

Table SI. Full list of canonical signaling pathways in facet joint osteoarthritis.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Salvage Pathways of Pyrimidine Ribonucleotides	2.60E-01	8.51E-02	NaN	PAK1, AK5, CMPK2, GRK6, TTK, NEK2, CDK1, APOBEC3A
Type II Diabetes Mellitus Signaling	2.75E-01	8.55E-02	-2.449	SOCS3, SLC27A5, ACSBG1, PKLR, CD36, PIK3CG, ACSL6, CACNA1H, PIK3R6, PIK3CD, TLR9, CACNA2D4, PRKCB
Endothelin-1 Signaling	2.88E-01	8.60E-02	-3	PLCB2, MAPK13, TLR9, PLA2G7, PLD4, MYC, HMOX1, GNA15, ADCY5, PLB1, PIK3CG, PIK3R6, PIK3CD, NOS2, PRKCB, CASP10
Erythropoietin Signaling	2.70E-01	8.64E-02	NaN	SOCS3, PTPN6, PIK3CG, PIK3R6, PIK3CD, TLR9, PRKCB
SAPK/JNK Signaling	2.89E-01	8.74E-02	-2.333	RAC2, LCK, PIK3CG, FCER1G, PIK3R6, MAP4K1, PIK3CD, TLR9, RAC3
Neuropathic Pain Signaling in Dorsal Horn Neurons	2.97E-01	8.77E-02	-1.897	PLCB2, CAMK2A, CAMK4, PIK3CG, PIK3R6, TAC1, PIK3CD, KCNH2, TLR9, PRKCB
HGF Signaling	2.97E-01	8.77E-02	-1.897	PAK1, PIK3CG, CDKN1A, PIK3R6, PIK3CD, IL6, TLR9, CCND1, ITGA4, PRKCB
G Beta Gamma Signaling	2.97E-01	8.77E-02	-0.632	BTK, PAK1, GNA15, CAV2, PIK3CG, CACNA1H, CAV1, HBEGF, CACNA2D4, PRKCB
FXR/RXR Activation	3.05E-01	8.80E-02	NaN	APOE, SLC27A5, FOXO1, PKLR, TF, IL1RN, PLTP, VLDLR, CLU, CETP, PPARGC1A
Oncostatin M Signaling	2.52E-01	8.82E-02	NaN	TIMP3, MMP3, CH13L1
Acute Phase Response Signaling	3.30E-01	8.88E-02	-1.667	SOCS3, ITIH3, MAPK13, IL6, HMOX1, HP, RBP7, TF, C4BPA, IL1RN, PIK3CG, PIK3CD, LBP, SERPINE1, CRABP2
PDGF Signaling	3.01E-01	8.89E-02	-2.121	MYC, PIK3CG, PIK3R6, CAV1, PIK3CD, TLR9, INPP5D, PRKCB
Glucocorticoid Receptor Signaling	3.84E-01	8.93E-02	NaN	CD247, BGLAP, CD3E, POU2F2, PRL, HSPA1A/HSPA1B, HSPA6, IL6, MAPK13, CD163, FCGR1A, TSC22D3, CXCL3, CCL13, KRT13, CCL2, PIK3CG, SERPINE1, NOS2, CXCL8, SELE, IL10, KRT23, TLR9, DUSP1, IL1RN, CDKN1A, PIK3R6, NFATC2, PIK3CD
Actin Nucleation by ARP-WASP Complex	2.83E-01	8.93E-02	-0.447	RHOB, RHOD, WAS, RHOH, ITGA4
Aldosterone Signaling in Epithelial Cells	3.48E-01	8.98E-02	-2.828	CRYAB, PLCB2, HSPH1, HSPA1A/HSPA1B, HSPB8, HSPA6, PIP5K1B, TLR9, DUSP1, PIK3CG, PIK3R6, PIK3CD, PIP4K2A, HSPB6, PRKCB
PAK Signaling	3.21E-01	9.00E-02	-2.333	PAK1, MYL2, PTK2B, PIK3CG, PIK3R6, MYL4, PIK3CD, TLR9, ITGA4
RANK Signaling in Osteoclasts	3.21E-01	9.00E-02	-2.121	CAMK4, PTK2B, PIK3CG, PIK3R6, NFATC2, PIK3CD, MAPK13, TLR9, GSN
P2Y Purigenic Receptor Signaling Pathway	3.41E-01	9.02E-02	-2.309	MYC, PLCB2, ITGA2B, P2RY4, ADCY5, PIK3CG, PIK3R6, P2RY1, PIK3CD, TLR9, ITGB3, PRKCB
LPS/IL-1 Mediated Inhibition of RXR Function	3.86E-01	9.09E-02	0.333	APOE, FMO3, IL1RL1, ACSL6, CETP, SLC27A5, ALDH1L1, ACSBG1, IL1RL2, IL1RN, CAT, CHST3, HS6ST3, PLTP, LBP, CPT1C, ABCC3, SULT1B1, PPARGC1A
eNOS Signaling	3.67E-01	9.09E-02	-1.941	CAMK4, HSPA1A/HSPA1B, FLT4, HSPA6, AQP1, TLR9, CCNA2, ADCY5, PIK3CG, LPAR5, PIK3R6, CAV1, CHRNA7, PIK3CD, PRKCB
Adipogenesis pathway	3.51E-01	9.09E-02	NaN	FZD10, ARNTL, WNT10B, LEP, PLIN1, FOXO1, FZD5, BMP7, RPS6KA1, FZD1, TCF7, FGF1
Renin-Angiotensin Signaling	3.45E-01	9.09E-02	-2.111	PTPN6, PAK1, CCL2, PTK2B, ADCY5, PIK3CG, PIK3R6, PIK3CD, MAPK13, TLR9, PRKCB
Amyotrophic Lateral Sclerosis Signaling	3.39E-01	9.09E-02	2.333	NAIP, PAK1, CAPN6, PIK3CG, GRIK3, CAT, PIK3R6, PIK3CD, TLR9, CAPN3
Purine Nucleotides De Novo Biosynthesis II	2.05E-01	9.09E-02	NaN	ADSSL1

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Dolichyl-1-diphosphooligosaccharide Biosynthesis	2.05E-01	9.09E-02	NaN	DPM2
Protein Kinase A Signaling	4.52E-01	9.11E-02	-0.73	HIST1H1C, PDE6G, PLCB2, CAMK4, PTK2B, MYL2, PPP1R3C, PTPN5, PTPRC, CDKN3, CAMK2A, PTPRJ, ADCY5, PTPRZ1, MYL4, PDE6B, CDC25A, SMPDL3A, PLN, PPP1R14C, PTPN7, PTPN6, PDE4C, ADD2, PPP1R1B, HIST1H3C, PDE1C, HIST1H1B, DUSP1, FLNC, HIST1H1D, NFATC2, LEF1, EBI3, PRKCB
p70S6K Signaling	3.61E-01	9.16E-02	-3.464	BTK, IL2RG, CD19, F2RL2, PLCB2, PIK3CG, SYK, PIK3R6, CD79A, PIK3CD, TLR9, PRKCB
Sperm Motility	3.56E-01	9.17E-02	-1.897	PLCB2, TXK, CAMK4, PTK2B, PDE4C, PLB1, CACNA1H, LTK, PLA2G7, PDE1C, PRKCB
LPS-stimulated MAPK Signaling	3.37E-01	9.20E-02	-2.646	PAK1, PIK3CG, PIK3R6, PIK3CD, LBP, MAPK13, TLR9, PRKCB
14-3-3-mediated Signaling	3.72E-01	9.23E-02	-2.333	TUBB1, PLCB2, FOXO1, PIK3CG, PIK3R6, GFAP, PIK3CD, RPS6KA1, TLR9, SNCA, PRKCB, TUBB2B
Netrin Signaling	3.21E-01	9.23E-02	NaN	RAC2, UNC5A, CACNA1H, NFATC2, RAC3, CACNA2D4
Sertoli Cell-Sertoli Cell Junction Signaling	4.01E-01	9.25E-02	NaN	SPTBN2, TUBB1, CLDN11, SPTA1, MAPK13, TUBB2B, EPB41, CDH1, ACTA2, CLDN1, WAS, SPTB, ACTG2, NOS2, ACTC1, ITGA4
Autophagy	3.11E-01	9.26E-02	NaN	CTSW, CTSG, CTSE, CTSC, MAP1LC3C
Opioid Signaling Pathway	4.42E-01	9.28E-02	-0.894	RAC2, RGS18, CAMK4, CACNA1H, RGS4, RAC3, PDE1C, FOSB, MYC, BLK, LCK, ARRB2, CAMK2A, ADCY5, PIK3CG, GRK6, HCK, RGS14, RPS6KA1, CACNA2D4, FGR, PRKCB
Role of JAK2 in Hormone-like Cytokine Signaling	2.86E-01	9.38E-02	NaN	SOCS3, PTPN6, PRL
Ethanol Degradation II	2.86E-01	9.38E-02	NaN	ALDH1L1, ACSS1, ADH4
Small Cell Lung Cancer Signaling	3.62E-01	9.41E-02	-1.342	MYC, CCNE1, PIK3CG, SUV39H1, PIK3R6, PIK3CD, TLR9, CCND1
Gap Junction Signaling	4.48E-01	9.42E-02	NaN	TUBB1, GJB6, BGLAP, PLCB2, GRIK3, TLR9, TUBB2B, ACTA2, ADCY5, PIK3CG, PIK3R6, CAV1, PIK3CD, ACTG2, ACTC1, GJB2, HTR2A, PRKCB
Chondroitin Sulfate Biosynthesis	3.26E-01	9.43E-02	NaN	CHPF, CHST9, CHST3, HS6ST3, SULT1B1
Thrombin Signaling	4.61E-01	9.45E-02	-2.357	PLCB2, F2RL2, CAMK4, GATA1, MYL2, MAPK13, TLR9, GATA2, RHOH, CAMK2A, GNA15, RHOB, ADCY5, RHOD, PIK3CG, PIK3R6, MYL4, PIK3CD, PRKCB
STAT3 Pathway	3.56E-01	9.46E-02	-1.134	MYC, SOCS3, PTPN6, CDKN1A, FLT4, MAPK13, CDC25A
Cellular Effects of Sildenafil (Viagra)	4.18E-01	9.52E-02	NaN	PLCB2, CAMK4, ACTA2, MYL2, PDE4C, ADCY5, MYL4, ACTG2, MYH11, KCNH2, ACTC1, PDE1C
Role of p14/p19ARF in Tumor Suppression	3.16E-01	9.52E-02	2	PIK3CG, PIK3R6, PIK3CD, TLR9
NAD Salvage Pathway II	2.66E-01	9.52E-02	NaN	ACP5, ACP
Ephrin B Signaling	3.70E-01	9.59E-02	-1	RAC2, PAK1, GNA15, CXCR4, CXCL12, VAV1, RAC3
Role of Cytokines in Mediating Communication between Immune Cells	3.42E-01	9.62E-02	NaN	CXCL8, IL10, IL1RN, IL6, CSF3
Sphingosine-1-phosphate Signaling	4.42E-01	9.68E-02	-1.732	S1PR4, PLCB2, RHOB, PTK2B, RHOD, ADCY5, PIK3CG, PIK3R6, PIK3CD, TLR9, RHOH, CASP10
fMLP Signaling in Neutrophils	4.68E-01	9.84E-02	-2.111	NOX4, NCF1, PLCB2, CAMK4, WAS, PIK3CG, FPR2, PIK3R6, NFATC2, PIK3CD, TLR9, PRKCB
FGF Signaling	4.36E-01	9.89E-02	-0.333	PTPN6, FGF18, PIK3CG, FGF9, PIK3R6, PIK3CD, MAPK13, TLR9, FGF1
Neuroinflammation Signaling	6.95E-01	9.97E-02	-2.043	AGER, MMP3, TLR8, CXCL12, MFGES8, MAPK13, IL6, FZD1, HMOX1, TLR10, CCL2, PIK3CG, TLR7,

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Pathway				
nNOS Signaling in Skeletal Muscle Cells	3.52E-01	1.00E-01	NaN	NOS2, CXCL8, NOX4, NLRP3, IL10, CD200R1, TLR9, CSF1R, BIRC5, GAD1, SYK, PIK3R6, NFATC2, PIK3CD, KLK1, SNCA, MMP9
Fatty Acid β -oxidation I	3.24E-01	1.00E-01	NaN	CAMK4, CACNA1H, CACNA2D4, CAPN3
Embryonic Stem Cell Differentiation into Cardiac Lineages	2.31E-01	1.00E-01	NaN	SLC27A5, ACSBG1, ACSL6
Glucose and Glucose-1-phosphate Degradation	2.31E-01	1.00E-01	NaN	NANOG
Ketogenesis	2.31E-01	1.00E-01	NaN	HK3
Oleate Biosynthesis II (Animals)	2.31E-01	1.00E-01	NaN	BDH1
Glycine Betaine Degradation	2.31E-01	1.00E-01	NaN	SCD
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	4.50E-01	1.01E-01	NaN	SDSL
Nitric Oxide Signaling in the Cardiovascular System	5.10E-01	1.02E-01	-1.508	CD247, CAMK4, CD3E, CARD11, ZAP70, LAT, NFATC2, VAV1
Phospholipases	4.14E-01	1.02E-01	NaN	PLN, CAMK4, PIK3CG, FLT4, PIK3R6, CAV1, ATP2A3, PIK3CD, TLR9, PDE1C, PRKCB
Breast Cancer Regulation by Stathmin1	6.85E-01	1.03E-01	NaN	PLD4, HMOX1, PLCB2, PLB1, PLA2G7, PLA1A
ErbB2-ErbB3 Signaling	4.50E-01	1.03E-01	-1.134	TUBB1, PPP1R14C, PLCB2, CAMK4, PPP1R3C, TLR9, CDK1, TUBB2B, STMN1, CCNE1, PAK1, CAMK2A, ADCY5, PIK3CG, CDKN1A, E2F7, PIK3R6, PIK3CD, E2F2, E2F8, PRKCB
Acetone Degradation I (to Methylglyoxal)	3.45E-01	1.03E-01	NaN	MYC, FOXO1, PIK3CG, PIK3R6, PIK3CD, TLR9, CCND1
Sonic Hedgehog Signaling	3.45E-01	1.03E-01	NaN	CYP4B1, CYP4X1, CYP2S1
CXCR4 Signaling	6.42E-01	1.04E-01	-2.324	ARRB2, CDK1, CCNB1
Lymphotoxin β Receptor Signaling	4.68E-01	1.04E-01	-2.646	PLCB2, MYL2, CXCR4, CXCL12, TLR9, RHOH, ELMO3, PAK1, GNA15, RHOB, ADCY5, RHOD, PIK3CG, PIK3R6, MYL4, PIK3CD, PRKCB
Chronic Myeloid Leukemia Signaling	5.57E-01	1.05E-01	NaN	PIK3CG, PIK3R6, LTB, CXCL1, PIK3CD, TLR9, TNFSF14
Mouse Embryonic Stem Cell Pluripotency	5.57E-01	1.05E-01	-1.508	MYC, PIK3CG, SUV39H1, E2F7, CDKN1A, PIK3R6, PIK3CD, TLR9, CCND1, E2F2, E2F8
Prostate Cancer Signaling	5.45E-01	1.05E-01	NaN	MYC, FZD10, NANOG, PIK3CG, PIK3R6, FZD5, LEF1, PIK3CD, MAPK13, FZD1, TLR9
GDNF Family Ligand-Receptor Interactions	5.01E-01	1.05E-01	-2.828	CCNE1, FOXO1, PIK3CG, SUV39H1, CDKN1A, PIK3R6, LEF1, PIK3CD, TLR9, CCND1
1D-myo-inositol Hexakisphosphate Biosynthesis II (Mammalian)	3.12E-01	1.05E-01	NaN	DOK6, DOK2, PIK3CG, GFRA1, PIK3R6, PIK3CD, DOK3, TLR9
D-myo-inositol (1,3,4)-trisphosphate Biosynthesis	3.12E-01	1.05E-01	NaN	ITPKC, INPP5D
			NaN	ITPKC, INPP5D

Table SI. Continued.

Inguinity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Hereditary Breast Cancer Signaling	6.66E-01	1.06E-01	NaN	GADD45B, TLR9, CCND1, CDK1, CCNB1, FANCD2, H2AFX, PIK3CG, CDKN1A, PIK3R6, BRCA2, SLC19A1, PIK3CD, BRCA1, BLM
Growth Hormone Signaling	5.32E-01	1.06E-01	-1.667	SOCS3, PTPN6, PRL, PIK3CG, PIK3R6, PIK3CD, RPS6KA1, TLR9, PRKCB
Leptin Signaling in Obesity	5.32E-01	1.06E-01	-1.89	SOCS3, PLCB2, LEP, FOXO1, ADCY5, PIK3CG, PIK3R6, PIK3CD, TLR9
Remodeling of Epithelial Adherens Junctions	4.86E-01	1.06E-01	NaN	DNM1, TUBB1, CDH1, ACTA2, ACTG2, ACTC1, TUBB2B
UVB-Induced MAPK Signaling	4.86E-01	1.06E-01	-2.449	PIK3CG, HIST1H3C, PIK3R6, PIK3CD, MAPK13, TLR9, PRKCB
Regulation of the Epithelial-Mesenchymal Transition Pathway	7.75E-01	1.07E-01	NaN	FZD10, WNT10B, FGF9, WNT16, FZD1, TLR9, FGF1, CDH1, GSC, FGF18, WNT7B, PIK3CG, PIK3R6, PIK3CD, LEF1, FZD5, HMGA2, MMP9, WNT5B, WNT11
Germ Cell-Sertoli Cell Junction Signaling	7.26E-01	1.07E-01	NaN	TUBB1, RAC2, LAMC3, GSN, TLR9, RAC3, RHOH, TUBB2B, CDH1, PAK1, RHOB, ACTA2, RHOD, PIK3CG, PIK3R6, PIK3CD, ACTG2, ACTC1
Gustation Pathway	6.92E-01	1.07E-01	NaN	SMPDL3A, PLCB2, PDE6G, P2RY4, PDE4C, P2RX1, CACNA1H, PDE1C, P2RY13, P2RY10, ADCY5, P2RX6, P2RY1, P2RY8, CACNA2D4, PDE6B
HMGB1 Signaling	6.56E-01	1.07E-01	-0.832	CXCL8, SELE, AGER, MAPK13, IL6, TLR9, RHOH, RHOB, CCL2, RHOD, PIK3CG, PIK3R6, PIK3CD, SERPINE1
Toll-like Receptor Signaling	5.19E-01	1.07E-01	-2.236	TLR10, IL1RN, IL1RL1, TLR7, TLR8, LBP, MAPK13, TLR9
RhoGDI Signaling	7.82E-01	1.08E-01	0.471	MYL2, CDH23, ARHGAP4, PIP5K1B, CDH15, RHOH, CDH1, PAK1, GNA15, ARHGAP9, ACTA2, RHOB, RHOD, MYL4, ACTG2, CDH13, ACTC1, PIP4K2A, ITGA4
Gai Signaling	6.63E-01	1.08E-01	-1.155	NPY1R, RXFP4, FPR2, ADORA3, RGS4, P2RY13, LTB4R, CCR4, ADRA2A, ADCY5, CAV1, RGS14, ADRA2C
CCR5 Signaling in Macrophages	5.79E-01	1.08E-01	-1.342	CD247, CCL4, CAMK4, PTK2B, CD3E, CACNA1H, FCER1G, MAPK13, CACNA2D4, PRKCB
IL-3 Signaling	5.68E-01	1.08E-01	-1.667	PTPN6, PAK1, FOXO1, PIK3CG, PIK3R6, PIK3CD, TLR9, INPP5D, PRKCB
FLT3 Signaling in Hematopoietic Progenitor Cells	5.68E-01	1.08E-01	-2.333	STAT4, PIK3CG, FLT3, PIK3R6, PIK3CD, RPS6KA1, MAPK13, TLR9, INPP5D
Prolactin Signaling	5.68E-01	1.08E-01	-1.667	MYC, SOCS3, PRL, PIK3CG, PIK3R6, PIK3CD, TLR9, TCF7, PRKCB
JAK/Stat Signaling	5.68E-01	1.08E-01	-1.667	STAT4, SOCS3, PTPN6, PIK3CG, CDKN1A, PIK3R6, PIK3CD, IL6, TLR9
BMP signaling pathway	5.37E-01	1.08E-01	-2.828	CAMK4, BMP3, BMP8A, BMP8B, BMP7, MAPK13, BMP5, CHRD
Thrombopoietin Signaling	5.05E-01	1.08E-01	-1.89	MYC, MPL, PIK3CG, PIK3R6, PIK3CD, TLR9, PRKCB
IL-6 Signaling	7.06E-01	1.09E-01	-1.387	SOCS3, CXCL8, TNFAIP6, IL1RL1, MAPK13, IL6, TLR9, COL1A1, IL1RL2, IL1RN, PIK3CG, PIK3R6, PIK3CD, LBP
Clathrin-mediated Endocytosis Signaling	9.34E-01	1.11E-01	NaN	APOE, FGF9, TLR9, ITGB3, FGF1, DNM1, ITGB2, LYZ, ARRB2, TF, ACTA2, FGF18, PIK3CG, AMPH, PIK3R6, TFRC, PIK3CD, S100A8, ACTG2, ACTC1, CLU, ITGB5
Pyrimidine Ribonucleotides De Novo Biosynthesis	4.76E-01	1.11E-01	NaN	AK5, CMPK2, RECQL4, RAD54L, BLM
Chondroitin Sulfate Biosynthesis (Late Stages)	4.76E-01	1.11E-01	NaN	CHPF, CHST9, CHST3, HS6ST3, SULF1B1
Purine Nucleotides Degradation II (Aerobic)	3.38E-01	1.11E-01	NaN	ADA2, ACP

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Pathogenesis of Multiple Sclerosis	2.60E-01	1.11E-01	NaN	CCL4
Prostanoid Biosynthesis	2.60E-01	1.11E-01	NaN	PTGES
Citrulline Biosynthesis	2.60E-01	1.11E-01	NaN	ARG1
GDP-glucose Biosynthesis	2.60E-01	1.11E-01	NaN	HK3
cAMP-mediated signaling	1.02E+00	1.12E-01	-1	PDE6G, RGS18, CAMK4, PTGDR, RXFP4, ADORA3, LTB4R, CAMK2A, ADCY5, RGS14, PDE6B, SMPDL3A, HRH2, PDE4C, NPY1R, FPR2, RGS4, CRHR1, PDE1C, P2RY13, CCR4, ADRA2A, DUSP1, ADRA2C, RPS6KA1
Role of BRCA1 in DNA Damage Response	6.26E-01	1.12E-01	0.707	FANCD2, E2F7, CDKN1A, BRCA2, SLC19A1, BRCA1, BLM, E2F2, E2F8
ErbB Signaling	7.02E-01	1.13E-01	-2.111	PAK1, FOXO1, BTC, PIK3CG, PIK3R6, HBEGF, PIK3CD, MAPK13, TLR9, EREG, PRKCB
Graft-vs.-Host Disease Signaling	4.99E-01	1.14E-01	NaN	HLA-G, GZMB, IL1RN, FCER1G, IL6
iNOS Signaling	4.99E-01	1.14E-01	NaN	CAMK4, LBP, MAPK13, HMGA1, NOS2
Coagulation System	4.61E-01	1.14E-01	NaN	SERPINA5, F13A1, SERPINE1, F3
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	8.41E-01	1.15E-01	-1.508	PTX3, CXCL8, NLRP3, IL10, SYK, PIK3CG, TLR8, TLR7, PIK3R6, PIK3CD, IL6, C1QB, TLR9, NLRCA4, PRKCB
Glioma Signaling	7.93E-01	1.15E-01	-1.89	CAMK2A, CAMK4, SUV39H1, PIK3CG, CDKN1A, E2F7, PIK3R6, PIK3CD, TLR9, CCND1, E2F2, E2F8, PRKCB
Semaphorin Signaling in Neurons	5.57E-01	1.15E-01	NaN	PAK1, SEMA4D, RHOB, RHOD, RHOH, SEMA7A
Antiproliferative Role of TOB in T Cell Signaling	4.19E-01	1.15E-01	NaN	CCNA2, CCNE1, RPS6KA1
Signaling by Rho Family GTPases	1.26E+00	1.16E-01	-1.134	MYL2, PTK2B, DIAPH3, CDH23, PIP5K1B, RHOH, STMN1, PAK1, GNA15, RHOB, RHOD, PIK3CG, CIT, MYL4, GFAP, ACTG2, ACTC1, CDH13, ITGA4, NOX4, CDH15, TLR9, DES, CDH1, ACTA2, WAS, PIK3R6, PIK3CD, PIP4K2A
T Helper Cell Differentiation	6.40E-01	1.16E-01	NaN	STAT4, IL2RG, IL10, IL10RA, FCER1G, IL2RA, IL6, TBX21
Pyrimidine Ribonucleotides Interconversion	5.23E-01	1.16E-01	NaN	AK5, CMPK2, RECQL4, RAD54L, BLM
p53 Signaling	8.34E-01	1.17E-01	1.508	GADD45B, BBC3, TP63, THBS1, PIK3CG, CDKN1A, PIK3R6, PIK3CD, TRIM29, TLR9, BRCA1, CCND1, BIRC5
Angiopoietin Signaling	6.90E-01	1.17E-01	-1.342	PAK1, FOXO1, DOK2, PIK3CG, PIK3R6, ANGPT4, PIK3CD, TLR9, BIRC5
Ephrin A Signaling	6.11E-01	1.17E-01	NaN	NGEF, PAK1, PIK3CG, PIK3R6, VAV1, PIK3CD, TLR9
3-phosphoinositide Degradation	1.03E+00	1.18E-01	NaN	SOC3, PTPN7, PTPN6, PPP1R1B, PPP1R1A, ACP5, PPFIA2, INPP5D, PTPRC, CA3, PHOSPHO1, PTPRJ, DUSP1, PPM1H, CILP, EYA4, ALPL, CDC25A
Oxidative Ethanol Degradation III	3.67E-01	1.18E-01	NaN	ALDH1L1, ACSS1
Phospholipase C Signaling	1.37E+00	1.19E-01	-2.985	CD247, BLNK, FCGR2C, PLCB2, CAMK4, CD3E, MYL2, RHOH, HMOX1, LCK, RHOB, RHOD, ADCY5, MYL4, ITGA4, ITK, FCGR2A, CD79A, BTK, PLD4, GRAP2, SYK, LAT, ZAP70, FCER1G, NFATC2, LCP2, PRKCB
Production of Nitric Oxide and	1.21E+00	1.19E-01	-2.236	APOE, PPP1R14C, PTPN6, PPP1R3C, MAPK13, NCF4, TLR9, RHOH, SPI1, NCF1, LYZ, MPO, RHOB,

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Reactive Oxygen Species in Macrophages				RHOD, PIK3CG, CAT, PIK3R6, PIK3CD, S100A8, IRF8, NOS2, CLU, PRKCB
ILK Signaling	1.21E+00	1.19E-01	-0.218	MYL2, MYH11, TLR9, CCND1, RHOH, ITGB3, MYC, ITGB2, CDH1, RHOB, ACTA2, FLNC, RHOD, PIK3CG, PIK3R6, MYL4, PIK3CD, LEF1, ACTG2, NOS2, ACTC1, ITGB5, MMP9
Gα12/13 Signaling	9.65E-01	1.19E-01	-2.5	F2RL2, MYL2, PTK2B, CDH23, CDH15, TLR9, TEC, BTK, CDH1, PIK3CG, LPAR5, PIK3R6, MYL4, VAV1, PIK3CD, CDH13
Autoimmune Thyroid Disease Signaling	5.49E-01	1.19E-01	NaN	HLA-G, GZMB, IL10, TSHR, FCER1G
Role of JAK family kinases in IL-6-type Cytokine Signaling	4.47E-01	1.20E-01	NaN	SOCS3, IL6, MAPK13
Axonal Guidance Signaling	2.32E+00	1.21E-01	NaN	RAC2, PAPP2, PLCB2, WNT10B, MMP3, MYL2, CXCL12, WNT16, ADAMTS2, PAK1, SEMA3D, GNA15, ADAM28, PIK3CG, WNT7B, MYL4, WNT5B, ITGA4, ADAMTS4, NGEF, BMP8A, BMP8B, L1CAM, KEL, TLR9, RAC3, ADAMTS6, ADAM12, PIK3R6, PIK3CD, FZD5, ERAP2, FZD10, MMP7, UNC5A, BMP3, FZD1, TUBB2B, RHOD, NTNG2, MMP8, SEMA3B, TUBB1, CXCR4, BMP5, SEMA4D, WAS, NFATC2, BMP7, SEMA3C, WNT11, MMP9, PRKCB, SEMA7A
HIF1α Signaling	9.43E-01	1.21E-01	NaN	MMP7, MMP3, MMP16, MAPK13, MMP25, TLR9, MMP8, SLC2A14, PIK3CG, PIK3R6, PIK3CD, MMP12, NOS2, MMP9
Rac Signaling	9.43E-01	1.21E-01	-3.051	IQGAP2, NOX4, PAK1, CYFIP2, PTK2B, PIK3CG, PIK3R6, PIK3CD, PIP5K1B, TLR9, PIP4K2A, ITGA4, IQGAP3, ANK1
Role of Hypercytokinemia/hyperchemokineemia in the Pathogenesis of Influenza	5.75E-01	1.22E-01	NaN	CXCL8, CCL4, CCL2, IL1RN, IL6
tRNA Splicing	5.75E-01	1.22E-01	NaN	SMPDL3A, PDE6G, PDE4C, PDE6B, PDE1C
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	1.12E+00	1.23E-01	NaN	SOCS3, PTPN7, PTPN6, PPP1R1B, PPP1R1A, ACP5, PPFIA2, PTPRC, CA3, PHOSPHO1, PTPRJ, DUSP1, PPM1H, CILP, EYA4, ALPL, CDC25A
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	1.12E+00	1.23E-01	NaN	SOCS3, PTPN7, PTPN6, PPP1R1B, PPP1R1A, ACP5, PPFIA2, PTPRC, CA3, PHOSPHO1, PTPRJ, DUSP1, PPM1H, CILP, EYA4, ALPL, CDC25A
RhoA Signaling	1.03E+00	1.23E-01	0	NGEF, MYL2, PTK2B, ANLN, RHPN1, ARHGAP4, PIP5K1B, ARHGAP9, ACTA2, CIT, LPAR5, MYL4, ACTG2, ACTC1, PIP4K2A
Macropinocytosis Signaling	8.33E-01	1.23E-01	-2.646	ITGB2, PAK1, PIK3CG, PIK3R6, PIK3CD, TLR9, CSF1R, ITGB5, ITGB3, PRKCB
Role of Wnt/GSK-3β Signaling in the Pathogenesis of Influenza	7.85E-01	1.23E-01	1.414	FZD10, WNT10B, WNT7B, WNT16, FZD5, LEF1, FZD1, WNT5B, WNT11
GM-CSF Signaling	7.85E-01	1.23E-01	-1.667	CAMK2A, PIK3CG, PIK3R6, HCK, PIK3CD, TLR9, BCL2A1, CCND1, PRKCB
IL-12 Signaling and Production in Macrophages	1.21E+00	1.25E-01	NaN	ALOX15, APOE, IL10, MST1, ALOX12, MAPK13, TLR9, SPI1, STAT4, LYZ, PIK3CG, PIK3R6, S100A8, PIK3CD, IRF8, NOS2, CLU, PRKCB
Neuroprotective Role of THO1 in Alzheimer's Disease	1.04E+00	1.25E-01	-2.309	PRSS57, GZMB, TPSD1, CMA1, CTSG, TAC1, KLK4, TPSAB1/TPSB2, HLA-G, PRTN3, KLK1, HTRA1, ST14, MMP9
Endometrial Cancer Signaling	7.62E-01	1.25E-01	-0.378	MYC, CDH1, PIK3CG, PIK3R6, LEF1, PIK3CD, TLR9, CCND1

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	Z-score	Molecules
Inhibition of Angiogenesis by TSP1	5.43E-01	1.25E-01	0	THBS1, CD36, MAPK13, MMP9
Tumoricidal Function of Hepatic Natural Killer Cells	4.77E-01	1.25E-01	NaN	GZMB, SRGN, ITGAL
Bupropion Degradation	4.77E-01	1.25E-01	NaN	CYP4B1, CYP4X1, CYP2S1
Glycolysis I	4.77E-01	1.25E-01	NaN	PKLR, ENO2, PFKP
Granzyme B Signaling	3.99E-01	1.25E-01	NaN	GZMB, LMNB1
Extrinsic Prothrombin Activation Pathway	3.99E-01	1.25E-01	NaN	FL3A1, F3
Parkinson's Signaling	3.99E-01	1.25E-01	NaN	MAPK13, SNCA
Histidine Degradation III	2.94E-01	1.25E-01	NaN	HAL
Superoxide Radicals Degradation	2.94E-01	1.25E-01	NaN	CAT
Ketolysis	2.94E-01	1.25E-01	NaN	BDH1
Glucocorticoid Biosynthesis	2.94E-01	1.25E-01	NaN	HSD3B7
Molecular Mechanisms of Cancer	2.49E+00	1.26E-01	NaN	RAC2, FZD10, PLCB2, WNT10B, SUV39H1, BMP3, WNT16, MAPK13, FZD1, CCND1, RHOH, MYC, PAK1, CAMK2A, BBC3, FANCD2, RHOB, GNA15, ADCY5, RHOD, PIK3CG, WNT7B, BRCA1, WNT5B, E2F2, E2F8, CASP10, CDC25A, ITGA4, NAIP, BMP8A, BMP8B, AURKA, TLR9, RAC3, BMP5, CDK1, CDH1, CCNE1, FOXO1, E2F7, CDKN1A, PIK3R6, BMP7, PIK3CD, FZD5, LEF1, WNT11, PRKCB
NF-κB Activation by Viruses	9.29E-01	1.26E-01	-2.714	ITGB2, LCK, PIK3CG, PIK3R6, PIK3CD, TLR9, ITGAL, ITGB5, ITGB3, ITGA4, PRKCB
Melanoma Signaling	7.39E-01	1.27E-01	-1.633	CDH1, PIK3CG, CDKN1A, PIK3R6, PIK3CD, TLR9, CCND1
Regulation of Cellular Mechanics by Calpain Protease	7.39E-01	1.27E-01	0	CCNA2, CCNE1, CAPN6, CCND1, CDK1, ITGA4, CAPN3
D-myo-inositol-5-phosphate Metabolism	1.38E+00	1.28E-01	NaN	SOC3, PTPN7, PTPN6, PLCB2, PPP1R1B, PPP1R1A, ACP5, PPFIA2, PTPRC, PLD4, CA3, PHOSPHO1, PTPRJ, DUSP1, PPM1H, CILP, EYA4, PIP4K2A, ALPL, CDC25A
IL-4 Signaling	9.55E-01	1.28E-01	NaN	IL2RG, PTPN6, IRF4, PIK3CG, PIK3R6, NFATC2, PIK3CD, HMGA1, TLR9, INPP5D, FCER2
IL-17A Signaling in Airway Cells	9.10E-01	1.28E-01	-1.633	CXCL3, PIK3CG, PIK3R6, CCL20, CXCL1, PIK3CD, CXCL5, IL6, MAPK13, TLR9
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	5.74E-01	1.29E-01	0	CD247, CD3E, GZMB, FCER1G
PKCθ Signaling in T Lymphocytes	1.43E+00	1.30E-01	-2.5	CD247, RAC2, CD3E, CACNA1H, TLR9, RAC3, LCK, CAMK2A, CARD11, GRAP2, PIK3CG, ZAP70, LAT, PIK3R6, FCER1G, NFATC2, PIK3CD, VAV1, CACNA2D4, LCP2
VEGF Signaling	1.10E+00	1.30E-01	-0.632	PTPN6, FOXO1, PTK2B, ACTA2, PIK3CG, FLT4, PIK3R6, PIK3CD, ACTG2, TLR9, ACTC1, EIF1AY, PRKCB
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I	5.09E-01	1.30E-01	NaN	AK5, CMPK2, RRM2
G-Protein Coupled Receptor Signaling	2.24E+00	1.31E-01	NaN	PDE6G, PLCB2, RGS18, CAMK4, PTK2B, PTGDR, RXFP4, ADORA3, AVPR1A, LTB4R, CAMK2A, GNA15, ADCY5, PIK3CG, RGS14, PDE6B, HTR2A, SMPDL3A, HRH2, PDE4C, NPY1R, FPR2, RGS4, CRHR1, TLR9, PDE1C, P2RY13, ADRA2A, CCR4, DUSP1, CALCR, PIK3R6, ADRA2C, PIK3CD, RPS6KA1, PRKCB
Th1 Pathway	1.31E+00	1.31E-01	-2.309	CD247, SOCS3, CD3E, IL10, LGALS9, IL6, TBX21, CD8A, TLR9, STAT4, ITGB2, PIK3CG, PIK3R6, IL10RA, NFATC2, PIK3CD, VAV1

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Gαq Signaling	1.55E+00	1.32E-01	-1.964	PLCB2, RGS18, CAMK4, PTK2B, RGS4, TLR9, AVPR1A, RHOH, BTK, PLD4, HMOX1, GNA15, RHOB, RHOD, PIK3CG, CALCR, PIK3R6, NFATC2, PIK3CD, HTR2A, PRKCB
Cdc42 Signaling	1.34E+00	1.32E-01	-2.324	CD247, FGD3, CD3E, MYL2, DIAPH3, MAPK13, EXOC6, HLA-G, IQGAP2, PAK1, WAS, FCER1G, MYL4, VAV1, ITGA4, IQGAP3, ITK
FAK Signaling	1.15E+00	1.33E-01	NaN	CAPN6, PAK1, ACTA2, WAS, PIK3CG, HMMR, PIK3R6, PIK3CD, ACTG2, TLR9, ACTC1, ITGA4, CAPN3
IL-9 Signaling	7.47E-01	1.33E-01	-2.449	SOCS3, IL2RG, PIK3CG, PIK3R6, PIK3CD, TLR9
Superpathway of Citrulline Metabolism	4.34E-01	1.33E-01	NaN	NOS2, ARG1
Adenosine Nucleotides Degradation II	4.34E-01	1.33E-01	NaN	ADA2, ACPP
Histidine Degradation VI	4.34E-01	1.33E-01	NaN	HAL, CYP4F11
ATM Signaling	1.18E+00	1.34E-01	0.632	GADD45B, FANCD2, SUV39H1, H2AFX, CDKN1A, CCNB2, HIST1H4J, MAPK13, BLM, BRCA1, CDK1, CCNB1, CDC25A
Docosahexaenoic Acid (DHA) Signaling	8.28E-01	1.35E-01	NaN	ALOX15, FOXO1, PIK3CG, PIK3R6, PIK3CD, TLR9, BCL2A1
Colorectal Cancer Metastasis Signaling	2.32E+00	1.36E-01	-0.87	FZD10, MMP7, WNT10B, MMP3, MMP16, TLR8, WNT16, IL6, FZD1, MMP25, CCND1, RHOH, MYC, TLR10, RHOB, RHOD, ADCY5, MMP8, WNT7B, PIK3CG, TLR7, NOS2, MMP12, WNT5B, TLR9, BIRC5, CDH1, PIK3R6, PIK3CD, FZD5, LEF1, WNT11, MMP9
Actin Cytoskeleton Signaling	2.16E+00	1.36E-01	-1.633	RAC2, FGD3, MYL2, DIAPH3, PIP5K1B, MYH11, IQGAP2, PAK1, CYFIP2, FGF18, PIK3CG, MYL4, LBP, ACTG2, ACTC1, ITGA4, IQGAP3, MATK, FGF9, GSN, TLR9, RAC3, FGF1, ACTA2, WAS, PIK3R6, PIK3CD, VAV1, NCKAP1L, PIP4K2A
HER-2 Signaling in Breast Cancer	1.17E+00	1.36E-01	NaN	ITGB2, CCNE1, FOXO1, PIK3CG, CDKN1A, PIK3R6, PIK3CD, TLR9, CCND1, ITGB5, ITGB3, PRKCB
Systemic Lupus Erythematosus Signaling	2.27E+00	1.38E-01	NaN	CD247, FCGR2C, CAMK4, CD3E, IL6, FCGR1A, PTPRC, HLA-G, LCK, PIK3CG, CD22, TLR7, C7, FCGR3A/FCGR3B, TNFSF13B, PTPN6, IL10, FCGR2A, SNRPF, CD79A, TLR9, INPP5D, IL1RN, LAT, FCER1G, PIK3R6, NFATC2, PIK3CD, KLR1, PIM2
FcγRIIB Signaling in B Lymphocytes	1.16E+00	1.39E-01	-2.333	BLNK, BTK, PIK3CG, SYK, CACNA1H, PIK3R6, CD79A, PIK3CD, TLR9, CACNA2D4, INPP5D
Ovarian Cancer Signaling	1.74E+00	1.40E-01	-2.449	FZD10, MMP7, WNT10B, FGF9, SUV39H1, WNT16, FZD1, TLR9, CCND1, WNT7B, PIK3CG, PIK3R6, BRCA2, PIK3CD, LEF1, FZD5, BRCA1, MMP9, WNT5B, WNT11
LXR/RXR Activation	1.57E+00	1.40E-01	0	APOE, SCD, IL1RL1, CD36, IL6, CETP, LYZ, IL1RL2, CCL2, TF, IL1RN, S100A8, PLTP, LBP, NOS2, CLU, MMP9
IL-7 Signaling Pathway	1.23E+00	1.40E-01	-1.897	PAX5, IL7R, MYC, IL2RG, FOXO1, PIK3CG, PIK3R6, PIK3CD, MAPK13, TLR9, CCND1, CDC25A
Acute Myeloid Leukemia Signaling	1.33E+00	1.41E-01	-0.577	CSF3R, FLT3, TLR9, CCND1, SPI1, CSF1R, MYC, PIK3CG, PIK3R6, KIT, LEF1, PIK3CD, PIM2
IL-17 Signaling	1.26E+00	1.41E-01	NaN	CXCL8, CCL2, MMP3, PIK3CG, PIK3R6, CXCL1, PIK3CD, CXCL5, IL6, MAPK13, TLR9, NOS2
Integrin Signaling	2.42E+00	1.42E-01	-0.962	RAC2, ITGA2B, MYL2, RHOH, ITGB3, PAK1, RHOB, RHOD, ITGA11, PIK3CG, CAV1, ACTG2, ACTC1, ITGB5, ITGA4, ITGAD, CAPN6, TSPAN5, TSPAN2, GSN, TLR9, ITGAL, RAC3, ITGB2, ITGAM, ACTA2, WAS, PIK3R6, PIK3CD, CAPN3
Wnt/β-catenin Signaling	2.06E+00	1.42E-01	-0.209	SOX7, FZD10, MMP7, WNT10B, FRZB, FRAT1, WNT16, FZD1, SOX11, CCND1, SOX17, MYC, CDH1, WIF1, DKK3, WNT7B, DKK2, SFRP5, LEF1, MAP4K1, FZD5, SFRP1, WNT5B, WNT11

Table S1. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Pancreatic Adenocarcinoma Signaling	1.60E+00	1.42E-01	-1.897	SUV39H1, HBEGF, TLR9, CCND1, BIRC5, PLD4, HMOX1, CCNE1, PIK3CG, CDKN1A, E2F7, PIK3R6, BRCA2, PIK3CD, E2F2, MMP9, E2F8
TR/RXR Activation	1.43E+00	1.43E-01	NaN	UCP2, CAMK4, NRG1, PFKF, TLR9, THRSP, KLF9, HP, COL6A3, PIK3CG, PIK3R6, PIK3CD, STRBP, PPARGC1A
VDR/RXR Activation	1.22E+00	1.43E-01	NaN	IGFBP6, BGLAP, CYP24A1, SPP1, CAMP, FOXO1, IL1RL1, CDKN1A, SEMA3B, KLF4, PRKCB
IL-17A Signaling in Fibroblasts	7.65E-01	1.43E-01	NaN	CCL2, LCN2, CXCL5, IL6, MAPK13
IL-15 Production	6.78E-01	1.43E-01	NaN	TXK, PTK2B, IL6, LTK
Ethanol Degradation IV	5.82E-01	1.43E-01	NaN	ALDH1L1, CAT, ACSS1
γ -glutamyl Cycle	4.74E-01	1.43E-01	NaN	GGT5, GCCLC
Ceramide Biosynthesis	3.35E-01	1.43E-01	NaN	SPTSSB
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	3.35E-01	1.43E-01	NaN	TDO2
Mineralocorticoid Biosynthesis	3.35E-01	1.43E-01	NaN	HSD3B7
Role of NFAT in Regulation of the Immune Response	2.25E+00	1.44E-01	-4.707	BLNK, CD247, FCGR2C, PLCB2, CAMK4, CD3E, FCER1A, FCGR1A, LCK, GNA15, PIK3CG, FCGR3A/FCGR3B, ITK, FCGR2A, CD79A, TLR9, BTK, SYK, LAT, ZAP70, MS4A2, FCER1G, PIK3R6, NFATC2, PIK3CD, LCP2
Superpathway of Inositol Phosphate Compounds	2.76E+00	1.45E-01	NaN	SOC3, PLCB2, PPP1R1A, TRAT1, PIP5K1B, ACP5, PP2A, PTPRC, CA3, LCK, PHOSPHO1, PTPRJ, PIK3CG, KIT, EYA4, ALPL, CDC25A, PTPN7, CD19, PTPN6, PPP1R1B, TLR9, INPP5D, PLD4, DUSP1, PPM1H, ITPKC, PIK3R6, CILP, PIK3AP1, PIK3CD, VAV1, PIP4K2A
Wnt/Ca+ pathway	1.11E+00	1.45E-01	0.333	FZD10, PDE6G, PLCB2, CAMK2A, NFATC2, FZD5, FZD1, PDE6B, WNT5B
Dendritic Cell Maturation	2.41E+00	1.46E-01	-1.633	FCGR2C, PLCB2, LEP, LTB, COL10A1, IL6, MAPK13, FCGR1A, COL1A2, CDID, IL1RL2, PIK3CG, CD1C, FCGR3A/FCGR3B, IL10, FCGR2A, COL2A1, TLR9, STAT4, COL1A1, COL5A3, IL1RN, FCER1G, PIK3R6, PIK3CD, IRF8, CCR7
Mechanisms of Viral Exit from Host Cells	8.85E-01	1.46E-01	NaN	ACTA2, CHMP4C, ACTG2, ACTC1, LMNB1, PRKCB
DNA Methylation and Transcriptional Repression Signaling	8.03E-01	1.47E-01	NaN	HIST1H4F, HIST1H4D, HIST1H4L, HIST1H4I, HIST1H4J
D-myo-inositol (1,4,5)-Trisphosphate Biosynthesis	7.17E-01	1.48E-01	NaN	PLD4, PLCB2, PIP5K1B, PIP4K2A
3-phosphoinositide Biosynthesis	2.71E+00	1.49E-01	NaN	SOC3, PPP1R1A, TRAT1, PIP5K1B, ACP5, PP2A, PTPRC, CA3, LCK, PHOSPHO1, PTPRJ, PIK3CG, KIT, EYA4, ALPL, CDC25A, PTPN7, PTPN6, CD19, PPP1R1B, TLR9, DUSP1, PPM1H, PIK3R6, CILP, PIK3AP1, PIK3CD, VAV1, PIP4K2A
Calcium-induced T Lymphocyte Apoptosis	1.19E+00	1.50E-01	-2.121	CD247, LCK, CAMK4, CD3E, ZAP70, FCER1G, NFATC2, ATP2A3, PRKCB
Inflammasome pathway	6.23E-01	1.50E-01	NaN	NAIP, NLRP3, NLRP4
Fc Epsilon RI Signaling	1.94E+00	1.51E-01	-3.153	RAC2, FCER1A, MAPK13, TLR9, RAC3, INPP5D, BTK, GRAP2, PIK3CG, SYK, LAT, PIK3R6, FCER1G, MS4A2, PIK3CD, VAV1, LCP2, PRKCB

Table S1. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Cyclins and Cell Cycle Regulation	1.47E+00	1.52E-01	-2.714	CCNA2, CCNE1, SUV39H1, E2F7, CDKN1A, CCNB2, CCND1, CDK1, E2F2, E2F8, CCNB1, CDC25A
nNOS Signaling in Neurons	1.04E+00	1.52E-01	NaN	NOS1AP, CAPN6, CAMK2A, CAMK4, RASD1, PRKCB, CAPN3
B Cell Receptor Signaling	2.92E+00	1.54E-01	-3.4	BLNK, FCGR2C, RAC2, CAMK4, PTK2B, POU2F2, MAPK13, PTPRC, PAX5, CAMK2A, PIK3CG, CD22, CD19, PTPN6, FCGR2A, CD79A, TLR9, INPP5D, BTK, DAPPI, FOXO1, SYK, PIK3R6, NFATC2, PIK3AP1, PIK3CD, VAV1, BCL2A1, PRKCB
Cell Cycle: G1/S Checkpoint Regulation	1.33E+00	1.54E-01	1.265	MYC, CCNE1, FOXO1, SUV39H1, E2F7, CDKN1A, CCND1, E2F2, E2F8, CDC25A
Thyroid Cancer Signaling	9.63E-01	1.54E-01	NaN	MYC, CXCL8, CDH1, CXCL12, LEF1, CCND1
Choline Biosynthesis III	5.18E-01	1.54E-01	NaN	PLD4, HMOX1
Bile Acid Biosynthesis, Neutral Pathway	5.18E-01	1.54E-01	NaN	SLC27A5, HSD3B7
Glioblastoma Multiforme Signaling	2.64E+00	1.55E-01	-0.218	FZD10, PLCB2, WNT10B, WNT16, FZD1, TLR9, CCND1, RHOH, MYC, CCNE1, RHOB, FOXO1, RHOD, PIK3CG, WNT7B, E2F7, CDKN1A, PIK3R6, LEF1, FZD5, PIK3CD, WNT5B, WNT11, E2F8, E2F2
Th1 and Th2 Activation Pathway	2.90E+00	1.56E-01	NaN	CD247, SOCS3, CD3E, IL1RL1, LGALS9, IL6, TBX21, CD8A, SPI1, PIK3CG, TIMD4, IL2RB, IL2RG, IL10, CXCR4, IKZF1, TLR9, TSLP, STAT4, ITGB2, CCR4, GF11, IL10RA, PIK3R6, NFATC2, PIK3CD, IL2RA, VAV1
IL-2 Signaling	1.37E+00	1.56E-01	-3.162	IL2RG, LCK, PTK2B, PIK3CG, SYK, PIK3R6, IL2RA, PIK3CD, TLR9, IL2RB
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	1.65E+00	1.57E-01	NaN	TLR10, SPPI1, IL10, IL1RN, PRTN3, TLR8, FCER1G, TLR7, LTB, CD79A, IL6, TLR9, TNFSF13B
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	4.73E+00	1.58E-01	NaN	FZD10, SOCS3, PLCB2, WNT10B, CAMK4, FRZB, MMP3, IL1RL1, CXCL12, TLR8, WNT16, LTB, IL6, FZD1, CCND1, FCGR1A, MYC, TLR10, CAMK2A, WIF1, CCL2, IL1RL2, DKK3, PIK3CG, WNT7B, TLR7, DKK2, SFRP5, NOS2, FCGR3A/FCGR3B, WNT5B, TNFSF13B, ADAMTS4, CXCL8, SELE, IL10, TLR9, CEBPE, IL1RN, PIK3R6, NFATC2, LEF1, FZD5, PIK3CD, SFRP1, SOST, WNT11, PRKCB
IL-8 Signaling	3.27E+00	1.58E-01	-2.556	RAC2, PLCB2, PTK2B, MYL2, CCND1, RHOH, ITGB3, HMOX1, RHOB, RHOD, PIK3CG, CXCL1, ITGB5, CXCL8, NOX4, FLT4, DEFA1 (includes others), HBEGF, TLR9, RAC3, AZU1, PLD4, ITGB2, ARRB2, CDH1, ITGAM, MPO, PIK3R6, PIK3CD, MMP9, PRKCB
IL-15 Signaling	1.59E+00	1.58E-01	NaN	CXCL8, IL2RG, LCK, PIK3CG, SYK, PIK3R6, PIK3CD, IL6, MAPK13, TLR9, RAC3, IL2RB
Role of CHK Proteins in Cell Cycle Checkpoint Control	1.31E+00	1.58E-01	1.633	E2F7, CDKN1A, SLC19A1, CLSPN, BRCA1, CDK1, E2F2, E2F8, CDC25A
Cardiomyocyte Differentiation via BMP Receptors	6.68E-01	1.58E-01	NaN	MYL2, BMP7, BMP5
PI3K Signaling in B Lymphocytes	2.33E+00	1.59E-01	-2.683	BLNK, CD19, PLCB2, CAMK4, ATF3, CD79A, INPP5D, PTPRC, BTK, BLK, CAMK2A, CD180, DAPPI, PIK3CG, SYK, NFATC2, PIK3AP1, PIK3CD, VAV1, PRKCB
Osteoarthritis Pathway	3.54E+00	1.60E-01	-1.826	MATN3, FZD10, BGLAP, LEP, FRZB, MMP3, AGER, IL1RL1, GDF5, COL10A1, WNT16, SP7, FZD1, FGF18, IL1RL2, S100A8, NOS2, MMP12, ALPL, ITGA4, ADAMTS4, CASP10, TIMP3, CXCL8, SPPI1, COL2A1, S100A9, FZD5, WISP1, LEF1, HTRA1, MMP9, PPARGC1A
IL-17A Signaling in Gastric Cells	8.03E-01	1.60E-01	NaN	CXCL8, CCL20, CXCL1, MAPK13

Table S1. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	Z-score	Molecules
Cell Cycle Regulation by BTG Family Proteins	1.05E+00	1.62E-01	-1.633	CCNE1, E2F7, BTG2, CCND1, E2F2, E2F8
Reelin Signaling in Neurons	1.99E+00	1.63E-01	NaN	APOE, VLDLR, TLR9, ITGAL, ITGB3, BLK, ITGB2, LCK, PIK3CG, HCK, PIK3R6, MAP4K1, PIK3CD, FGR, ITGA4
Th2 Pathway	2.90E+00	1.64E-01	-2.065	CD247, SOCS3, IL2RG, CD3E, IL10, CXCR4, IL1RL1, IKZF1, TBX21, TLR9, TSLP, SPI1, STAT4, ITGB2, CCR4, PIK3CG, GF11, PIK3R6, NFATC2, PIK3CD, VAV1, IL2RA, TIMD4, IL2RB
Aggrin Interactions at Neuromuscular Junction	1.61E+00	1.64E-01	-0.632	RAC2, ITGB2, PAK1, ACTA2, PKLR, ACTG2, ACTC1, RAC3, ITGAL, ITGB3, ITGA4
Role of NANOG in Mammalian Embryonic Stem Cell Pluripotency	2.58E+00	1.67E-01	-2.646	FZD10, WNT10B, BMP3, BMP8A, BMP8B, WNT16, FZD1, TLR9, BMP5, NANOG, WNT7B, PIK3CG, PIK3R6, BMP7, PIK3CD, FZD5, WNT5B, WNT11, TCL1A, SALL4
Role of Tissue Factor in Cancer	2.58E+00	1.67E-01	NaN	CXCL8, PTK2B, HBEGF, MAPK13, TLR9, F3, ITGB3, BLK, LCK, PAK1, ARRB2, GNA15, PIK3CG, HCK, PIK3R6, CXCL1, PIK3CD, RPS6KA1, ITGB5, FGR
PCP pathway	1.54E+00	1.67E-01	1.667	NDP, FZD10, WNT10B, WNT7B, WNT16, CTHRC1, FZD5, FZD1, WNT5B, WNT11
Transcriptional Regulatory Network in Embryonic Stem Cells	1.44E+00	1.67E-01	NaN	HIST1H4F, NANOG, HIST1H4D, HIST1H4L, HIST1H4I, HIST1H4J, L1CAM, EOMES, SIX3
Role of IL-17F in Allergic Inflammatory Airway Diseases	1.21E+00	1.67E-01	-0.378	CXCL8, CCL4, CCL2, CXCL1, CXCL5, IL6, RPS6KA1
Complement System	1.10E+00	1.67E-01	NaN	ITGB2, CR1, ITGAM, C4BPA, C7, C1QB
Lipid Antigen Presentation by CDI	8.50E-01	1.67E-01	NaN	CD1D, CD3E, FCER1G, CD1C
BER pathway	5.67E-01	1.67E-01	NaN	LIG1, FEN1
Arginine Biosynthesis IV	3.84E-01	1.67E-01	NaN	GLUD2
Urea Cycle	3.84E-01	1.67E-01	NaN	ARG1
Chondroitin and Dermatan Biosynthesis	3.84E-01	1.67E-01	NaN	CHPF
Adenine and Adenosine Salvage III	3.84E-01	1.67E-01	NaN	ADA2
Purine Ribonucleosides Degradation to Ribose-1-phosphate	3.84E-01	1.67E-01	NaN	ADA2
Zymosterol Biosynthesis	3.84E-01	1.67E-01	NaN	LBR
Factors Promoting Cardiogenesis in Vertebrates	2.12E+00	1.69E-01	NaN	FZD10, NOX4, MYL2, BMP3, BMP8A, CDC6, BMP8B, FZD1, BMP5, CCNE1, BMP7, LEF1, FZD5, WNT11, PRKCB
Eicosanoid Signaling	1.70E+00	1.69E-01	-2.449	ALOX15, PTGES, LTB4R, PTGDR, PLB1, FPR2, ALOX5AP, ALOX12, ALOX5, PLA2G7, DPEP2
Human Embryonic Stem Cell Pluripotency	3.16E+00	1.71E-01	NaN	FZD10, WNT10B, BMP3, BMP8A, BMP8B, WNT16, FZD1, TLR9, LEFTY2, BMP5, INHBA, SIPR4, NANOG, FOXO1, WNT7B, PIK3CG, PIK3R6, BMP7, PIK3CD, LEF1, FZD5, WNT11, WNT5B, SALL4
Communication between Innate and Adaptive Immune Cells	2.21E+00	1.72E-01	NaN	HLA-G, CXCL8, TLR10, CCL4, IL10, IL1RN, TLR8, FCER1G, TLR7, CD79A, IL6, CD8A, TLR9, TNFSF13B, CCR7

Table S1. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
B Cell Development	1.02E+00	1.72E-01	NaN	PTPRC, IL7R, CD19, SPN, CD79A
Tec Kinase Signaling	3.74E+00	1.73E-01	-3.402	PTK2B, FCER1A, RHOH, BLK, LCK, PAK1, TXK, GNA15, RHOB, RHOD, PIK3CG, HCK, ACTG2, ACTC1, FGR, ITGA4, ITK, TLR9, TEC, STAT4, BTK, ACTA2, WAS, MS4A2, FCER1G, PIK3R6, PIK3CD, VAV1, PRKCB
Paxillin Signaling	2.66E+00	1.73E-01	-1.508	ITGAD, ITGA2B, PTK2B, MAPK13, TLR9, ITGAL, ITGB3, ITGB2, PAK1, ITGAM, ACTA2, ITGA11, PIK3CG, PIK3R6, PIK3CD, ACTG2, ACTC1, ITGB5, ITGA4
γ -linolenate Biosynthesis II (Animals)	7.69E-01	1.76E-01	NaN	SLC27A5, ACSBG1, ACSL6
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	1.47E+00	1.78E-01	NaN	NR2F1, NR6A1, SPP1, NANOG, CCNF, NR2F6, BRCA1, SALL4
Cell Cycle Control of Chromosomal Replication	1.74E+00	1.79E-01	NaN	LIG1, CDC45, MCM2, CDT1, CDC6, ORC6, TOP2A, CDK1, MCM4, ORC1
CD28 Signaling in T Helper Cells	3.40E+00	1.81E-01	-3.13	CD247, PTPN6, CAMK4, CD3E, TLR9, CTLA4, PTPRC, LCK, PAK1, WAS, GRAP2, CARD11, SYK, PIK3CG, ZAP70, LAT, PIK3R6, FCER1G, NFATC2, PIK3CD, VAV1, LCP2, ITK
UDP-N-acetyl-D-galactosamine Biosynthesis II	6.23E-01	1.82E-01	NaN	HK3, UAPI
CTLA4 Signaling in Cytotoxic T Lymphocytes	2.86E+00	1.84E-01	NaN	CD247, PTPN6, CD3E, API3, TRAT1, TLR9, CD8A, CTLA4, LCK, GRAP2, PIK3CG, SYK, ZAP70, LAT, PIK3R6, FCER1G, PIK3CD, LCP2
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	1.68E+00	1.84E-01	1.667	CDKN1A, TOP2A, CCNB2, PKMYT1, RPS6KA1, AURKA, BRCA1, CDK1, CCNB1
Regulation of Actin-based Motility by Rho	2.66E+00	1.86E-01	-0.258	RAC2, MYL2, PIP5K1B, GSN, RHOH, RAC3, PAK1, RHOB, ACTA2, RHOD, WAS, MYL4, ACTG2, ACTC1, PIP4K2A, ITGA4
Glioma Invasiveness Signaling	2.26E+00	1.86E-01	-1.941	TIMP3, TIMP4, RHOB, RHOD, PIK3CG, HMMR, PIK3R6, PIK3CD, TLR9, RHOH, MMP9, ITGB5, ITGB3
IL-10 Signaling	2.31E+00	1.88E-01	NaN	SOCS3, FCGR2C, IL10, IL1RL1, FCGR2A, BLVRB, IL6, MAPK13, HMOX1, IL1RL2, IL1RN, IL10RA, LBP
Role of IL-17A in Arthritis	2.31E+00	1.88E-01	NaN	CXCL8, CCL20, CXCL5, MAPK13, TLR9, CXCL3, CCL2, PIK3CG, PIK3R6, PIK3CD, CXCL1, RPS6KA1, NOS2
Role of JAK1 and JAK3 in γ Cytokine Signaling	2.31E+00	1.88E-01	NaN	BLNK, SOCS3, IL2RG, PTK2B, TLR9, TSLP, IL7R, PIK3CG, SYK, PIK3R6, IL2RA, PIK3CD, IL2RB
Mismatch Repair in Eukaryotes	8.26E-01	1.88E-01	NaN	SLC19A1, FEN1, EXO1
Mitotic Roles of Polo-Like Kinase	2.21E+00	1.90E-01	-1.897	KIF23, PLK4, ESPL1, CDC20, PTTG1, PRC1, CCNB2, PKMYT1, CDK1, KIF11, CCNB1, CDC25A
Hematopoiesis from Pluripotent Stem Cells	1.64E+00	1.90E-01	NaN	CD247, CXCL8, CD3E, IL10, FCER1G, IL6, CSF3, CD8A
Crosstalk between Dendritic Cells and Natural Killer Cells	2.93E+00	1.91E-01	NaN	CD209, IL2RG, CD69, LTB, IL6, TLR9, ITGAL, HLA-G, CAMK2A, ACTA2, ICAM3, CD226, TLR7, ACTG2, ACTC1, CCR7, IL2RB
Chemokine Signaling	2.37E+00	1.91E-01	-1.387	PLCB2, CAMK4, MYL2, PTK2B, CXCR4, CXCL12, MAPK13, CCL4, CCL13, CAMK2A, CCL2, PIK3CG, PRKCB

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
iCOS-iCOSL Signaling in T Helper Cells	3.89E+00	1.95E-01	-3.13	CD247, IL2RG, CAMK4, CD3E, TRAT1, TLR9, INPP5D, PTPRC, LCK, CAMK2A, GRAP2, PIK3CG, ZAP70, LAT, PIK3R6, FCER1G, NFATC2, PIK3CD, IL2RA, VAV1, LCP2, ITK, IL2RB
Bladder Cancer Signaling	3.04E+00	1.95E-01	2.236	CXCL8, MMP7, MMP3, MMP16, FGF9, SUV39H1, MMP25, CCND1, FGF1, MYC, CDH1, FGF18, THBS1, MMP8, CDKN1A, MMP12, MMP9
Intrinsic Prothrombin Activation Pathway	1.70E+00	1.95E-01	0.707	COL1A2, COL1A1, COL5A3, COL2A1, F13A1, COL10A1, KLK1, KLK4
Virus Entry via Endocytic Pathways	3.49E+00	1.96E-01	NaN	RAC2, TLR9, RAC3, ITGAL, ITGB3, DNMI1, ITGB2, ACTA2, FLNC, PIK3CG, PIK3R6, CAV1, TFRC, PIK3CD, ACTG2, CXADR, ACTC1, ITGB5, ITGA4, PRKCB
Calcium Transport I	6.86E-01	2.00E-01	NaN	ATP2A3, ATP2C2
NAD Phosphorylation and Dephosphorylation	6.86E-01	2.00E-01	NaN	ACP5, ACP
Trehalose Degradation II (Trehalase)	4.46E-01	2.00E-01	NaN	HK3
Protein Citrullination	4.46E-01	2.00E-01	NaN	PADI4
Citrulline-Nitric Oxide Cycle	4.46E-01	2.00E-01	NaN	NOS2
Lactose Degradation III	4.46E-01	2.00E-01	NaN	GLB1L3
dTMP De Novo Biosynthesis	4.46E-01	2.00E-01	NaN	DHFR
Glutamate Degradation III (via 4-aminobutyrate)	4.46E-01	2.00E-01	NaN	GAD1
Basal Cell Carcinoma Signaling	2.76E+00	2.03E-01	1	FZD10, WNT10B, BMP3, BMP8A, BMP8B, WNT16, FZD1, BMP5, WNT7B, LEF1, FZD5, BMP7, WNT5B, WNT11
Leukocyte Extravasation Signaling	7.13E+00	2.04E-01	-4.542	RAC2, CLDN11, MMP7, SPN, PTK2B, MMP3, MMP16, CXCL12, MAPK13, MMP25, RHOH, ITGB3, TXK, MMP8, PIK3CG, ACTG2, MMP12, ACTC1, ITGA4, ITK, TIMP3, CXCR4, ARHGAP4, NCF4, TLR9, ITGAL, BTK, TEC, ITGB2, TIMP4, NCF1, ITGAM, ARHGAP9, ACTA2, CLDN1, WAS, ICAM3, PIK3R6, VAV1, PIK3CD, MMP9, PRKCB
Agranulocyte Adhesion and Diapedesis	6.24E+00	2.05E-01	NaN	CLDN11, MMP7, SELL, MMP3, MYL2, MMP16, CXCL12, CCL20, MYH11, CXCL5, MMP25, CCL4L1/ CCL4L2, CXCL3, CCL13, CCL2, CCL8, MMP8, CXCL14, MYL4, CXCL1, ACTG2, MMP12, ACTC1, ITGA4, CXCL8, SELE, CXCR4, PPBP, PF4, ITGB2, CCL4, ACTA2, CLDN1, IL1RN, CCL18, MMP9
Natural Killer Cell Signaling	4.68E+00	2.08E-01	NaN	CD247, RAC2, LCK, PAK1, SH2D1A, PIK3CG, FCGR3A/FCGR3B, PTPN6, LAIR1, FCGR2A, TLR9, RAC3, LILRB1, INPP5D, SIGLEC7, SYK, LAT, ZAP70, CD244, FCER1G, PIK3R6, PIK3CD, VAV1, LCP2, PRKCB
MSP-RON Signaling Pathway	3.05E+00	2.08E-01	NaN	MST1, CCR2, TLR9, KLK4, ITGB2, ITGAM, ACTA2, CCL2, PIK3CG, PIK3R6, PIK3CD, ACTG2, KLK1, NOS2, ACTC1
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	8.52E+00	2.11E-01	NaN	FZD10, BGLAP, WNT10B, CAMK4, FRZB, PTK2B, MMP3, IL1RL1, BMP3, WNT16, SP7, ACP5, IL6, FZD1, ITGB3, WIF1, IL1RL2, DKK3, MMP8, PIK3CG, WNT7B, DKK2, SFRP5, ALPL, WNT5B, ADAMTS4, NAIP, SPP1, IL10, BMP8A, BMP8B, GSN, TLR9, BMP5, CSF1R, COL1A1, FOXO1, IL1RN, PIK3R6, CALCR, NFATC2, LEF1, BMP7, FZD5, PIK3CD, SFRP1, SOST, WNT11

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Phagosome Formation	4.96E+00	2.11E-01	NaN	FCAR, FCGR2C, PLCB2, TLR8, FCER1A, FCGR1A, RHOH, TLR10, RHOB, RHOD, PIK3CG, TLR7, FCGR3A/FCGR3B, FCER2, ITGA4, FCGR2A, TLR9, INPP5D, ITGB2, CR1, ITGAM, SYK, FCER1G, PIK3R6, PIK3CD, PRKCB
Caveolar-mediated Endocytosis Signaling	3.11E+00	2.11E-01	NaN	ITGAD, ITGA2B, CD48, ITGAL, ITGB3, ITGB2, ITGAM, ACTA2, ITGA11, FLNC, CAV1, ACTG2, ACTC1, ITGB5, ITGA4
Hepatic Fibrosis/Hepatic Stellate Cell Activation	7.20E+00	2.13E-01	NaN	COL8A2, LEP, MYL2, IL1RL1, COL9A3, COL8A1, COL10A1, IL6, MYH11, COL17A1, COL15A1, COL5A1, COL1A2, CXCL3, COL6A1, CCL2, IL1RL2, COL22A1, MYL4, LBP, SERPINE1, CXCL8, COL5A2, COL6A2, IL10, COL12A1, FLT4, COL2A1, FGF1, COL1A1, COL5A3, ACTA2, COL6A3, COL23A1, IL10RA, COL9A2, MMP9, CCR7, COL7A1
T Cell Receptor Signaling	4.51E+00	2.13E-01	NaN	CD247, PTPN7, CAMK4, CD3E, CD8A, TLR9, CTLA4, PTPRC, TEC, BTK, LCK, TXK, GRAP2, CARD11, PIK3CG, ZAP70, LAT, PIK3R6, NFATC2, PIK3CD, VAV1, LCP2, ITK
Fatty Acid Activation	1.04E+00	2.31E-01	NaN	SLC27A5, ACSBG1, ACSL6
Leukotriene Biosynthesis	1.04E+00	2.31E-01	NaN	GGT5, ALOX5, DPEP2
Granulocyte Adhesion and Diapedesis	8.45E+00	2.35E-01	NaN	CLDN11, MMP7, SELL, MMP3, IL1RL1, MMP16, CXCL12, CCL20, CXCL5, MMP25, CCL4L1/CCL4L2, ITGB3, CXCL3, CCL13, CCL2, CCL8, IL1RL2, MMP8, CXCL14, CXCL1, MMP12, ITGA4, CSF3R, CXCL8, HRH2, SELE, CXCR4, PPBP, PF4, FPR2, CSF3, ITGAL, ITGB2, ITGAM, CCL4, CLDN1, IL1RN, CCL18, MMP9
Granzyme A Signaling	1.30E+00	2.35E-01	NaN	HIST1H1B, HIST1H1C, HIST1H1D, HMGB2
Mitochondrial L-carnitine Shuttle Pathway	1.30E+00	2.35E-01	NaN	SLC27A5, ACSBG1, ACSL6, CPT1C
Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes	5.66E+00	2.47E-01	-3.128	RAC2, PTK2B, FCGR2A, FYB1, RAC3, FCGR1A, INPP5D, PLD4, HMOX1, PAK1, NCF1, ACTA2, WAS, SYK, PIK3CG, HCK, VAV1, ACTG2, ACTC1, FCGR3A/FCGR3B, LCP2, FGR, PRKCB
Atherosclerosis Signaling	7.52E+00	2.50E-01	NaN	APOE, MMP3, CMA1, CD36, CXCL12, COL10A1, ALOX12, IL6, CCR2, PLA2G7, COL1A2, LYZ, CCL2, PLB1, S100A8, ITGA4, ALOX15, CXCL8, SELE, CXCR4, COL2A1, F3, TPSAB1/TPSB2, ITGB2, COL1A1, COL5A3, IL1RN, ALOX5, CLU, MMP9, TNFSF14
Salvage Pathways of Pyrimidine Deoxyribonucleotides	8.44E-01	2.50E-01	NaN	APOBEC3A, TK1
Retinoate Biosynthesis II	5.25E-01	2.50E-01	NaN	RBP7
α-tocopherol Degradation	5.25E-01	2.50E-01	NaN	CYP4F3
Proline Biosynthesis I	5.25E-01	2.50E-01	NaN	PYCR1
Arginine Degradation I (Arginase Pathway)	5.25E-01	2.50E-01	NaN	ARG1
Acetate Conversion to Acetyl-CoA	5.25E-01	2.50E-01	NaN	ACSS1
Inhibition of Matrix Metalloproteases	3.01E+00	2.63E-01	2.53	TIMP3, TIMP4, MMP7, ADAM12, MMP3, MMP16, MMP8, MMP12, MMP25, MMP9
DNA damage-induced 14-3-3σ Signaling	1.73E+00	2.63E-01	NaN	CCNE1, CCNB2, BRCA1, CDK1, CCNB1
TREM1 Signaling	5.43E+00	2.71E-01	-2.524	CXCL8, TREM1, NLRP6, NLRP3, IL10, IL1RL1, CITA, TLR8, LAT2, IL6, TLR9, CXCL3, TLR10, MPO, CCL2, NLRP12, NLR3, TLR7, NLR4

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
DNA Double-Strand Break Repair by Homologous Recombination	1.59E+00	2.86E-01	NaN	LIG1, GEN1, BRCA2, BRCA1
Superpathway of Serine and Glycine Biosynthesis I	9.45E-01	2.86E-01	NaN	PSAT1, PHGDH
GP6 Signaling Pathway	1.11E+01	2.90E-01	0.164	COL8A2, ITGA2B, CAMK4, GP6, COL9A3, COL8A1, COL10A1, COL17A1, COL15A1, ITGB3, COL5A1, COL1A2, COL6A1, PIK3CG, COL22A1, RASGRP2, COL5A2, COL6A2, COL12A1, COL2A1, LAMC3, TLR9, BTK, COL1A1, COL5A3, COL6A3, GRAP2, COL23A1, SYK, LAT, FCER1G, LAMA3, PIK3R6, PIK3CD, COL9A2, LCP2, COL7A1, PRKCB
Primary Immunodeficiency Signaling	4.32E+00	2.95E-01	NaN	BLNK, PTPRC, IL7R, BTK, CD19, LCK, IL2RG, CD3E, ZAP70, IGLL1/IGLL5, CIITA, CD79A, CD8A
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	2.64E+00	3.04E-01	NaN	CCL4, CCL2, IL10, LCN2, CXCL1, DEFB1, CSF3
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	2.55E+00	3.33E-01	NaN	CCL4, CCL2, IL10, CXCL1, IL6, CSF3
Proline Biosynthesis II (from Arginine)	1.07E+00	3.33E-01	NaN	PADI4, PYCR1
Arginine Degradation VI (Arginase 2 Pathway)	1.07E+00	3.33E-01	NaN	ARG1, PYCR1
UDP-N-acetyl-D-glucosamine Biosynthesis II	1.07E+00	3.33E-01	NaN	FMO3, UAP1
Glutathione Biosynthesis	6.32E-01	3.33E-01	NaN	GCLC
L-serine Degradation	6.32E-01	3.33E-01	NaN	SDSL
GADD45 Signaling	3.20E+00	3.68E-01	NaN	CCNE1, GADD45B, CDKN1A, BRCA1, CCND1, CDK1, CCNB1
Estrogen-mediated S-phase Entry	4.55E+00	3.85E-01	-1.897	MYC, CCNA2, CCNE1, E2F7, CDKN1A, CCND1, CDK1, E2F2, E2F8, CDC25A
Creatine-phosphate Biosynthesis	1.22E+00	4.00E-01	NaN	CKB, CKM
Serine Biosynthesis	1.22E+00	4.00E-01	NaN	PSAT1, PHGDH
Tetrapyrrole Biosynthesis II	1.22E+00	4.00E-01	NaN	ALAS2, HMBS
Airway Pathology in Chronic Obstructive Pulmonary Disease	2.56E+00	5.00E-01	NaN	CXCL8, CXCL3, MMP8, MMP9
Heme Degradation	1.42E+00	5.00E-01	NaN	HMOX1, BLVRB
Asparagine Degradation I	7.89E-01	5.00E-01	NaN	ASRGL1
Alanine Degradation III	7.89E-01	5.00E-01	NaN	GPT
Alanine Biosynthesis II	7.89E-01	5.00E-01	NaN	GPT
Glutamate Biosynthesis II	7.89E-01	5.00E-01	NaN	GLUD2
Glutamate Degradation X	7.89E-01	5.00E-01	NaN	GLUD2

Table SI. Continued.

Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules
Glutamate Dependent Acid Resistance	7.89E-01	5.00E-01	NaN	GAD1
Role of IL-17A in Psoriasis	4.47E+00	5.38E-01	NaN	CXCL8, CXCL3, S100A9, CCL20, CXCL1, S100A8, CXCL5
Heme Biosynthesis II	3.39E+00	5.56E-01	NaN	UROD, FECH, ALAS2, CPOX, HMBS
Heme Biosynthesis from Uroporphyrinogen-III I	2.64E+00	7.50E-01	NaN	UROD, FECH, CPOX
Melatonin Degradation III	1.07E+00	1.00E+00	NaN	MPO
Histamine Biosynthesis	1.07E+00	1.00E+00	NaN	HDC
Ingenuity canonical pathways	-log(P-value)	Ratio	z-score	Molecules