T
rs3024505	1	206939904	<i>IL10</i>	T
rs9782955	1	236039877	<i>LYST</i>	C
rs2111485	2	163110536	<i>IFIH1</i>	G
rs3768792	2	213871709	<i>IKZF2</i>	C
rs6740462	2	65667272	<i>SPRED2</i>	A
rs11889341	2	191943742	<i>STAT4</i>	T
rs9311676	3	58470351	<i>ABHD6-PXK</i>	C
rs564799	3	159728987	<i>IL12A</i>	C
rs10028805	4	102737250	<i>BANK1</i>	G
rs7726414	5	133431834	<i>TCF7-SKP1</i>	T
rs10036748	5	150458146	<i>TNIP1</i>	T
rs2431697	5	159879978	<i>MIR146A</i>	T
rs9462027	6	34797241	<i>UHRF1BP1</i>	A
rs6568431	6	106588806	<i>PRDM1-ATG5</i>	A
rs6932056	6	138242437	<i>TNFAIP3</i>	C
rs1270942	6	31918860	<i>MHC class III</i>	C
rs849142	7	28185891	<i>JAZF1</i>	A
rs4917014	7	50305863	<i>IKZF1</i>	T
rs10488631	7	128594183	<i>IRF5</i>	C
rs2736340	8	11343973	<i>BLK</i>	T
rs2663052	10	50069395	<i>WDFY4</i>	C
rs4948496	10	63805617	<i>ARID5B</i>	C
rs3794060	11	71187679	<i>DHCR7-NADSYN1</i>	C
rs2732549	11	35088399	<i>CD44</i>	T
rs7941765	11	128499000	<i>ETS1-FLI1</i>	C
rs12802200	11	566936	<i>IRF7</i>	C
rs10774625	12	111910219	<i>SH2B3</i>	A
rs1059312	12	129278864	<i>SLC15A4</i>	C
rs4902562	14	68731458	<i>RAD51B</i>	A
rs2289583	15	75311036	<i>CSK</i>	A
rs9652601	16	11174365	<i>CIITA-SOCS1</i>	G
rs34572943	16	31272353	<i>ITGAM</i>	A
rs11644034	16	85972612	<i>IRF8</i>	G
rs2286672	17	4712617	<i>PLD2</i>	T
rs2941509	17	37921194	<i>IKZF3</i>	A
rs2304256	19	10475652	<i>TYK2</i>	C
rs7444	22	21976934	<i>UBE2L3</i>	C
rs887369	X	30577846	<i>CXorf21</i>	C
rs1734787	X	153325446	<i>IRAK1-MECP2</i>	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
CACAM_PATHWAY	BIOCARTA	16
CDMAC_PATHWAY	BIOCARTA	16
EIF_PATHWAY	BIOCARTA	16
GATA3_PATHWAY	BIOCARTA	16
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
CK1_PATHWAY	BIOCARTA	17
PML_PATHWAY	BIOCARTA	17
41BB_PATHWAY	BIOCARTA	17
ARF_PATHWAY	BIOCARTA	17
ARAP_PATHWAY	BIOCARTA	18
MCM_PATHWAY	BIOCARTA	18
ETS_PATHWAY	BIOCARTA	18
NGF_PATHWAY	BIOCARTA	18
PTEN_PATHWAY	BIOCARTA	18
CARDIACEGF_PATHWAY	BIOCARTA	18
ERK5_PATHWAY	BIOCARTA	18
SPRY_PATHWAY	BIOCARTA	18
TEL_PATHWAY	BIOCARTA	18
TNFR2_PATHWAY	BIOCARTA	18
UCALPAIN_PATHWAY	BIOCARTA	18
TID_PATHWAY	BIOCARTA	19
COMP_PATHWAY	BIOCARTA	19
MTA3_PATHWAY	BIOCARTA	19
EPO_PATHWAY	BIOCARTA	19
MAL_PATHWAY	BIOCARTA	19
STATHMIN_PATHWAY	BIOCARTA	19
TGF $\beta$ _PATHWAY	BIOCARTA	19
TH1TH2_PATHWAY	BIOCARTA	19
AMI_PATHWAY	BIOCARTA	20
ATM_PATHWAY	BIOCARTA	20
CCR5_PATHWAY	BIOCARTA	20
NKCELLS_PATHWAY	BIOCARTA	20
IGF1MOTOR_PATHWAY	BIOCARTA	20
ACTINY_PATHWAY	BIOCARTA	20
CALCINEURIN_PATHWAY	BIOCARTA	21
NDKDYNAMIN_PATHWAY	BIOCARTA	21
IGF1_PATHWAY	BIOCARTA	21
ATRBRCA_PATHWAY	BIOCARTA	21
MITOCHONDRIA_PATHWAY	BIOCARTA	21
TOB1_PATHWAY	BIOCARTA	21
CTLA4_PATHWAY	BIOCARTA	21
TFF_PATHWAY	BIOCARTA	21
AKT_PATHWAY	BIOCARTA	22
CHEMICAL_PATHWAY	BIOCARTA	22
SPPA_PATHWAY	BIOCARTA	22
CERAMIDE_PATHWAY	BIOCARTA	22
GCR_PATHWAY	BIOCARTA	22
CYTOKINE_PATHWAY	BIOCARTA	22
DC_PATHWAY	BIOCARTA	22
IL2_PATHWAY	BIOCARTA	22
IL6_PATHWAY	BIOCARTA	22
INSULIN_PATHWAY	BIOCARTA	22
HER2_PATHWAY	BIOCARTA	22
CASPASE_PATHWAY	BIOCARTA	23
CCR3_PATHWAY	BIOCARTA	23
CTCF_PATHWAY	BIOCARTA	23
CELLCYCLE_PATHWAY	BIOCARTA	23
P53HYPOXIA_PATHWAY	BIOCARTA	23
IL12_PATHWAY	BIOCARTA	23
GLEEVEC_PATHWAY	BIOCARTA	23
INTRINSIC_PATHWAY	BIOCARTA	23
MTOR_PATHWAY	BIOCARTA	23
IGF1R_PATHWAY	BIOCARTA	23
NFKB_PATHWAY	BIOCARTA	23
PTDINS_PATHWAY	BIOCARTA	23
RAC1_PATHWAY	BIOCARTA	23
RAS_PATHWAY	BIOCARTA	23
MEF2D_PATHWAY	BIOCARTA	23
CSK_PATHWAY	BIOCARTA	24
G2_PATHWAY	BIOCARTA	24
CXCR4_PATHWAY	BIOCARTA	24
ECM_PATHWAY	BIOCARTA	24
NTH1_PATHWAY	BIOCARTA	24
NOS1_PATHWAY	BIOCARTA	24
EIF4_PATHWAY	BIOCARTA	24
TPO_PATHWAY	BIOCARTA	24
MCALPAIN_PATHWAY	BIOCARTA	25
STRESS_PATHWAY	BIOCARTA	25
RACCYCD_PATHWAY	BIOCARTA	26
BAD_PATHWAY	BIOCARTA	26
PGC1A_PATHWAY	BIOCARTA	26
WNT_PATHWAY	BIOCARTA	26

GSK3_PATHWAY	BIOCARTA	27
EDG1_PATHWAY	BIOCARTA	27
CREB_PATHWAY	BIOCARTA	27
G1_PATHWAY	BIOCARTA	28
ERK_PATHWAY	BIOCARTA	28
GH_PATHWAY	BIOCARTA	28
PROTEASOME_PATHWAY	BIOCARTA	28
INFLAM_PATHWAY	BIOCARTA	29
VIP_PATHWAY	BIOCARTA	29
NKT_PATHWAY	BIOCARTA	29
TNFR1_PATHWAY	BIOCARTA	29
VEGF_PATHWAY	BIOCARTA	29
FAS_PATHWAY	BIOCARTA	30
EGF_PATHWAY	BIOCARTA	31
PYK2_PATHWAY	BIOCARTA	31
MYOSIN_PATHWAY	BIOCARTA	31
HDAC_PATHWAY	BIOCARTA	32
PDGF_PATHWAY	BIOCARTA	32
RHO_PATHWAY	BIOCARTA	32
NO1_PATHWAY	BIOCARTA	33
DEATH_PATHWAY	BIOCARTA	33
IL1R_PATHWAY	BIOCARTA	33
MPR_PATHWAY	BIOCARTA	34
CARM_ER_PATHWAY	BIOCARTA	35
AGR_PATHWAY	BIOCARTA	36
AT1R_PATHWAY	BIOCARTA	36
ALK_PATHWAY	BIOCARTA	37
BCR_PATHWAY	BIOCARTA	37
MET_PATHWAY	BIOCARTA	37
GPCR_PATHWAY	BIOCARTA	37
PAR1_PATHWAY	BIOCARTA	37
TOLL_PATHWAY	BIOCARTA	37
IL2RB_PATHWAY	BIOCARTA	38
INTEGRIN_PATHWAY	BIOCARTA	38
FMLP_PATHWAY	BIOCARTA	39
P38MAPK_PATHWAY	BIOCARTA	40
FCER1_PATHWAY	BIOCARTA	41
CHREBP2_PATHWAY	BIOCARTA	42
BIOPEPTIDES_PATHWAY	BIOCARTA	45
KERATINOCYTE_PATHWAY	BIOCARTA	46
TCR_PATHWAY	BIOCARTA	49
NFAT_PATHWAY	BIOCARTA	56
HIVNEF_PATHWAY	BIOCARTA	58
PPARA_PATHWAY	BIOCARTA	58
MAPK_PATHWAY	BIOCARTA	87
PRIMARY_BILE_ACID_BIOSYNTHESIS	KEGG	16
OTHER_GLYCAN_DEGRADATION	KEGG	16
GLYOXYLATE_AND_DICARBOXYLATE_METABOLISM	KEGG	16
RIBOFLAVIN_METABOLISM	KEGG	16
PANTOTHENATE_AND_COA_BIOSYNTHESIS	KEGG	16
STEROID_BIOSYNTHESIS	KEGG	17
ONE_CARBON_POOL_BY_FOLATE	KEGG	17
RENIN_ANGIOTENSIN_SYSTEM	KEGG	17
PHENYLALANINE_METABOLISM	KEGG	18
ALPHA_LINOLENIC_ACID_METABOLISM	KEGG	19
GLYCOSAMINOGLYCAN_DEGRADATION	KEGG	21
BETA_ALANINE_METABOLISM	KEGG	22
GLYCOSAMINOGLYCAN_BIOSYNTHESIS_CHONDROITIN_SULFATE	KEGG	22
BIOSYNTHESIS_OF_UNSATURATED_FATTY_ACIDS	KEGG	22
NITROGEN_METABOLISM	KEGG	23
MISMATCH_REPAIR	KEGG	23
PROXIMAL_TUBULE_BICARBONATE_RECLAMATION	KEGG	23
NICOTINATE_AND_NICOTINAMIDE_METABOLISM	KEGG	24
PROTEIN_EXPORT	KEGG	24
ASCORBATE_AND_ALDARATE_METABOLISM	KEGG	25
GLYCOSYLPHOSPHATIDYLINOSITOL_GPI_ANCHOR_BIOSYNTHESIS	KEGG	25
DORSO_VENTRAL_AXIS_FORMATION	KEGG	25
MATURITY_ONSET_DIABETES_OF_THE_YOUNG	KEGG	25
GALACTOSE_METABOLISM	KEGG	26
SELENOAMINO_ACID_METABOLISM	KEGG	26
GLYCOSAMINOGLYCAN_BIOSYNTHESIS_HEPARAN_SULFATE	KEGG	26
GLYCOSPHINGOLIPID_BIOSYNTHESIS_LACTO_AND_NEOLACTO_SERIES	KEGG	26
PENTOSE_PHOSPHATE_PATHWAY	KEGG	27
PENTOSE_AND_GLUCURONATE_INTERCONVERSIONS	KEGG	28
HOMOLOGOUS_RECOMBINATION	KEGG	28
HISTIDINE_METABOLISM	KEGG	29
LINOLEIC_ACID_METABOLISM	KEGG	29
RNA_POLYMERASE	KEGG	29
THYROID_CANCER	KEGG	29
O_GLYCAN_BIOSYNTHESIS	KEGG	30
ASTHMA	KEGG	30
GLYCINE_SERINE_AND_THREONINE_METABOLISM	KEGG	31
CITRATE_CYCLE_TCA_CYCLE	KEGG	32
ALANINE_ASPARTATE_AND_GLUTAMATE_METABOLISM	KEGG	32
ETHER_LIPID_METABOLISM	KEGG	33
PROPANOATE_METABOLISM	KEGG	33
FRUCTOSE_AND_MANNOSE_METABOLISM	KEGG	34
CYSTEINE_AND_METHIONINE_METABOLISM	KEGG	34
BUTANOATE_METABOLISM	KEGG	34
BASE_EXCISION_REPAIR	KEGG	35
REGULATION_OF_AUTOPHAGY	KEGG	35
PRION_DISEASES	KEGG	35
PRIMARY_IMMUNODEFICIENCY	KEGG	35
BASAL_TRANSCRIPTION_FACTORS	KEGG	36
DNA_REPLICATION	KEGG	36
SNARE_INTERACTIONS_IN_VESICULAR_TRANSPORT	KEGG	38
ALLOGRAFT_REJECTION	KEGG	38
TRYPTOPHAN_METABOLISM	KEGG	40
SPHINGOLIPID_METABOLISM	KEGG	40
PYRUVATE_METABOLISM	KEGG	40
PORPHYRIN_AND_CHLOROPHYLL_METABOLISM	KEGG	41

AMINOACYL_TRNA_BIOSYNTHESIS	KEGG	41
FATTY_ACID_METABOLISM	KEGG	42
TYROSINE_METABOLISM	KEGG	42
ALDOSTERONE_REGULATED_SODIUM_REABSORPTION	KEGG	42
BLADDER_CANCER	KEGG	42
GRAFT_VERSUS_HOST_DISEASE	KEGG	42
VALINE_LEUCINE_AND_ISOLEUCINE_DEGRADATION	KEGG	44
LYSINE_DEGRADATION	KEGG	44
AMINO_SUGAR_AND_NUCLEOTIDE_SUGAR_METABOLISM	KEGG	44
ABC_TRANSPORTERS	KEGG	44
NUCLEOTIDE_EXCISION_REPAIR	KEGG	44
TYPE_I_DIABETES_MELLITUS	KEGG	44
VASOPRESSIN_REGULATED_WATER_REABSORPTION	KEGG	44
N_GLYCAN_BIOSYNTHESIS	KEGG	46
NOTCH_SIGNALING_PATHWAY	KEGG	47
TYPE_II_DIABETES_MELLITUS	KEGG	47
PROTEASOME	KEGG	48
INTESTINAL_IMMUNE_NETWORK_FOR_IGA_PRODUCTION	KEGG	48
GLYCEROLIPID_METABOLISM	KEGG	49
GLUTATHIONE_METABOLISM	KEGG	50
DRUG_METABOLISM_OTHER_ENZYMES	KEGG	51
STARCH_AND_SUCROSE_METABOLISM	KEGG	52
MTOR_SIGNALING_PATHWAY	KEGG	52
TASTE_TRANSDUCTION	KEGG	52
ENDOMETRIAL_CANCER	KEGG	52
AMYOTROPHIC_LATERAL_SCLEROSIS_ALS	KEGG	53
AUTOIMMUNE_THYROID_DISEASE	KEGG	53
ARGININE_AND_PROLINE_METABOLISM	KEGG	54
INOSITOL_PHOSPHATE_METABOLISM	KEGG	54
NON_SMALL_CELL_LUNG_CANCER	KEGG	54
STEROID_HORMONE_BIOSYNTHESIS	KEGG	55
BASAL_CELL_CARCINOMA	KEGG	55
HEDGEHOG_SIGNALING_PATHWAY	KEGG	56
CYTOSOLIC_DNA_SENSING_PATHWAY	KEGG	56
VIBRIO_CHOLERAE_INFECTION	KEGG	56
ARACHIDONIC_ACID_METABOLISM	KEGG	58
RNA_DEGRADATION	KEGG	59
PATHOGENIC_ESCHERICHIA_COLI_INFECTION	KEGG	59
ACUTE_MYELOID_LEUKEMIA	KEGG	60
GLYCOLYSIS_GLUCCONEOGENESIS	KEGG	62
NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY	KEGG	62
COLORRECTAL_CANCER	KEGG	62
RETINOL_METABOLISM	KEGG	64
GLIOMA	KEGG	65
ADIPOCYTOKINE_SIGNALING_PATHWAY	KEGG	67
EPITHELIAL_CELL_SIGNALING_IN_HELICOBACTER_PYLORI_INFECTION	KEGG	68
PPAR_SIGNALING_PATHWAY	KEGG	69
P53_SIGNALING_PATHWAY	KEGG	69
COMPLEMENT_AND_COAGULATION_CASCADES	KEGG	69
METABOLISM_OF_XENOBIOTICS_BY_CYTOCHROME_P450	KEGG	70
LONG_TERM_POTENTIATION	KEGG	70
LONG_TERM_DEPRESSION	KEGG	70
RENAL_CELL_CARCINOMA	KEGG	70
PANCREATIC_CANCER	KEGG	70
RIG_I_LIKE_RECEPTOR_SIGNALING_PATHWAY	KEGG	71
MELANOMA	KEGG	71
DRUG_METABOLISM_CYTOCHROME_P450	KEGG	72
LEISHMANIA_INFECTION	KEGG	72
CHRONIC_MYELOID_LEUKEMIA	KEGG	73
VIRAL_MYOCARDITIS	KEGG	73
ADHERENS_JUNCTION	KEGG	75
B_CELL_RECEPTOR_SIGNALING_PATHWAY	KEGG	75
PHOSPHATIDYLINOSITOL_SIGNALING_SYSTEM	KEGG	76
VEGF_SIGNALING_PATHWAY	KEGG	76
ARRHYTHMOGENIC_RIGHT_VENTRICULAR_CARDIOMYOPATHY_ARVC	KEGG	76
GLYCEROPHOSPHOLIPID_METABOLISM	KEGG	77
PEROXISOME	KEGG	78
FC_EPSILON_R1_SIGNALING_PATHWAY	KEGG	79
CARDIAC_MUSCLE_CONTRACTION	KEGG	80
ECM_RECEPTOR_INTERACTION	KEGG	84
SMALL_CELL_LUNG_CANCER	KEGG	84
HYPERTROPHIC_CARDIOMYOPATHY_HCM	KEGG	85
TGF_BETA_SIGNALING_PATHWAY	KEGG	86
PROGESTERONE_MEDIATED_OOCYTE_MATURATION	KEGG	86
ERBB_SIGNALING_PATHWAY	KEGG	87
RIBOSOME	KEGG	88
APOPTOSIS	KEGG	88
HEMATOPOIETIC_CELL_LINEAGE	KEGG	88
ANTIGEN_PROCESSING_AND_PRESENTATION	KEGG	89
PROSTATE_CANCER	KEGG	89
GAP_JUNCTION	KEGG	90
DILATED_CARDIOMYOPATHY	KEGG	92
FC_GAMMA_R_MEDIATED_PHAGOCYTOSIS	KEGG	97
PYRIMIDINE_METABOLISM	KEGG	98
GNRH_SIGNALING_PATHWAY	KEGG	101
TOLL_LIKE_RECEPTOR_SIGNALING_PATHWAY	KEGG	102
MELANOGENESIS	KEGG	102
T_CELL_RECEPTOR_SIGNALING_PATHWAY	KEGG	108
OOCYTE_MEIOSIS	KEGG	114
VASCULAR_SMOOTH_MUSCLE_CONTRACTION	KEGG	115
LEUKOCYTE_TRANSENDOTHELIAL_MIGRATION	KEGG	118
LYSOSOME	KEGG	121
NEUROTROPIN_SIGNALING_PATHWAY	KEGG	126
SPLICEOSOME	KEGG	128
CELL_CYCLE	KEGG	128
AXON_GUIDANCE	KEGG	129
PARKINSONS_DISEASE	KEGG	133
CELL_ADHESION_MOLECULES_CAMS	KEGG	134
TIGHT_JUNCTION	KEGG	134
OXIDATIVE_PHOSPHORYLATION	KEGG	135
NATURAL_KILLER_CELL_MEDIATED_CYTOTOXICITY	KEGG	137

INSULIN_SIGNALING_PATHWAY	KEGG	137
UBIQUITIN_MEDIATED_PROTEOLYSIS	KEGG	138
SYSTEMIC_LUPUS_ERYTHEMATOSUS	KEGG	140
WNT_SIGNALING_PATHWAY	KEGG	151
JAK_STAT_SIGNALING_PATHWAY	KEGG	155
PURINE_METABOLISM	KEGG	159
ALZHEIMERS_DISEASE	KEGG	169
CALCIUM_SIGNALING_PATHWAY	KEGG	178
ENDOCYTOSIS	KEGG	183
HUNTINGTONS_DISEASE	KEGG	185
CHEMOKINE_SIGNALING_PATHWAY	KEGG	190
FOCAL_ADHESION	KEGG	201
REGULATION_OF_ACTIN_CYTOSKELETON	KEGG	216
MAPK_SIGNALING_PATHWAY	KEGG	267
CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	KEGG	267
NEUROACTIVE_LIGAND_RECEPTOR_INTERACTION	KEGG	272
CTNNB1_PHOSPHORYLATION_CASCADE	REACTOME	16
PRE_NOTCH_PROCESSING_IN_GOLGI	REACTOME	16
TGF_BETA_RECEPTOR_SIGNALING_IN_EMT_EPITHELIAL_TO_MESENCHYMAL_TRANSITION	REACTOME	16
ACTIVATED_POINT_MUTANTS_OF_FGFR2	REACTOME	16
ACYL_CHAIN_REMODELLING_OF_PG	REACTOME	16
PHOSPHORYLATION_OF_CD3_AND_TCR_ZETA_CHAINS	REACTOME	16
XENOBIOTICS	REACTOME	16
REGULATION_OF_INSULIN_LIKE_GROWTH_FACTOR_IGF_ACTIVITY_BY_INSULIN_LIKE_GROWTH_FACTOR_BINDING_PROTEINS_IGFBPS	REACTOME	16
ACETYLCHOLINE_BINDING_AND_DOWNSTREAM_EVENTS	REACTOME	16
NUCLEOTIDE_LIKE_PURINERGIC_RECEPTORS	REACTOME	16
EICOSANOID_LIGAND_BINDING_RECEPTORS	REACTOME	16
TRAFFICKING_OF_GLR2_CONTAINING_AMPA_RECEPTORS	REACTOME	16
SYNTHESIS_SECRETION_AND_DEACYLATION_OF_GHRELIN	REACTOME	16
JNK_C_JUN_KINASES_PHOSPHORYLATION_AND_ACTIVATION_MEDIATED_BY_ACTIVATED_HUMAN_TAK1	REACTOME	16
PLATELET_SENSITIZATION_BY_LDL	REACTOME	16
FORMATION_OF_ATP_BY_CHEMIOSMOTIC_COUPLING	REACTOME	16
CHYLOMICRON_MEDIATED_LIPID_TRANSPORT	REACTOME	16
INTEGRATION_OF_PROVIRUS	REACTOME	16
INITIAL_TRIGGERING_OF_COMPLEMENT	REACTOME	16
REGULATION_OF_KIT_SIGNALING	REACTOME	17
PROTEOLYTIC_CLEAVAGE_OF_SNARE_COMPLEX_PROTEINS	REACTOME	17
RESOLUTION_OF_AP_SITES_VIA_THE_MULTIPLE_NUCLEOTIDE_PATCH_REPLACEMENT_PATHWAY	REACTOME	17
ARMS_MEDIATED_ACTIVATION	REACTOME	17
SYNTHESIS_OF_PIPS_AT_THE_GOLGI_MEMBRANE	REACTOME	17
TIE2_SIGNALING	REACTOME	17
HOMOLOGOUS_RECOMBINATION_REPAIR_OF_REPLICATION_INDEPENDENT_DOUBLE_STRAND_BREAKS	REACTOME	17
BRANCHED_CHAIN_AMINO_ACID_CATABOLISM	REACTOME	17
NA_CL_DEPENDENT_NEUROTRANSMITTER_TRANSPORTERS	REACTOME	17
RAS_ACTIVATION_UOPN_CA2_INFUX_THROUGH_NMDA_RECEPTOR	REACTOME	17
AMINO_ACID_SYNTHESIS_AND_INTERCONVERSION_TRANSAMINATION	REACTOME	17
RAP1_SIGNALING	REACTOME	17
GABA_SYNTHESIS_RELEASE_REUPTAKE_AND_DEGRADATION	REACTOME	17
DESTABILIZATION_OF_MRNA_BY_BRF1	REACTOME	17
DESTABILIZATION_OF_MRNA_BY_KSRP	REACTOME	17
DESTABILIZATION_OF_MRNA_BY_TRISTETRAPROLIN_TTP	REACTOME	17
INTRINSIC_PATHWAY	REACTOME	17
ACTIVATION_OF_BH3_ONLY_PROTEINS	REACTOME	17
RNA_POL_III_CHAIN_ELONGATION	REACTOME	17
INFLAMMASOMES	REACTOME	17
SYNTHESIS_OF_GLYCOSYLPHOSPHATIDYLINOSITOL_GPI	REACTOME	17
SHC_RELATED_EVENTS	REACTOME	17
GLYCOGEN_BREAKDOWN_GLYCOGENOLYSIS	REACTOME	18
SIGNALING_BY_NODAL	REACTOME	18
ABCA_TRANSPORTERS_IN_LIPID_HOMEOSTASIS	REACTOME	18
SIGNALING_BY_CONSTITUTIVELY_ACTIVE_EGFR	REACTOME	18
RIP_MEDIATED_NFKB_ACTIVATION_VIA_DAI	REACTOME	18
OXYGEN_DEPENDENT_PROLINE_HYDROXYLATION_OF_HYPOXIA_INDUCIBLE_FACTOR_ALPHA	REACTOME	18
SYNTHESIS_OF_PC	REACTOME	18
FATTY_ACYL_COA_BIOSYNTHESIS	REACTOME	18
PKA_MEDIATED_PHOSPHORYLATION_OF_CREB	REACTOME	18
PD1_SIGNALING	REACTOME	18
ENERGY_DEPENDENT_REGULATION_OF_MTOR_BY_LKB1_AMPK	REACTOME	18
ACTIVATED_TAK1_MEDIATES_P38_MAPK_ACTIVATION	REACTOME	18
REGULATION_OF_SIGNALING_BY_CBL	REACTOME	18
PLATELET_CALCIIUM_HOMEOSTASIS	REACTOME	18
N_GLYCAN_ANTENNAE_ELONGATION_IN_THE_MEDIAL_TRANS_GOLGI	REACTOME	18
GLUCURONIDATION	REACTOME	18
GAP_JUNCTION_ASSEMBLY	REACTOME	18
BASE_EXCISION_REPAIR	REACTOME	19
SYNTHESIS_OF_BILE_ACIDS_AND_BILE_SALTS	REACTOME	19
ACTIVATED_AMPK_STIMULATES_FATTY_ACID_OXIDATION_IN_MUSCLE	REACTOME	19
BOTULINUM_NEUROTOXICITY	REACTOME	19
PROLONGED_ERK_ACTIVATION_EVENTS	REACTOME	19
SIGNALING_BY_FGFR1_FUSION_MUTANTS	REACTOME	19
POST_CHAPERONIN_TUBULIN_FOLDING_PATHWAY	REACTOME	19
PYRUVATE_METABOLISM	REACTOME	19
SYNTHESIS_AND_INTERCONVERSION_OF_NUCLEOTIDE_DI_AND_TRIPHOSPHATES	REACTOME	19
CGMP_EFFECTS	REACTOME	19
PROSTACYCLIN_SIGNALING_THROUGH_PROSTACYCLIN_RECEPTOR	REACTOME	19
SYNTHESIS_SECRETION_AND_INACTIVATION_OF_GLP1	REACTOME	19
LAGGING_STRAND_SYNTHESIS	REACTOME	19
RNA_POL_III_TRANSCRIPTION_TERMINATION	REACTOME	19
G1_S_SPECIFIC_TRANSCRIPTION	REACTOME	19
SHC1_EVENTS_IN_ERBB4_SIGNALING	REACTOME	20
HS_GAG_DEGRADATION	REACTOME	20
DOWNREGULATION_OF_SMAD2_3_SMAD4_TRANSCRIPTIONAL_ACTIVITY	REACTOME	20
ENOS_ACTIVATION_AND_REGULATION	REACTOME	20
REGULATION_OF_GENE_EXPRESSION_IN_BETA_CELLS	REACTOME	20
G_BETA_GAMMA_SIGNALING_THROUGH_PLG_BETA	REACTOME	20
NEPHRIN_INTERACTIONS	REACTOME	20
NEF_MEDIATES_DOWN_MODULATION_OF_CELL_SURFACE_RECEPTORS_BY_RECRUITING_THEM_TO_CLATHRIN_ADAPTERS	REACTOME	21
CHONDROITIN_SULFATE_BIOSYNTHESIS	REACTOME	21
ACYL_CHAIN_REMODELLING_OF_PE	REACTOME	21
ERK_MAPK_TARGETS	REACTOME	21
MITOCHONDRIAL_TRNA_AMINOACYLATION	REACTOME	21

INSULIN_SYNTHESIS_AND_PROCESSING	REACTOME	21
PEROXISOMAL_LIPID_METABOLISM	REACTOME	21
CTLA4_INHIBITORY_SIGNALING	REACTOME	21
ADP_SIGNALING_THROUGH_P2RY12	REACTOME	21
TRAF6_MEDIATED_NFKB_ACTIVATION	REACTOME	21
LIGAND_GATED_ION_CHANNEL_TRANSPORT	REACTOME	21
EARLY_PHASE_OF_HIV_LIFE_CYCLE	REACTOME	21
ANTIGEN_PRESENTATION_FOLDING_ASSEMBLY_AND_PEPTIDE_LOADING_OF_CLASS_I_MHC	REACTOME	21
RNA_POL_I_TRANSCRIPTION_TERMINATION	REACTOME	22
GRB2_EVENTS_IN_ERBB2_SIGNALING	REACTOME	22
SIGNALING_BY_HIPPO	REACTOME	22
ACYL_CHAIN_REMODELLING_OF_PC	REACTOME	22
FORMATION_OF_TUBULIN_FOLDING_INTERMEDIATES_BY_CCT_TRIC	REACTOME	22
CD28_DEPENDENT_PI3K_AKT_SIGNALING	REACTOME	22
DEADENYLATION_OF_MRNA	REACTOME	22
METAL_ION_SLC_TRANSPORTERS	REACTOME	22
INCRETIN_SYNTHESIS_SECRETION_AND_INACTIVATION	REACTOME	22
CONVERSION_FROM_APC_C_CD20_TO_APC_C_CDH1_IN_LATE_ANAPHASE	REACTOME	22
FGFR_LIGAND_BINDING_AND_ACTIVATION	REACTOME	22
RNA_POL_III_TRANSCRIPTION_INITIATION_FROM_TYPE_2_PROMOTER	REACTOME	23
INSULIN_RECEPTOR_RECYCLING	REACTOME	23
CIRCADIAN_REPRESSION_OF_EXPRESSION_BY_REV_ERBA	REACTOME	23
SIGNALING_BY_BMP	REACTOME	23
DOWNREGULATION_OF_TGF_BETA_RECEPTOR_SIGNALING	REACTOME	23
MICRORNA_MIRNA_BIOGENESIS	REACTOME	23
PROCESSING_OF_CAPPED_INTRONLESS_PRE_MRNA	REACTOME	23
LYSOSOME_VESICLE_BIOGENESIS	REACTOME	23
THROMBOXANE_SIGNALING_THROUGH_TP_RECEPTOR	REACTOME	23
TAK1_ACTIVATES_NFKB_BY_PHOSPHORYLATION_AND_ACTIVATION_OF_IKKS_COMPLEX	REACTOME	23
INTERACTION_BETWEEN_L1_AND_ANKYRINS	REACTOME	23
FORMATION_OF_INCISION_COMPLEX_IN_GG_NER	REACTOME	23
ABORTIVE_ELONGATION_OF_HIV1_TRANSCRIPT_IN_THE_ABSENCE_OF_TAT	REACTOME	23
PHOSPHORYLATION_OF_THE_APC_C	REACTOME	23
GLUTATHIONE_CONJUGATION	REACTOME	23
INHIBITION_OF_THE_PROTEOLYTIC_ACTIVITY_OF_APC_C_REQUIRED_FOR_THE_ONSET_OF_ANAPHASE_BY_MITOTIC_SPINDLE_CHECKPOINT_COMPONENTS	REACTOME	24
GROWTH_HORMONE_RECEPTOR_SIGNALING	REACTOME	24
SULFUR_AMINO_ACID_METABOLISM	REACTOME	24
TERMINATION_OF_O_GLYCAN_BIOSYNTHESIS	REACTOME	24
RORA_ACTIVATES_CIRCADIAN_EXPRESSION	REACTOME	24
YAP1_AND_WWTR1_TAZ_STIMULATED_GENE_EXPRESSION	REACTOME	24
NUCLEAR_EVENTS_KINASE_AND_TRANSCRIPTION_FACTOR_ACTIVATION	REACTOME	24
CYTOSOLIC_TRNA_AMINOACYLATION	REACTOME	24
DOUBLE_STRAND_BREAK_REPAIR	REACTOME	24
KINESINS	REACTOME	24
REGULATION_OF_IFNA_SIGNALING	REACTOME	24
CHOLESTEROL_BIOSYNTHESIS	REACTOME	24
PYRIMIDINE_METABOLISM	REACTOME	24
G0_AND_EARLY_G1	REACTOME	25
REGULATION_OF_HYPOXIA_INDUCIBLE_FACTOR_HIF_BY_OXYGEN	REACTOME	25
A_TETRASACCHARIDE_LINKER_SEQUENCE_IS_REQUIRED_FOR_GAG_SYNTHESIS	REACTOME	25
EGFR_DOWNREGULATION	REACTOME	25
DARPP_32_EVENTS	REACTOME	25
INHIBITION_OF_INSULIN_SECRETION_BY_ADRENALINE_NORADRENALINE	REACTOME	25
FANCONI_ANEMIA_PATHWAY	REACTOME	25
ADP_SIGNALING_THROUGH_P2RY1	REACTOME	25
G_BETA_GAMMA_SIGNALING_THROUGH_PI3KGAMMA	REACTOME	25
SMOOTH_MUSCLE_CONTRACTION	REACTOME	25
EFFECTS_OF_PIP2_HYDROLYSIS	REACTOME	25
NITRIC_OXIDE_STIMULATES_GUANYLATE_CYCLASE	REACTOME	25
INHIBITION_OF_VOLTAGE_GATED_CA2_CHANNELS_VIA_GBETA_GAMMA_SUBUNITS	REACTOME	25
TRANSFERRIN_ENDOCYTOSIS_AND_RECYCLING	REACTOME	25
RNA_POL_I_TRANSCRIPTION_INITIATION	REACTOME	25
TGF_BETA_RECEPTOR_SIGNALING_ACTIVATES_SMADS	REACTOME	26
KERATAN_SULFATE_BIOSYNTHESIS	REACTOME	26
REGULATORY_RNA_PATHWAYS	REACTOME	26
CITRIC_ACID_CYCLE_TCA_CYCLE	REACTOME	26
ACTIVATION_OF_GENES_BY_ATF4	REACTOME	26
POST_TRANSLATIONAL_MODIFICATION_SYNTHESIS_OF_GPI_ANCHORED_PROTEINS	REACTOME	26
RNA_POL_III_TRANSCRIPTION_INITIATION_FROM_TYPE_3_PROMOTER	REACTOME	26
APC_C_CD20_MEDIATED_DEGRADATION_OF_CYCLIN_B	REACTOME	26
PTM_GAMMA_CARBOXYLATION_HYPUSINE_FORMATION_AND_ARYLSULFATASE_ACTIVATION	REACTOME	27
BILE_ACID_AND_BILE_SALT_METABOLISM	REACTOME	27
ACTIVATED_NOTCH1_TRANSMITS_SIGNAL_TO_THE_NUCLEUS	REACTOME	27
SIGNALING_TO_RAS	REACTOME	27
SMAD2_SMAD3_SMAD4_HETEROTRIMER_REGULATES_TRANSCRIPTION	REACTOME	27
SYNTHESIS_OF_PA	REACTOME	27
GENERATION_OF_SECOND_MESSENGER_MOLECULES	REACTOME	27
G_PROTEIN_ACTIVATION	REACTOME	27
INTEGRIN_ALPHAIIIB_BETA3_SIGNALING	REACTOME	27
ASSOCIATION_OF_TRIC_CCT_WITH_TARGET_PROTEINS_DURING_BIOSYNTHESIS	REACTOME	27
STRIATED_MUSCLE_CONTRACTION	REACTOME	27
ADHERENS_JUNCTIONS_INTERACTIONS	REACTOME	27
SEMA4D_INDUCED_CELL_MIGRATION_AND_GROWTH_CONE_COLLAPSE	REACTOME	27
CREB_PHOSPHORYLATION_THROUGH_THE_ACTIVATION_OF_RAS	REACTOME	27
AMINE_COMPOUND_SLC_TRANSPORTERS	REACTOME	27
RECYCLING_PATHWAY_OF_L1	REACTOME	27
IL_RECEPTOR_SHC_SIGNALING	REACTOME	27
ENDOSOMAL_SORTING_COMPLEX_REQUIRED_FOR_TRANSPORT_ESCRT	REACTOME	27
NEP_NS2_INTERACTS_WITH_THE_CELLULAR_EXPORT_MACHINERY	REACTOME	27
TRANSPORT_OF_RIBONUCLEOPROTEINS_INTO_THE_HOST_NUCLEUS	REACTOME	27
REGULATION_OF_GLUKOKINASE_BY_GLUKOKINASE_REGULATORY_PROTEIN	REACTOME	27
EXTENSION_OF_TELOMERES	REACTOME	27
GAP_JUNCTION_TRAFFICKING	REACTOME	27
PREFOLDIN_MEDIATED_TRANSFER_OF_SUBSTRATE_TO_CCT_TRIC	REACTOME	28
TRAFFICKING_OF_AMPA_RECEPTORS	REACTOME	28
G_PROTEIN_BETA_GAMMA_SIGNALING	REACTOME	28
MYOGENESIS	REACTOME	28
SHC_MEDIATED_CASCADE	REACTOME	28
LIPOPROTEIN_METABOLISM	REACTOME	28
THE_ROLE_OF_NEF_IN_HIV1_REPLICATION_AND_DISEASE_PATHOGENESIS	REACTOME	28
APC_CD20_MEDIATED_DEGRADATION_OF_NEK2A	REACTOME	28

PRE_NOTCH_TRANSCRIPTION_AND_TRANSLATION	REACTOME	29
DEGRADATION_OF_THE_EXTRACELLULAR_MATRIX	REACTOME	29
ANTIGEN_ACTIVATES_B_CELL_RECEPTOR_LEADING_TO_GENERATION_OF_SECOND_MESSENGERS	REACTOME	29
GLYCOLYSIS	REACTOME	29
STEROID_HORMONES	REACTOME	29
PERK_REGULATED_GENE_EXPRESSION	REACTOME	29
TIGHT_JUNCTION_INTERACTIONS	REACTOME	29
BIOSYNTHESIS_OF_THE_N_GLYCAN_PRECURSOR_DOLICHOL_LIPID_LINKED_OLIGOSACCHARIDE_LLO_AND_TRANSFER_TO_A_NASCENT_PROTEIN	REACTOME	29
PKB_MEDIATED_EVENTS	REACTOME	29
PIP3_ACTIVATES_AKT_SIGNALING	REACTOME	29
SIGNALING_BY_FGFR1_MUTANTS	REACTOME	30
KERATAN_SULFATE_KERATIN_METABOLISM	REACTOME	30
BASIGIN_INTERACTIONS	REACTOME	30
REGULATION_OF_BETA_CELL_DEVELOPMENT	REACTOME	30
MRNA_CAPPING	REACTOME	30
CA_DEPENDENT_EVENTS	REACTOME	30
SIGNALING_BY_ROBO_RECEPTOR	REACTOME	30
FORMATION_OF_TRANSCRIPTION_COUPLED_NER_TC_NER_REPAIR_COMPLEX	REACTOME	30
MAPK_TARGETS_NUCLEAR_EVENTS_MEDIATED_BY_MAP_KINASES	REACTOME	30
TRAF6_MEDIATED_IRF7_ACTIVATION	REACTOME	30
NOD1_2_SIGNALING_PATHWAY	REACTOME	30
DNA_STRAND_ELONGATION	REACTOME	30
INTRINSIC_PATHWAY_FOR_APOPTOSIS	REACTOME	30
ACTIVATION_OF_THE_PRE_REPLICATIVE_COMPLEX	REACTOME	31
SPHINGOLIPID_DE_NOVO_BIOSYNTHESIS	REACTOME	31
SYNTHESIS_OF_PIP3_AT_THE_PLASMA_MEMBRANE	REACTOME	31
HS_GAG_BIOSYNTHESIS	REACTOME	31
AMINO_ACID_TRANSPORT_ACROSS_THE_PLASMA_MEMBRANE	REACTOME	31
GPVI_MEDIATED_ACTIVATION_CASCADE	REACTOME	31
SIGNAL_AMPLIFICATION	REACTOME	31
ACTIVATION_OF_KAINATE_RECEPTORS_UPON_Glutamate_BINDING	REACTOME	31
TRANSPORT_OF_VITAMINS_NUCLEOSIDES_AND_RELATED_MOLECULES	REACTOME	31
NEGATIVE_REGULATORS_OF_RIG_I_MDA5_SIGNALING	REACTOME	31
INWARDLY_RECTIFYING_K_CHANNELS	REACTOME	31
DAG_AND_IP3_SIGNALING	REACTOME	32
ELONGATION_ARREST_AND_RECOVERY	REACTOME	32
CD28_CO_STIMULATION	REACTOME	32
SEMA4D_IN_SEMAPHORIN_SIGNALING	REACTOME	32
FORMATION_OF_FIBRIN_CLOT_CLOTTING_CASCADE	REACTOME	32
THROMBIN_SIGNALING_THROUGH_PROTEINASE_ACTIVATED_RECEPTORS_PARS	REACTOME	32
COMPLEMENT_CASCADE	REACTOME	32
LATENT_INFECTION_OF_HOMO_SAPIENS_WITH_MYCOBACTERIUM_TUBERCULOSIS	REACTOME	33
RNA_POL_III_TRANSCRIPTION	REACTOME	33
TRANSPORT_OF_MATURE_MRNA_DERIVED_FROM_AN_INTRONLESS_TRANSCRIPT	REACTOME	33
GLUCAGON_TYPE_LIGAND_RECEPTORS	REACTOME	33
POST_NMDA_RECEPTOR_ACTIVATION_EVENTS	REACTOME	33
TRANSPORT_TO_THE_GOLGI_AND_SUBSEQUENT_MODIFICATION	REACTOME	33
PURINE_METABOLISM	REACTOME	33
INTERACTIONS_OF_VPR_WITH_HOST_CELLULAR_PROTEINS	REACTOME	33
NEUROTRANSMITTER_RELEASE_CYCLE	REACTOME	34
GLUCONEOGENESIS	REACTOME	34
ABC_FAMILY_PROTEINS_MEDIATED_TRANSPORT	REACTOME	34
GLUCAGON_SIGNALING_IN_METABOLIC_REGULATION	REACTOME	34
SIGNAL_TRANSDUCTION_BY_L1	REACTOME	34
ION_TRANSPORT_BY_P_TYPE_ATPASES	REACTOME	34
FORMATION_OF_THE_HIV1_EARLY_ELONGATION_COMPLEX	REACTOME	34
METABOLISM_OF_STEROID_HORMONES_AND_VITAMINS_A_AND_D	REACTOME	35
MRNA_3_END_PROCESSING	REACTOME	35
GLOBAL_GENOMIC_NER_GG_NER	REACTOME	35
E2F_MEDIATED_REGULATION_OF_DNA_REPLICATION	REACTOME	35
BMAL1_CLOCK_NPAS2_ACTIVATES_CIRCADIAN_EXPRESSION	REACTOME	36
SIGNALING_TO_ERKS	REACTOME	36
FRS2_MEDIATED_CASCADE	REACTOME	36
IRON_UPTAKE_AND_TRANSPORT	REACTOME	36
PLATELET_AGGREGATION_PLUG_FORMATION	REACTOME	36
NEGATIVE_REGULATION_OF_FGFR_SIGNALING	REACTOME	37
DOWNSTREAM_TCR_SIGNALING	REACTOME	37
ACTIVATION_OF_NMDA_RECEPTOR_UPON_Glutamate_BINDING_AND_POSTSYNAPTIC_EVENTS	REACTOME	37
PI3K_EVENTS_IN_ERBB4_SIGNALING	REACTOME	38
NUCLEAR_SIGNALING_BY_ERBB4	REACTOME	38
GLYCOSPHINGOLIPID_METABOLISM	REACTOME	38
TRIGLYCERIDE_BIOSYNTHESIS	REACTOME	38
TRANSCRIPTIONAL_ACTIVITY_OF_SMAD2_SMAD3_SMAD4_HETEROTRIMER	REACTOME	38
PI3K_AKT_ACTIVATION	REACTOME	38
GAB1_SIGNALOSOME	REACTOME	38
G1_PHASE	REACTOME	38
AMINE_LIGAND_BINDING_RECEPTORS	REACTOME	38
GLUCOSE_TRANSPORT	REACTOME	38
GABA_B_RECEPTOR_ACTIVATION	REACTOME	38
ACTIVATION_OF_ATR_IN_RESPONSE_TO_REPLICATION_STRESS	REACTOME	38
NCAM1_INTERACTIONS	REACTOME	39
IL1_SIGNALING	REACTOME	39
APOPTOTIC_CLEAVAGE_OF_CELLULAR_PROTEINS	REACTOME	40
RNA_POL_II_TRANSCRIPTION_PRE_INITIATION_AND_PROMOTER_OPENING	REACTOME	41
NETRIN1_SIGNALING	REACTOME	41
IL_2_SIGNALING	REACTOME	41
BETA_DEFENSINS	REACTOME	42
TRNA_AMINOACYLATION	REACTOME	42
NRAGE_SIGNALS_DEATH_THROUGH_JNK	REACTOME	43
PLC_BETA_MEDIATED_EVENTS	REACTOME	43
REGULATION_OF_INSULIN_SECRETION_BY_GLUcAGON LIKE PEPTIDE1	REACTOME	43
IL_3_5_AND_GM-CSF_SIGNALING	REACTOME	43
VOLTAGE_GATED_POTASSIUM_CHANNELS	REACTOME	43
PI3K_EVENTS_IN_ERBB2_SIGNALING	REACTOME	44
PRE_NOTCH_EXPRESSION_AND_PROCESSING	REACTOME	44
SIGNALING_BY_FGFR_MUTANTS	REACTOME	44
G_ALPHA_Z_SIGNALING_EVENTS	REACTOME	44
REGULATION_OF_WATER_BALANCE_BY_RENAL_AQUAPORINS	REACTOME	44
CLEAVAGE_OF_GROWING_TRANSCRIPT_IN_THE_TERMINATION_REGION	REACTOME	44
TRANSCRIPTION_COUPLED_NER_TC_NER	REACTOME	45
MRNA_SPLICING_MINOR_PATHWAY	REACTOME	45

FORMATION_OF_RNA_POL_II_ELONGATION_COMPLEX_	REACTOME	45
G2_M_CHECKPOINTS	REACTOME	45
NOTCH1_INTRACELLULAR_DOMAIN_REGULATES_TRANSCRIPTION	REACTOME	46
ACTIVATION_OF_CHAPERONE_GENES_BY_XBP1S	REACTOME	46
LIPID_DIGESTION_MOBILIZATION_AND_TRANSPORT	REACTOME	46
NUCLEOTIDE_BINDING_DOMAIN_LEUCINE_RICH_REPEAT_CONTAINING_RECEPTOR_NLR_SIGNALING_PATHWAYS	REACTOME	46
PYRUVATE_METABOLISM_AND_CITRIC_ACID_TCA_CYCLE	REACTOME	48
CROSS_PRESENTATION_OF_SOLUBLE_EXOGENOUS_ANTIGENS_ENDOSOMES	REACTOME	48
PI_METABOLISM	REACTOME	48
CDK_MEDIATED_PHOSPHORYLATION_AND_REMOVAL_OF_CDC6	REACTOME	48
MUSCLE_CONTRACTION	REACTOME	48
DEADENYLATION_DEPENDENT_MRNA_DECAY	REACTOME	48
PACKAGING_OF_TELOMERE_ENDS	REACTOME	48
METABOLISM_OF_NON_CODING_RNA	REACTOME	49
CHONDROITIN_SULFATE_DERMATAN_SULFATE_METABOLISM	REACTOME	49
REGULATION_OF_ORNITHINE_DECARBOXYLASE_ODC	REACTOME	49
NUCLEAR_RECEPTOR_TRANSCRIPTION_PATHWAY	REACTOME	49
AMINO_ACID_AND_OLIGOPEPTIDE_SLC_TRANSPORTERS	REACTOME	49
MAP_KINASE_ACTIVATION_IN_TLR_CASCADE	REACTOME	50
METABOLISM_OF_VITAMINS_AND_COFACTORS	REACTOME	51
DEFENSINS	REACTOME	51
P53_INDEPENDENT_G1_S_DNA_DAMAGE_CHECKPOINT	REACTOME	51
CYTOCHROME_P450_ARRANGED_BY_SUBSTRATE_TYPE	REACTOME	51
NUCLEOTIDE_EXCISION_REPAIR	REACTOME	51
AUTODEGRADATION_OF_THE_E3_UBIQUITIN_LIGASE_COP1	REACTOME	51
AQUAPORIN_MEDIATED_TRANSPORT	REACTOME	51
SCF_BETA_TRCP_MEDIATED_DEGRADATION_OF_EMI1	REACTOME	51
HEPARAN_SULFATE_HEPARIN_HS_GAG_METABOLISM	REACTOME	52
GABA_RECEPTOR_ACTIVATION	REACTOME	52
VIF_MEDIATED_DEGRADATION_OF_APOBEC3G	REACTOME	52
PROTEIN_FOLDING	REACTOME	53
GOLGI_ASSOCIATED_VESICLE_BIOGENESIS	REACTOME	53
CIRCADIAN_CLOCK	REACTOME	53
DESTABILIZATION_OF_MRNA_BY_AUF1_HNRNP_D0	REACTOME	53
TCR_SIGNALING	REACTOME	54
TRANSPORT_OF_MATURE_TRANSCRIPT_TO_CYTOPLASM	REACTOME	54
PHOSPHOLIPASE_C_MEDIATED_CASCADE	REACTOME	54
APOPTOTIC_EXECUTION_PHASE	REACTOME	54
ION_CHANNEL_TRANSPORT	REACTOME	55
CELL_CELL_JUNCTION_ORGANIZATION	REACTOME	56
CDT1_ASSOCIATION_WITH_THE_CDC6_ORC_ORIGIN_COMPLEX	REACTOME	56
PI_3K_CASCADE	REACTOME	56
SCFSKP2_MEDIATED_DEGRADATION_OF_P27_P21	REACTOME	56
CHEMOKINE_RECEPTORS_BIND_CHEMOKINES	REACTOME	57
P53_DEPENDENT_G1_DNA_DAMAGE_RESPONSE	REACTOME	57
MITOCHONDRIAL_PROTEIN_IMPORT	REACTOME	58
COLLAGEN_FORMATION	REACTOME	58
REGULATION_OF_APOPTOSIS	REACTOME	58
O_LINKED_GLYCOSYLATION_OF_MUCINS	REACTOME	59
LOSS_OF_NLP_FROM_MITOTIC_CENTROSOMES	REACTOME	59
TRANS_GOLGI_NETWORK_VESICLE_BUDDING	REACTOME	60
CELL_DEATH_SIGNALLING_VIA_NRAE_NRF1_AND_NADE	REACTOME	60
ER_PHAGOSOME_PATHWAY	REACTOME	61
RNA_POL_II_PRE_TRANSCRIPTION_EVENTS	REACTOME	61
RNA_POL_I_PROMOTER_OPENING	REACTOME	62
COSTIMULATION_BY_THE_CD28_FAMILY	REACTOME	63
INTERFERON_GAMMA_SIGNALING	REACTOME	63
SIGNALING_BY_TGF_BETA_RECEPTOR_COMPLEX	REACTOME	63
ACTIVATION_OF_NF_KAPPAB_IN_B_CELLS	REACTOME	64
NCAM_SIGNALING_FOR_NEURITE_OUT_GROWTH	REACTOME	64
DEPOSITION_OF_NEW_CENPA_CONTAINING_NUCLEOSOMES_AT_THE_CENTROMERE	REACTOME	64
INTERFERON_ALPHA_BETA_SIGNALING	REACTOME	64
AUTODEGRADATION_OF_CDH1_BY_CDH1_APC_C	REACTOME	64
SIGNALING_BY_WNT	REACTOME	65
CYCLIN_E_ASSOCIATED_EVENTS_DURING_G1_S_TRANSITION_	REACTOME	65
ASSEMBLY_OF_THE_PRE_REPLICATIVE_COMPLEX	REACTOME	65
ANTIVIRAL_MECHANISM_BY_IFN1_STIMULATED_GENES	REACTOME	66
RECRUITMENT_OF_MITOTIC_CENTROSOME_PROTEINS_AND_COMPLEXES	REACTOME	66
ORC1_REMOVAL_FROM_CHROMATIN	REACTOME	67
SEMAPHORIN_INTERACTIONS	REACTOME	68
SPHINGOLIPID_METABOLISM	REACTOME	69
GLUCOSE_METABOLISM	REACTOME	69
IMMUNOREGULATORY_INTERACTIONS_BETWEEN_A_LYMPHOID_AND_A_NON_LYMPHOID_CELL	REACTOME	70
SIGNALING_BY_NOTCH1	REACTOME	70
PHASE1_FUNCTIONALIZATION_OF_COMPOUNDS	REACTOME	70
PHASE_II_CONJUGATION	REACTOME	70
PI3K_CASCADE	REACTOME	71
METABOLISM_OF_NUCLEOTIDES	REACTOME	72
NFKB_AND_MAP_KINASES_ACTIVATION_MEDIATED_BY_TLR4_SIGNALING_REPERTOIRE	REACTOME	72
TRANSCRIPTIONAL_REGULATION_OF_WHITE_ADIPOCYTE_DIFFERENTIATION	REACTOME	72
APC_C_CDH1_MEDIATED_DEGRADATION_OF_CDC20_AND_OTHER_APC_C_CDH1_TARGETED_PROTEINS_IN_LATE_MITOSIS_EARLY_G1	REACTOME	72
RIG_I_MDA5_MEDIATED_INDUCION_OF_IFN_ALPHA_BETA_PATHWAYS	REACTOME	73
APC_C_CDC20_MEDIATED_DEGRADATION_OF_MITOTIC_PROTEINS	REACTOME	73
MEIOTIC_SYNAPSIS	REACTOME	73
FORMATION_OF_THE_TERNARY_COMPLEX_AND_SUBSEQUENTLY_THE_43S_COMPLEX	REACTOME	74
TRIF_MEDIATED_TLR3_SIGNALING	REACTOME	74
G_ALPHA1213_SIGNALING_EVENTS	REACTOME	74
TELOMERE_MAINTENANCE	REACTOME	75
ANTIGEN_PROCESSING_CROSS_PRESENTATION	REACTOME	76
TRAF6_MEDIATED_INDUCION_OF_NFKB_AND_MAP_KINASES_UPON_TLR7_8_OR_9_ACTIVATION	REACTOME	77
SIGNALING_BY_SCF_KIT	REACTOME	78
OPIOID_SIGNALLING	REACTOME	78
CELL_JUNCTION_ORGANIZATION	REACTOME	78
PLATELET_HOMEOSTASIS	REACTOME	78
INTEGRIN_CELL_SURFACE_INTERACTIONS	REACTOME	79
RESPIRATORY_ELECTRON_TRANSPORT	REACTOME	79
UNFOLDED_PROTEIN_RESPONSE	REACTOME	80
P75_NTR_RECEPTOR_MEDIATED_SIGNALLING	REACTOME	81
M_G1_TRANSITION	REACTOME	81
MITOTIC_G2_G2_M_PHASES	REACTOME	81
ASPARAGINE_N_LINKED_GLYCOSYLATION	REACTOME	81

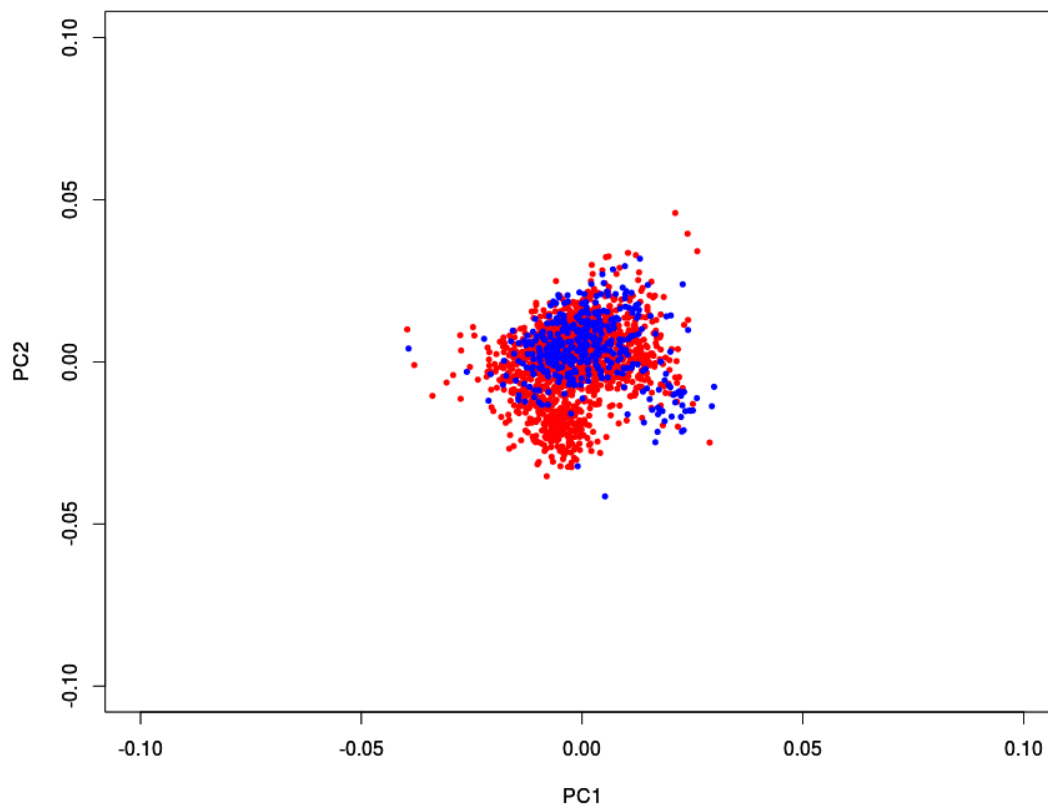
GLYCEROPHOSPHOLIPID_BIOSYNTHESIS	REACTOME	82
MYD88_MAL_CASCADE_INITIATED_ON_PLASMA_MEMBRANE	REACTOME	83
AMYLOIDS	REACTOME	83
ACTIVATION_OF_THE_MRNA_UPON_BINDING_OF_THE_CAP_BINDING_COMPLEX_AND_EIFS_AND_SUBSEQUENT_BINDING_TO_43S	REACTOME	84
REGULATION_OF_MRNA_STABILITY_BY_PROTEINS_THAT_BIND_AU_RICH_ELEMENTS	REACTOME	84
REGULATION_OF_MITOTIC_CELL_CYCLE	REACTOME	85
L1CAM_INTERACTIONS	REACTOME	86
MEIOTIC_RECOMBINATION	REACTOME	86
EXTRACELLULAR_MATRIX_ORGANIZATION	REACTOME	87
INSULIN_RECEPTOR_SIGNALLING_CASCADE	REACTOME	87
MITOTIC_PROMETAPHASE	REACTOME	87
CLASS_B_2_SECRETIN_FAMILY_RECEPTORS	REACTOME	88
RESPONSE_TO_ELEVATED_PLATELET_CYTOSOLIC_CA2	REACTOME	89
RNA_POL_I_TRANSCRIPTION	REACTOME	89
TRANSPORT_OF_GLUCOSE_AND_OTHER_SUGARS_BILE_SALTS_AND_ORGANIC_ACIDS_METAL_IONS_AND_AMINE_COMPOUNDS	REACTOME	89
SIGNALING_BY_ERBB4	REACTOME	90
CELL_SURFACE_INTERACTIONS_AT_THE_VASCULAR_WALL	REACTOME	91
MHC_CLASS_II_ANTIGEN_PRESENTATION	REACTOME	91
SYNTHESIS_OF_DNA	REACTOME	92
REGULATION_OF_INSULIN_SECRETION	REACTOME	93
ACTIVATED_TLR4_SIGNALLING	REACTOME	93
TRANSPORT_OF_INORGANIC_CATIONS_ANIONS_AND_AMINO_ACIDS_OLIGOPEPTIDES	REACTOME	94
DOWNSTREAM_SIGNAL_TRANSDUCTION	REACTOME	95
DOWNSTREAM_SIGNALING_EVENTS_OF_B_CELL_RECEPTOR_BCR	REACTOME	97
RESPIRATORY_ELECTRON_TRANSPORT_ATP_SYNTHESIS_BY_CHEMIOSMOTIC_COUPLING_AND_HEAT_PRODUCTION_BY_UNCOUPLING_PROTEINS	REACTOME	98
POTASSIUM_CHANNELS	REACTOME	98
DOWNSTREAM_SIGNALING_OF_ACTIVATED_FGFR	REACTOME	100
SIGNALING_BY_ERBB2	REACTOME	101
SIGNALING_BY_NOTCH	REACTOME	103
PPARA_ACTIVATES_GENE_EXPRESSION	REACTOME	104
LATE_PHASE_OF_HIV_LIFE_CYCLE	REACTOME	104
RNA_POL_II_TRANSCRIPTION	REACTOME	105
SIGNALING_BY_ILS	REACTOME	107
SIGNALING_BY_INSULIN_RECEPTOR	REACTOME	108
SIGNALING_BY_EGFR_IN_CANCER	REACTOME	109
S_PHASE	REACTOME	109
GLYCOSAMINOGLYCAN_METABOLISM	REACTOME	111
MRNA_SPLICING	REACTOME	111
G1_S_TRANSITION	REACTOME	112
DNA_REPAIR	REACTOME	112
SIGNALING_BY_FGFR	REACTOME	112
SIGNALING_BY_RHO_GTPASES	REACTOME	113
MEIOSIS	REACTOME	116
TOLL_RECEPTOR_CASCADES	REACTOME	118
CELL_CELL_COMMUNICATION	REACTOME	120
INTEGRATION_OF_ENERGY_METABOLISM	REACTOME	120
G_ALPHA_S_SIGNALLING_EVENTS	REACTOME	121
SIGNALING_BY_PDGF	REACTOME	122
RNA_POL_I_RNA_POL_III_AND_MITOCHONDRIAL_TRANSCRIPTION	REACTOME	122
CHROMOSOME_MAINTENANCE	REACTOME	122
CELL_CYCLE_CHECKPOINTS	REACTOME	124
HIV_LIFE_CYCLE	REACTOME	125
SIGNALING_BY_THE_B_CELL_RECEPTOR_BCR	REACTOME	126
SIGNALING_BY_FGFR_IN_DISEASE	REACTOME	127
MEMBRANE_TRAFFICKING	REACTOME	129
FACTORS_INVOLVED_IN_MEGAKARYOCYTE_DEVELOPMENT_AND_PLATELET_PRODUCTION	REACTOME	132
HOST_INTERACTIONS_OF_HIV_FACTORS	REACTOME	132
DIABETES_PATHWAYS	REACTOME	133
NGF_SIGNALLING_VIA_TRKA_FROM_THE_PLASMA_MEMBRANE	REACTOME	137
NEUROTRANSMITTER_RECEPTOR_BINDING_AND_DOWNSTREAM_TRANSMISSION_IN_THE_POSTSYNAPTIC_CELL	REACTOME	137
MITOTIC_G1_S_PHASES	REACTOME	137
BIOLOGICAL_OXIDATIONS	REACTOME	139
PROCESSING_OF_CAPPED_INTRON_CONTAINING_PRE_MRNA	REACTOME	140
TCA_CYCLE_AND_RESPIRATORY_ELECTRON_TRANSPORT	REACTOME	141
APOPTOSIS	REACTOME	148
PEPTIDE_CHAIN_ELONGATION	REACTOME	153
INTERFERON_SIGNALING	REACTOME	159
MRNA_PROCESSING	REACTOME	161
FATTY_ACID_TRIACYLGLYCEROL_AND_KETONE_BODY_METABOLISM	REACTOME	168
INFLUENZA_VIRAL_RNA_TRANSCRIPTION_AND_REPLICATION	REACTOME	169
MITOTIC_M_M_G1_PHASES	REACTOME	172
3_UTR_MEDIATED_TRANSLATIONAL_REGULATION	REACTOME	176
NONSENSE_MEDIATED_DECAY_ENHANCED_BY_THE_EXON_JUNCTION_COMPLEX	REACTOME	176
SRP_DEPENDENT_COTRANSLATIONAL_PROTEIN_TARGETING_TO_MEMBRANE	REACTOME	179
G_ALPHA_Q_SIGNALLING_EVENTS	REACTOME	184
TRANSMISSION_ACROSS_CHEMICAL_SYNAPSES	REACTOME	186
PEPTIDE_LIGAND_BINDING_RECEPTORS	REACTOME	188
POST_TRANSLATIONAL_PROTEIN_MODIFICATION	REACTOME	188
DNA_REPLICATION	REACTOME	192
G_ALPHA_I_SIGNALLING_EVENTS	REACTOME	195
PHOSPHOLIPID_METABOLISM	REACTOME	198
METABOLISM_OF_AMINO_ACIDS_AND_DERIVATIVES	REACTOME	200
INFLUENZA_LIFE_CYCLE	REACTOME	203
GASTRIN_CREB_SIGNALLING_PATHWAY_VIA_PKC_AND_MAPK	REACTOME	205
HIV_INFECTION	REACTOME	207
PLATELET_ACTIVATION_SIGNALING_AND_AGGREGATION	REACTOME	208
TRANSCRIPTION	REACTOME	210
ANTIGEN_PROCESSING_UBIQUITINATION_PROTEASOME_DEGRADATION	REACTOME	212
SIGNALING_BY_NGF	REACTOME	217
TRANSLATION	REACTOME	222
SLC_MEDIATED_TRANSMEMBRANE_TRANSPORT	REACTOME	241
METABOLISM_OF_CARBHYDRATES	REACTOME	247
AXON_GUIDANCE	REACTOME	251
CLASS_I_MHC_MEDIATED_ANTIGEN_PROCESSING_PRESENTATION	REACTOME	251
CYTOKINE_SIGNALING_IN_IMMUNE_SYSTEM	REACTOME	270
NEURONAL_SYSTEM	REACTOME	279
INNATE_IMMUNE_SYSTEM	REACTOME	279
METABOLISM_OF_MRNA	REACTOME	284

**Abbreviations:** Genes, number of genes contained in each particular pathway.



### 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.

## 4. References

1. Julia A, Tortosa R, Hernanz JM, Canete JD, Fonseca E, Ferrandiz C, Unamuno P, Puig L, Fernandez-Sueiro JL, Sanmarti R *et al*: Risk variants for psoriasis vulgaris in a large case-control collection and association with clinical subphenotypes. *Hum Mol Genet* 2012, 21(20):4549-4557. Epub 2012 Jul 4519.
2. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, Schaller JG, Talal N, Winchester RJ: The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982, 25(11):1271-1277.
3. Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, Maller J, Sklar P, de Bakker PI, Daly MJ *et al*: PLINK: a tool set for whole-genome association and population-based linkage analyses. *Am J Hum Genet* 2007, 81(3):559-575. Epub 2007 Jul 2025.
4. Aterido A, Julia A, Ferrandiz C, Puig L, Fonseca E, Fernandez-Lopez E, Dauden E, Sanchez-Carazo JL, Lopez-Estebarez JL, Moreno-Ramirez D *et al*: Genome-Wide Pathway Analysis Identifies Genetic Pathways Associated with Psoriasis. *J Invest Dermatol* 2016, 136(3):593-602. doi: 510.1016/j.jid.2015.1011.1026. Epub 2015 Dec 1029.
5. Price AL, Patterson NJ, Plenge RM, Weinblatt ME, Shadick NA, Reich D: Principal components analysis corrects for stratification in genome-wide association studies. *Nat Genet* 2006, 38(8):904-909. Epub 2006 Jul 2023.
6. Delaneau O, Zagury JF, Marchini J: Improved whole-chromosome phasing for disease and population genetic studies. *Nature methods* 2013, 10(1):5-6.
7. Howie B, Marchini J, Stephens M: Genotype imputation with thousands of genomes. *G3 (Bethesda, Md)* 2011, 1(6):457-470.
8. Abecasis GR, Auton A, Brooks LD, DePristo MA, Durbin RM, Handsaker RE, Kang HM, Marth GT, McVean GA: An integrated map of genetic variation from 1,092 human genomes. *Nature* 2012, 491(7422):56-65.
9. Edgar R, Domrachev M, Lash AE: Gene Expression Omnibus: NCBI gene expression and hybridization array data repository. *Nucleic Acids Res* 2002, 30(1):207-210.
10. Chang AY, Werth VP: Treatment of cutaneous lupus. *Curr Rheumatol Rep* 2011, 13(4):300-307. doi: 310.1007/s11926-11011-10180-z.
11. Khandpur S, Sharma VK, Sumanth K: Topical immunomodulators in dermatology. *J Postgrad Med* 2004, 50(2):131-139.
12. Allison DB, Cui X, Page GP, Sabripour M: Microarray data analysis: from disarray to consolidation and consensus. *Nat Rev Genet* 2006, 7(1):55-65.
13. Bolstad BM, Irizarry RA, Astrand M, Speed TP: A comparison of normalization methods for high density oligonucleotide array data based on variance and bias. *Bioinformatics* 2003, 19(2):185-193.
14. Ihaka R, Gentleman G: R: A language for data analysis and graphics. *Journal of Computational and Graphical Statistics* 1996, 5(5):299-314.