

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Aldosterone Signaling in Epithelial Cells	2.26	0.09	1.20	0.06	0.98	0.19
Prolactin Signaling	2.09	0.11	1.65	0.09	2.01	0.26
LPS/IL-1 Mediated Inhibition of RXR Function	2.07	0.08	1.95	0.06	0.97	0.18
NRF2-mediated Oxidative Stress Response	1.98	0.08	2.10	0.07	1.30	0.20
Aryl Hydrocarbon Receptor Signaling	1.98	0.08	1.52	0.06	2.38	0.22
Heme Degradation	1.88	0.18	N/A	N/A	0.85	0.18
Serine Biosynthesis	1.88	0.15	2.07	0.15	0.85	0.15
ErbB4 Signaling	1.68	0.10	1.62	0.09	1.48	0.24
Neuregulin Signaling	1.68	0.09	0.96	0.06	1.81	0.23
ErbB Signaling	1.68	0.10	0.96	0.07	2.76	0.30
Pyruvate Fermentation to Lactate	1.68	0.22	0.75	0.11	0.21	0.11
Estrogen-mediated S-phase Entry	1.58	0.14	1.90	0.14	1.84	0.32
HER-2 Signaling in Breast Cancer	1.53	0.10	0.77	0.06	1.52	0.25
ERK/MAPK Signaling	1.52	0.07	1.02	0.05	0.71	0.18
Superpathway of Serine and Glycine Biosynthesis I	1.51	0.11	1.70	0.11	0.56	0.11
Ceramide Biosynthesis	1.51	0.13	1.70	0.13	0.56	0.13
Superoxide Radicals Degradation	1.51	0.25	N/A	N/A	0.56	0.25
Macropinocytosis Signaling	1.38	0.09	0.94	0.07	1.23	0.22
Mechanisms of Viral Exit from Host Cells	1.38	0.11	N/A	N/A	0.62	0.20
Xenobiotic Metabolism Signaling	1.35	0.06	1.31	0.05	1.43	0.18
Thrombopoietin Signaling	1.32	0.10	1.22	0.08	0.85	0.21
Glutamate Removal from Folates	1.32	0.33	N/A	N/A	0.76	0.33
Sorbitol Degradation I	1.32	0.20	1.41	0.20	0.76	0.20
Sulfite Oxidation IV	1.32	0.25	1.41	0.25	0.76	0.25
Synaptic Long Term Potentiation	1.29	0.08	1.11	0.06	0.91	0.19
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	1.19	0.08	0.26	0.03	0.71	0.18
Stearate Biosynthesis I (Animals)	1.18	0.08	2.15	0.10	1.83	0.22
Leucine Degradation I	1.18	0.08	1.35	0.08	0.32	0.08
Acute Myeloid Leukemia Signaling	1.14	0.09	0.47	0.05	0.82	0.21
Glutathione-mediated Detoxification	1.11	0.07	2.11	0.09	1.73	0.18
Sperm Motility	1.08	0.06	1.20	0.06	0.49	0.15
p38 MAPK Signaling	1.06	0.08	0.86	0.06	N/A	N/A
UDP-D-xylose and UDP-D-glucuronate Biosynthesis	1.03	0.14	1.12	0.14	0.50	0.14
Dolichol and Dolichyl Phosphate Biosynthesis	1.03	0.08	N/A	N/A	0.50	0.08

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Beta-alanine Degradation I	1.03	0.10	1.12	0.10	1.53	0.20
Spermine Biosynthesis	1.03	0.14	1.12	0.14	0.50	0.14
Palmitate Biosynthesis I (Animals)	1.03	0.03	1.12	0.03	0.50	0.03
Sulfate Activation for Sulfonation	1.03	0.13	N/A	N/A	0.50	0.13
Anandamide Degradation	1.03	0.20	1.12	0.20	1.53	0.40
Fatty Acid Biosynthesis Initiation II	1.03	0.14	1.12	0.14	0.50	0.14
Putrescine Biosynthesis III	1.03	0.25	N/A	N/A	0.50	0.25
FXR/RXR Activation	1.02	0.07	1.03	0.06	0.65	0.17
Agrin Interactions at Neuromuscular Junction	1.01	0.09	0.33	0.04	1.28	0.25
Hepatic Cholestasis	0.96	0.06	0.39	0.03	0.69	0.16
Melanocyte Development and Pigmentation Signaling	0.96	0.08	1.36	0.08	1.60	0.24
Leukotriene Biosynthesis	0.95	0.08	2.01	0.12	0.47	0.12
Gamma-glutamyl Cycle	0.95	0.07	2.01	0.11	0.86	0.15
P2Y Purigenic Receptor Signaling Pathway	0.94	0.07	1.06	0.06	1.16	0.20
Thyroid Cancer Signaling	0.90	0.10	1.74	0.12	0.86	0.24
CDK5 Signaling	0.90	0.07	0.61	0.05	1.44	0.23
Cholesterol Biosynthesis I	0.90	0.05	2.93	0.10	0.41	0.08
Cholesterol Biosynthesis II (via 24,25-dihydrostanosterol)	0.90	0.05	2.93	0.10	0.41	0.08
Cholesterol Biosynthesis III (via Desmosterol)	0.90	0.05	2.93	0.10	0.41	0.08
Antiproliferative Role of TOB in T Cell Signaling	0.89	0.12	N/A	N/A	0.55	0.23
D-myo-inositol (1,4,5)-Trisphosphate Biosynthesis	0.89	0.08	0.58	0.05	0.55	0.16
Virus Entry via Endocytic Pathways	0.88	0.07	0.60	0.05	0.77	0.19
Actin Nucleation by ARP-WASP Complex	0.88	0.08	0.77	0.06	1.04	0.21
ErbB2-ErbB3 Signaling	0.88	0.08	0.43	0.05	0.81	0.22
NF-kappaB Activation by Viruses	0.88	0.07	0.28	0.04	0.78	0.20
UVC-Induced MAPK Signaling	0.87	0.10	0.68	0.07	1.77	0.31
L-carnitine Biosynthesis	0.86	0.08	N/A	N/A	0.36	0.08
Glutathione Biosynthesis	0.86	0.09	0.95	0.09	0.36	0.09
Tetrahydrobiopterin Biosynthesis I	0.86	0.09	0.95	0.09	0.36	0.09
Glutathione Redox Reactions II	0.86	0.14	N/A	N/A	0.36	0.14
D-glucuronate Degradation I	0.86	0.08	0.95	0.08	1.10	0.15
Spermidine Biosynthesis I	0.86	0.13	0.95	0.13	0.36	0.13
Tetrahydrobiopterin Biosynthesis II	0.86	0.08	0.95	0.08	0.36	0.08
4-aminobutyrate Degradation I	0.86	0.10	0.95	0.10	0.36	0.10

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Epithelial Adherens Junction Signaling	0.86	0.07	0.53	0.05	N/A	N/A
Superpathway of Cholesterol Biosynthesis	0.86	0.03	1.72	0.05	0.77	0.08
Glioma Invasiveness Signaling	0.86	0.08	0.42	0.05	0.99	0.23
Corticotropin Releasing Hormone Signaling	0.86	0.06	0.41	0.04	1.04	0.18
VEGF Family Ligand-Receptor Interactions	0.84	0.07	1.18	0.07	0.74	0.19
Dopamine Receptor Signaling	0.82	0.06	0.25	0.03	0.86	0.18
Cell Cycle: G1/S Checkpoint Regulation	0.81	0.08	0.72	0.06	1.73	0.26
D-myo-inositol-5-phosphate Metabolism	0.81	0.06	0.67	0.04	0.50	0.15
Chronic Myeloid Leukemia Signaling	0.81	0.07	0.55	0.05	1.20	0.21
Fatty Acid Beta-oxidation I	0.79	0.07	0.51	0.04	2.72	0.27
PDGF Signaling	0.78	0.07	0.46	0.05	0.34	0.17
nNOS Signaling in Neurons	0.77	0.08	0.60	0.06	N/A	N/A
Wnt/Beta-catenin Signaling	0.76	0.06	0.52	0.05	0.73	0.19
Pyridoxal 5'-phosphate Salvage Pathway	0.75	0.07	0.66	0.05	0.99	0.21
Glutathione Redox Reactions I	0.75	0.08	0.90	0.08	0.90	0.21
14-3-3-mediated Signaling	0.73	0.07	0.56	0.05	0.63	0.19
Sertoli Cell-Sertoli Cell Junction Signaling	0.70	0.06	0.48	0.04	N/A	N/A
Germ Cell-Sertoli Cell Junction Signaling	0.70	0.06	0.43	0.04	0.42	0.17
Retinol Biosynthesis	0.70	0.05	0.45	0.03	N/A	N/A
HGF Signaling	0.70	0.07	0.27	0.04	1.11	0.22
Cholecystokinin/Gastrin-mediated Signaling	0.70	0.07	0.27	0.04	0.63	0.19
Growth Hormone Signaling	0.67	0.07	0.33	0.04	0.66	0.18
Valine Degradation I	0.67	0.06	0.82	0.06	0.42	0.11
D-myo-inositol (1,4,5)-trisphosphate Degradation	0.67	0.09	0.29	0.04	0.42	0.17
Pyrimidine Ribonucleotides Interconversion	0.67	0.06	0.29	0.03	2.18	0.24
Superpathway of Inositol Phosphate Compounds	0.66	0.05	0.45	0.04	0.54	0.15
Tetrahydrofolate Salvage from 5,10-methenyltetrahydrofolate	0.66	0.10	0.75	0.10	0.68	0.20
Selenocysteine Biosynthesis II (Archaea and Eukaryotes)	0.66	0.06	N/A	N/A	0.68	0.12
Tyrosine Degradation I	0.66	0.07	3.27	0.20	2.42	0.27
Glutamate Degradation III (via 4-aminobutyrate)	0.66	0.08	0.75	0.08	0.21	0.08
Folate Polyglutamylation	0.66	0.06	0.75	0.06	0.21	0.06
Amyloid Processing	0.66	0.07	0.90	0.07	0.45	0.18
Erythropoietin Signaling	0.66	0.06	0.59	0.05	0.99	0.21
JAK/Stat Signaling	0.66	0.07	0.32	0.04	0.78	0.21

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Oncostatin M Signaling	0.65	0.09	0.85	0.09	0.66	0.23
Alpha-Adrenergic Signaling	0.65	0.06	0.38	0.04	1.07	0.19
GDNF Family Ligand-Receptor Interactions	0.64	0.07	1.81	0.10	1.73	0.26
Endometrial Cancer Signaling	0.64	0.07	0.88	0.07	1.05	0.23
1D-myo-inositol Hexakisphosphate Biosynthesis II (Mammalian)	0.63	0.07	0.78	0.07	0.66	0.18
D-myo-inositol (1,3,4)-trisphosphate Biosynthesis	0.63	0.08	0.28	0.04	0.38	0.16
Factors Promoting Cardiogenesis in Vertebrates	0.63	0.06	N/A	N/A	0.28	0.16
Fc Epsilon RI Signaling	0.63	0.06	0.97	0.06	1.15	0.21
Apoptosis Signaling	0.60	0.06	0.60	0.05	1.16	0.22
Pyrimidine Ribonucleotides De Novo Biosynthesis	0.60	0.04	0.26	0.02	1.86	0.17
Glioblastoma Multiforme Signaling	0.60	0.05	0.73	0.05	1.36	0.20
PPAR-alpha/RXR-alpha Activation	0.59	0.05	0.36	0.04	1.09	0.18
UDP-N-acetyl-D-glucosamine Biosynthesis II	0.59	0.06	0.68	0.06	N/A	N/A
Zymosterol Biosynthesis	0.59	0.05	2.98	0.14	0.56	0.09
Pregnenolone Biosynthesis	0.59	0.08	0.68	0.08	0.56	0.15
PEDF Signaling	0.59	0.06	N/A	N/A	1.03	0.22
Regulation of Cellular Mechanics by Calpain Protease	0.58	0.06	1.25	0.07	0.90	0.18
Toll-like Receptor Signaling	0.58	0.06	N/A	N/A	0.49	0.18
3-phosphoinositide Degradation	0.58	0.05	0.67	0.04	0.29	0.14
Notch Signaling	0.58	0.07	1.28	0.09	0.34	0.16
Renin-Angiotensin Signaling	0.58	0.06	0.39	0.04	1.59	0.22
Fc-gamma Receptor-mediated Phagocytosis in Macrophages and Monocytes	0.58	0.06	0.34	0.04	0.58	0.18
Polyamine Regulation in Colon Cancer	0.57	0.07	0.25	0.03	0.30	0.14
NAD Salvage Pathway II	0.57	0.06	0.71	0.06	N/A	N/A
LPS-stimulated MAPK Signaling	0.56	0.06	0.27	0.04	0.94	0.21
Dermatan Sulfate Biosynthesis (Late Stages)	0.56	0.06	1.24	0.09	1.57	0.26
Endothelin-1 Signaling	0.55	0.05	0.72	0.05	1.87	0.21
Glioma Signaling	0.55	0.05	0.84	0.05	1.43	0.21
Tec Kinase Signaling	0.55	0.05	0.29	0.03	0.47	0.16
Thrombin Signaling	0.54	0.05	0.54	0.04	2.24	0.22
Type II Diabetes Mellitus Signaling	0.54	0.04	N/A	N/A	1.93	0.18
HMGB1 Signaling	0.54	0.06	N/A	N/A	0.61	0.19
Mouse Embryonic Stem Cell Pluripotency	0.54	0.06	0.31	0.04	0.67	0.19
RAR Activation	0.54	0.05	N/A	N/A	0.34	0.16

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Gap Junction Signaling	0.53	0.05	N/A	N/A	0.56	0.17
Transcriptional Regulatory Network in Embryonic Stem Cells	0.52	0.08	0.70	0.08	N/A	N/A
Nicotine Degradation II	0.52	0.04	0.34	0.02	0.42	0.10
Fc-gamma-RIIB Signaling in B Lymphocytes	0.50	0.05	1.14	0.07	1.77	0.22
Chondroitin Sulfate Biosynthesis (Late Stages)	0.50	0.06	1.14	0.07	1.33	0.22
Role of NFAT in Cardiac Hypertrophy	0.50	0.05	N/A	N/A	1.23	0.18
Synaptic Long Term Depression	0.50	0.05	1.13	0.06	0.84	0.18
Integrin Signaling	0.49	0.05	0.49	0.04	0.87	0.19
Triacylglycerol Degradation	0.49	0.06	0.63	0.06	0.65	0.19
Superpathway of D-myo-inositol (1,4,5)-trisphosphate Metabolism	0.49	0.06	0.21	0.03	0.40	0.15
Phosphatidylethanolamine Biosynthesis II	0.49	0.06	0.57	0.06	N/A	N/A
Histidine Degradation III	0.49	0.06	0.57	0.06	N/A	N/A
ERK5 Signaling	0.48	0.06	1.56	0.09	0.48	0.19
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	0.48	0.06	0.31	0.04	1.97	0.29
CCR5 Signaling in Macrophages	0.47	0.04	0.38	0.03	0.31	0.12
Estrogen-Dependent Breast Cancer Signaling	0.47	0.06	1.07	0.07	1.04	0.21
p70S6K Signaling	0.47	0.05	1.06	0.06	1.36	0.22
Prostate Cancer Signaling	0.47	0.05	1.05	0.06	1.30	0.20
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	0.47	0.05	N/A	N/A	0.40	0.15
HIF1-alpha Signaling	0.47	0.06	0.47	0.05	0.60	0.19
Dopamine-DARPP32 Feedback in cAMP Signaling	0.46	0.05	0.39	0.04	0.53	0.16
Hypoxia Signaling in the Cardiovascular System	0.46	0.06	0.37	0.05	N/A	N/A
GM-CSF Signaling	0.46	0.06	0.66	0.06	1.52	0.25
Natural Killer Cell Signaling	0.45	0.05	0.47	0.04	0.54	0.16
GABA Receptor Signaling	0.45	0.05	0.29	0.04	N/A	N/A
Acyl-CoA Hydrolysis	0.45	0.07	0.53	0.07	0.32	0.13
Oleate Biosynthesis II (Animals)	0.45	0.06	1.35	0.11	1.99	0.28
Histidine Degradation VI	0.45	0.05	0.53	0.05	0.32	0.10
UDP-N-acetyl-D-galactosamine Biosynthesis II	0.45	0.04	1.35	0.08	0.32	0.08
Folate Transformations I	0.45	0.03	0.53	0.03	0.32	0.06
Salvage Pathways of Pyrimidine Ribonucleotides	0.44	0.05	0.41	0.04	0.99	0.19
Heparan Sulfate Biosynthesis (Late Stages)	0.43	0.05	1.02	0.07	1.07	0.20
TGF-beta Signaling	0.43	0.06	N/A	N/A	0.45	0.18
Bladder Cancer Signaling	0.42	0.05	0.65	0.05	0.91	0.21

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Ketogenesis	0.41	0.05	N/A	N/A	0.62	0.14
Dolichyl-diphosphooligosaccharide Biosynthesis	0.41	0.03	N/A	N/A	N/A	N/A
TNFR2 Signaling	0.41	0.06	N/A	N/A	0.71	0.21
NGF Signaling	0.40	0.05	0.66	0.05	0.73	0.19
FAK Signaling	0.40	0.05	0.62	0.05	1.25	0.21
UVA-Induced MAPK Signaling	0.40	0.05	0.62	0.05	1.49	0.24
Melatonin Signaling	0.39	0.05	0.32	0.04	N/A	N/A
GNRH Signaling	0.38	0.05	0.26	0.03	1.20	0.19
Breast Cancer Regulation by Stathmin1	0.38	0.05	0.36	0.04	0.70	0.18
Ubiquinol-10 Biosynthesis (Eukaryotic)	0.38	0.03	0.45	0.03	0.54	0.10
Methylglyoxal Degradation III	0.38	0.04	1.19	0.09	0.98	0.17
G Beta Gamma Signaling	0.38	0.04	0.35	0.03	0.95	0.17
Chondroitin Sulfate Biosynthesis	0.37	0.04	0.92	0.06	0.85	0.17
Superpathway of Methionine Degradation	0.37	0.03	N/A	N/A	N/A	N/A
Serotonin Receptor Signaling	0.37	0.04	N/A	N/A	N/A	N/A
Calcium-induced T Lymphocyte Apoptosis	0.36	0.04	0.24	0.03	N/A	N/A
IL-3 Signaling	0.36	0.05	0.29	0.04	0.37	0.18
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	0.36	0.04	0.38	0.04	0.38	0.14
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	0.36	0.04	0.38	0.04	0.38	0.14
G Protein Signaling Mediated by Tubby	0.35	0.05	0.47	0.05	N/A	N/A
Mevalonate Pathway I	0.35	0.04	N/A	N/A	0.47	0.11
Guanosine Nucleotides Degradation III	0.35	0.05	0.42	0.05	N/A	N/A
IL-1 Signaling	0.35	0.05	N/A	N/A	0.67	0.18
Dermatan Sulfate Biosynthesis	0.35	0.04	0.88	0.06	0.76	0.17
FLT3 Signaling in Hematopoietic Progenitor Cells	0.35	0.05	0.86	0.07	0.48	0.18
Small Cell Lung Cancer Signaling	0.35	0.04	0.28	0.03	1.27	0.20
p53 Signaling	0.34	0.05	N/A	N/A	0.64	0.20
Circadian Rhythm Signaling	0.34	0.05	0.90	0.08	N/A	N/A
Role of JAK2 in Hormone-like Cytokine Signaling	0.34	0.06	N/A	N/A	0.35	0.17
Semaphorin Signaling in Neurons	0.34	0.06	N/A	N/A	1.00	0.25
Heparan Sulfate Biosynthesis	0.34	0.04	0.85	0.05	0.72	0.16
Cardiac Hypertrophy Signaling	0.33	0.05	N/A	N/A	0.89	0.18
Phospholipase C Signaling	0.33	0.04	0.88	0.05	0.68	0.16
Ephrin B Signaling	0.33	0.05	N/A	N/A	0.74	0.20

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Phospholipases	0.32	0.05	0.83	0.06	0.26	0.14
Fatty Acid Activation	0.32	0.05	0.40	0.05	0.76	0.21
Thyroid Hormone Metabolism II (via Conjugation and/or Degradation)	0.32	0.02	0.40	0.02	0.76	0.08
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I	0.32	0.03	0.40	0.03	0.76	0.12
Urate Biosynthesis/Inosine 5'-phosphate Degradation	0.32	0.05	0.40	0.05	N/A	N/A
Bile Acid Biosynthesis, Neutral Pathway	0.32	0.02	1.06	0.03	0.41	0.05
Nicotine Degradation III	0.32	0.03	N/A	N/A	0.29	0.08
Protein Kinase A Signaling	0.32	0.05	N/A	N/A	N/A	N/A
IGF-1 Signaling	0.31	0.05	N/A	N/A	N/A	N/A
ILK Signaling	0.31	0.05	0.42	0.04	0.30	0.16
3-phosphoinositide Biosynthesis	0.31	0.04	N/A	N/A	0.51	0.15
Melatonin Degradation I	0.31	0.03	N/A	N/A	0.66	0.13
Telomerase Signaling	0.31	0.05	0.29	0.04	0.85	0.20
nNOS Signaling in Skeletal Muscle Cells	0.30	0.03	0.37	0.03	0.35	0.10
Isoleucine Degradation I	0.30	0.03	0.37	0.03	0.35	0.10
Phenylalanine Degradation IV (Mammalian, via Side Chain)	0.30	0.03	0.37	0.03	N/A	N/A
Colanic Acid Building Blocks Biosynthesis	0.30	0.03	1.00	0.06	1.11	0.14
Cyclins and Cell Cycle Regulation	0.29	0.04	0.46	0.04	1.46	0.23
Neuropathic Pain Signaling In Dorsal Horn Neurons	0.29	0.05	N/A	N/A	N/A	N/A
Acute Phase Response Signaling	0.29	0.04	N/A	N/A	N/A	N/A
IL-8 Signaling	0.29	0.04	N/A	N/A	N/A	N/A
PXR/RXR Activation	0.28	0.03	N/A	N/A	0.57	0.14
The Visual Cycle	0.28	0.04	N/A	N/A	N/A	N/A
Adenosine Nucleotides Degradation II	0.28	0.04	0.35	0.04	0.31	0.12
Methionine Degradation I (to Homocysteine)	0.28	0.04	N/A	N/A	N/A	N/A
Myc Mediated Apoptosis Signaling	0.27	0.05	0.41	0.05	1.20	0.25
Death Receptor Signaling	0.27	0.05	N/A	N/A	0.54	0.19
Mitochondrial L-carnitine Shuttle Pathway	0.26	0.05	0.33	0.05	0.90	0.23
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)	0.26	0.03	N/A	N/A	0.53	0.11
Cellular Effects of Sildenafil (Viagra)	0.26	0.04	N/A	N/A	0.34	0.15
Estrogen Receptor Signaling	0.26	0.04	0.47	0.04	N/A	N/A
Serotonin Degradation	0.26	0.03	N/A	N/A	N/A	N/A
Role of BRCA1 in DNA Damage Response	0.25	0.05	0.39	0.05	1.09	0.23
Rac Signaling	0.25	0.04	N/A	N/A	0.50	0.16

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Docosahexaenoic Acid (DHA) Signaling	0.25	0.04	N/A	N/A	0.92	0.20
Neuroprotective Role of THOP1 in Alzheimer's Disease	0.25	0.04	N/A	N/A	N/A	N/A
Superpathway of Melatonin Degradation	0.25	0.03	N/A	N/A	0.45	0.10
Cardiomyocyte Differentiation via BMP Receptors	0.25	0.05	N/A	N/A	N/A	N/A
Granzyme A Signaling	0.25	0.05	N/A	N/A	N/A	N/A
Gamma-linolenate Biosynthesis II (Animals)	0.25	0.04	0.86	0.08	1.24	0.25
Cysteine Biosynthesis III (mammalia)	0.25	0.03	N/A	N/A	N/A	N/A
IL-15 Signaling	0.25	0.04	N/A	N/A	0.31	0.16
Antiproliferative Role of Somatostatin Receptor 2	0.25	0.04	N/A	N/A	0.31	0.16
Role of RIG1-like Receptors in Antiviral Innate Immunity	0.24	0.04	N/A	N/A	N/A	N/A
Purine Nucleotides Degradation II (Aerobic)	0.23	0.03	0.29	0.03	N/A	N/A
Endoplasmic Reticulum Stress Pathway	0.23	0.06	0.82	0.11	N/A	N/A
Lipid Antigen Presentation by CD1	0.22	0.04	N/A	N/A	N/A	N/A
DNA Methylation and Transcriptional Repression Signaling	0.20	0.04	N/A	N/A	0.34	0.17
Axonal Guidance Signaling	N/A	N/A	N/A	N/A	0.29	0.15
Amyotrophic Lateral Sclerosis Signaling	N/A	N/A	0.50	0.04	N/A	N/A
Actin Cytoskeleton Signaling	N/A	N/A	N/A	N/A	0.47	0.16
Coagulation System	N/A	N/A	0.41	0.05	N/A	N/A
Mitochondrial Dysfunction	N/A	N/A	0.59	0.04	1.48	0.17
Ceramide Signaling	N/A	N/A	0.45	0.04	0.95	0.20
Tight Junction Signaling	N/A	N/A	0.29	0.04	N/A	N/A
TR/RXR Activation	N/A	N/A	0.68	0.05	0.48	0.17
Regulation of Actin-based Motility by Rho	N/A	N/A	N/A	N/A	0.50	0.18
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	N/A	N/A	N/A	N/A	0.73	0.18
TREM1 Signaling	N/A	N/A	N/A	N/A	1.77	0.23
MIF Regulation of Innate Immunity	N/A	N/A	0.35	0.04	0.49	0.16
Role of NFAT in Regulation of the Immune Response	N/A	N/A	0.26	0.03	0.40	0.14
CD40 Signaling	N/A	N/A	N/A	N/A	0.77	0.20
Lymphotoxin-beta Receptor Signaling	N/A	N/A	N/A	N/A	0.34	0.16
IL-17 Signaling	N/A	N/A	0.28	0.04	1.22	0.24
CXCR4 Signaling	N/A	N/A	N/A	N/A	1.85	0.22
Induction of Apoptosis by HIV1	N/A	N/A	N/A	N/A	0.51	0.19
B Cell Activating Factor Signaling	N/A	N/A	N/A	N/A	0.26	0.16
IL-9 Signaling	N/A	N/A	N/A	N/A	0.43	0.18

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
CCR3 Signaling in Eosinophils	N/A	N/A	0.37	0.04	0.59	0.17
CD28 Signaling in T Helper Cells	N/A	N/A	N/A	N/A	0.27	0.14
Dendritic Cell Maturation	N/A	N/A	N/A	N/A	0.50	0.14
Reelin Signaling in Neurons	N/A	N/A	0.24	0.04	1.26	0.23
Angiopietin Signaling	N/A	N/A	0.34	0.04	1.34	0.23
CNTF Signaling	N/A	N/A	0.57	0.05	0.55	0.18
Molecular Mechanisms of Cancer	N/A	N/A	0.27	0.03	1.82	0.19
Cell Cycle Regulation by BTG Family Proteins	N/A	N/A	0.41	0.06	0.61	0.22
Role of CHK Proteins in Cell Cycle Checkpoint Control	N/A	N/A	0.45	0.05	0.64	0.21
ATM Signaling	N/A	N/A	0.40	0.05	0.51	0.20
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	N/A	N/A	0.28	0.04	0.31	0.18
CREB Signaling in Neurons	N/A	N/A	0.48	0.04	0.64	0.16
Melanoma Signaling	N/A	N/A	0.31	0.04	0.76	0.22
Renal Cell Carcinoma Signaling	N/A	N/A	N/A	N/A	0.94	0.22
Type I Diabetes Mellitus Signaling	N/A	N/A	N/A	N/A	0.35	0.15
Non-Small Cell Lung Cancer Signaling	N/A	N/A	0.35	0.04	2.75	0.27
G-alpha-12/13 Signaling	N/A	N/A	N/A	N/A	0.48	0.18
Colorectal Cancer Metastasis Signaling	N/A	N/A	N/A	N/A	0.82	0.18
mTOR Signaling	N/A	N/A	N/A	N/A	0.82	0.17
Pancreatic Adenocarcinoma Signaling	N/A	N/A	N/A	N/A	1.04	0.20
Sphingosine-1-phosphate Signaling	N/A	N/A	N/A	N/A	1.08	0.20
April Mediated Signaling	N/A	N/A	N/A	N/A	0.31	0.16
AMPK Signaling	N/A	N/A	N/A	N/A	0.36	0.14
PAK Signaling	N/A	N/A	N/A	N/A	1.16	0.20
Hereditary Breast Cancer Signaling	N/A	N/A	0.38	0.04	0.77	0.18
RhoA Signaling	N/A	N/A	N/A	N/A	0.58	0.18
Ovarian Cancer Signaling	N/A	N/A	N/A	N/A	0.83	0.19
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	N/A	N/A	0.41	0.04	0.45	0.15
Regulation of eIF4 and p70S6K Signaling	N/A	N/A	N/A	N/A	0.37	0.14
Leptin Signaling in Obesity	N/A	N/A	N/A	N/A	0.74	0.19
RANK Signaling in Osteoclasts	N/A	N/A	N/A	N/A	0.41	0.17
PKC-delta Signaling in T Lymphocytes	N/A	N/A	N/A	N/A	0.61	0.15
TNFR1 Signaling	N/A	N/A	N/A	N/A	1.30	0.25
Role of MAPK Signaling in the Pathogenesis of Influenza	N/A	N/A	0.63	0.06	0.94	0.22

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
PI3K Signaling in B Lymphocytes	N/A	N/A	0.49	0.04	1.24	0.20
MIF-mediated Glucocorticoid Regulation	N/A	N/A	0.47	0.05	0.38	0.14
Assembly of RNA Polymerase II Complex	N/A	N/A	0.25	0.04	N/A	N/A
Role of Tissue Factor in Cancer	N/A	N/A	N/A	N/A	1.24	0.22
IL-17A Signaling in Fibroblasts	N/A	N/A	N/A	N/A	0.87	0.23
Role of IL-17F in Allergic Inflammatory Airway Diseases	N/A	N/A	0.68	0.06	N/A	N/A
Paxillin Signaling	N/A	N/A	0.50	0.05	1.00	0.20
Signaling by Rho Family GTPases	N/A	N/A	N/A	N/A	0.83	0.17
RhoGDI Signaling	N/A	N/A	N/A	N/A	0.58	0.17
eNOS Signaling	N/A	N/A	N/A	N/A	0.82	0.17
Ephrin A Signaling	N/A	N/A	N/A	N/A	0.35	0.17
Netrin Signaling	N/A	N/A	N/A	N/A	0.98	0.18
Bupropion Degradation	N/A	N/A	0.21	0.03	0.40	0.15
Estrogen Biosynthesis	N/A	N/A	N/A	N/A	0.40	0.14
Triacylglycerol Biosynthesis	N/A	N/A	0.44	0.04	0.29	0.13
Glycolysis I	N/A	N/A	0.24	0.03	0.27	0.10
Gluconeogenesis I	N/A	N/A	0.23	0.02	0.24	0.09
Noradrenaline and Adrenaline Degradation	N/A	N/A	0.47	0.04	N/A	N/A
Acetone Degradation I (to Methylglyoxal)	N/A	N/A	0.60	0.06	0.60	0.17
Ethanol Degradation II	N/A	N/A	0.51	0.05	N/A	N/A
Antioxidant Action of Vitamin C	N/A	N/A	0.55	0.05	0.84	0.19
G-alpha-q Signaling	N/A	N/A	N/A	N/A	0.59	0.17
UVB-Induced MAPK Signaling	N/A	N/A	0.23	0.04	1.05	0.24
EGF Signaling	N/A	N/A	N/A	N/A	0.30	0.16
SAPK/JNK Signaling	N/A	N/A	N/A	N/A	0.49	0.17
Cardiac Beta-adrenergic Signaling	N/A	N/A	N/A	N/A	0.39	0.16
Protein Ubiquitination Pathway	N/A	N/A	0.32	0.04	N/A	N/A
FGF Signaling	N/A	N/A	N/A	N/A	0.91	0.21
IL-4 Signaling	N/A	N/A	0.31	0.04	N/A	N/A
B Cell Receptor Signaling	N/A	N/A	0.26	0.04	0.69	0.18
Insulin Receptor Signaling	N/A	N/A	0.27	0.04	0.29	0.16
Chemokine Signaling	N/A	N/A	0.32	0.04	0.44	0.18
Neurotrophin/TRK Signaling	N/A	N/A	0.94	0.07	0.44	0.17
Sonic Hedgehog Signaling	N/A	N/A	N/A	N/A	0.24	0.15

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
PPAR Signaling	N/A	N/A	N/A	N/A	0.31	0.15
NF-kappaB Signaling	N/A	N/A	N/A	N/A	0.96	0.19
VEGF Signaling	N/A	N/A	N/A	N/A	0.27	0.15
T Cell Receptor Signaling	N/A	N/A	N/A	N/A	0.36	0.16
BMP signaling pathway	N/A	N/A	0.28	0.04	0.45	0.18
Eicosanoid Signaling	N/A	N/A	0.40	0.04	N/A	N/A
Ephrin Receptor Signaling	N/A	N/A	N/A	N/A	0.37	0.15
IL-22 Signaling	N/A	N/A	N/A	N/A	0.65	0.24
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	N/A	N/A	N/A	N/A	0.29	0.09
4-1BB Signaling in T Lymphocytes	N/A	N/A	N/A	N/A	0.35	0.17
Mitotic Roles of Polo-Like Kinase	N/A	N/A	N/A	N/A	0.99	0.21
RAN Signaling	N/A	N/A	N/A	N/A	1.00	0.21
Granzyme B Signaling	N/A	N/A	N/A	N/A	0.90	0.31
B Cell Development	N/A	N/A	0.26	0.03	N/A	N/A
TWEAK Signaling	N/A	N/A	N/A	N/A	0.47	0.18
Inhibition of Angiogenesis by TSP1	N/A	N/A	N/A	N/A	0.47	0.18
Tumoricidal Function of Hepatic Natural Killer Cells	N/A	N/A	N/A	N/A	0.98	0.29
Cell Cycle Control of Chromosomal Replication	N/A	N/A	0.71	0.06	4.38	0.39
Mismatch Repair in Eukaryotes	N/A	N/A	N/A	N/A	0.31	0.13
DNA Double-Strand Break Repair by Homologous Recombination	N/A	N/A	N/A	N/A	0.35	0.18
DNA Double-Strand Break Repair by Non-Homologous End Joining	N/A	N/A	N/A	N/A	0.68	0.21
IL-17A Signaling in Airway Cells	N/A	N/A	N/A	N/A	0.94	0.21
Role of IL-17A in Arthritis	N/A	N/A	N/A	N/A	0.90	0.21
IL-17A Signaling in Gastric Cells	N/A	N/A	N/A	N/A	0.90	0.28
Role of IL-17A in Psoriasis	N/A	N/A	N/A	N/A	0.41	0.23
Differential Regulation of Cytokine Production in Macrophages & T Helper Cells by IL-17A & IL-17F	N/A	N/A	N/A	N/A	0.24	0.17
Role of JAK family kinases in IL-6-type Cytokine Signaling	N/A	N/A	N/A	N/A	0.90	0.26
Embryonic Stem Cell Differentiation into Cardiac Lineages	N/A	N/A	N/A	N/A	0.32	0.20
Dopamine Degradation	N/A	N/A	0.28	0.03	0.38	0.11
Glutaryl-CoA Degradation	N/A	N/A	N/A	N/A	0.54	0.13
Protein Citrullination	N/A	N/A	N/A	N/A	0.85	0.33
CDP-diacylglycerol Biosynthesis I	N/A	N/A	0.35	0.04	0.31	0.11
Superpathway of Citrulline Metabolism	N/A	N/A	N/A	N/A	0.35	0.08
Pentose Phosphate Pathway (Oxidative Branch)	N/A	N/A	N/A	N/A	0.28	0.09

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Thio-molybdenum Cofactor Biosynthesis	N/A	N/A	N/A	N/A	0.76	0.20
PRPP Biosynthesis I	N/A	N/A	N/A	N/A	0.36	0.14
Methylglyoxal Degradation I	N/A	N/A	0.95	0.09	1.10	0.18
Guanine and Guanosine Salvage I	N/A	N/A	N/A	N/A	0.50	0.11
Heme Biosynthesis from Uroporphyrinogen-III I	N/A	N/A	N/A	N/A	0.28	0.09
Tetrapyrrole Biosynthesis II	N/A	N/A	N/A	N/A	0.21	0.08
5-aminoimidazole Ribonucleotide Biosynthesis I	N/A	N/A	N/A	N/A	0.36	0.06
CMP-N-acetylneuraminate Biosynthesis I (Eukaryotes)	N/A	N/A	N/A	N/A	0.21	0.06
All-trans-decaprenyl Diphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.50	0.17
Thioredoxin Pathway	N/A	N/A	0.68	0.13	0.56	0.25
Coenzyme A Biosynthesis	N/A	N/A	N/A	N/A	1.10	0.14
S-methyl-5'-thioadenosine Degradation II	N/A	N/A	N/A	N/A	0.76	0.17
Proline Degradation	N/A	N/A	N/A	N/A	1.53	0.29
Thyronamine and Iodothyronamine Metabolism	N/A	N/A	0.95	0.08	0.36	0.08
Catecholamine Biosynthesis	N/A	N/A	N/A	N/A	0.28	0.07
L-DOPA Degradation	N/A	N/A	1.12	0.08	0.50	0.08
Calcium Transport I	N/A	N/A	N/A	N/A	0.32	0.15
Phosphatidylglycerol Biosynthesis II (Non-plastidic)	N/A	N/A	0.33	0.03	0.24	0.09
Glycine Cleavage Complex	N/A	N/A	N/A	N/A	0.21	0.07
Pentose Phosphate Pathway	N/A	N/A	N/A	N/A	0.27	0.09
Taurine Biosynthesis	N/A	N/A	N/A	N/A	0.50	0.11
Citrulline Biosynthesis	N/A	N/A	N/A	N/A	0.38	0.08
Adenine and Adenosine Salvage III	N/A	N/A	N/A	N/A	1.17	0.19
Inosine-5'-phosphate Biosynthesis II	N/A	N/A	0.95	0.06	0.36	0.06
Heme Biosynthesis II	N/A	N/A	N/A	N/A	0.32	0.09
4-hydroxyproline Degradation I	N/A	N/A	N/A	N/A	0.76	0.07
Myo-inositol Biosynthesis	N/A	N/A	N/A	N/A	0.28	0.13
Purine Ribonucleosides Degradation to Ribose-1-phosphate	N/A	N/A	N/A	N/A	0.56	0.11
Tryptophan Degradation III (Eukaryotic)	N/A	N/A	N/A	N/A	0.38	0.08
Geranylgeranyldiphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.28	0.13
Ketolysis	N/A	N/A	N/A	N/A	0.38	0.11
Biotin-carboxyl Carrier Protein Assembly	N/A	N/A	0.84	0.07	0.28	0.07
Purine Nucleotides De Novo Biosynthesis II	N/A	N/A	0.45	0.02	0.54	0.07
Thyroid Hormone Biosynthesis	N/A	N/A	0.95	0.14	0.36	0.14

Table S25. Subtype 1 (LAR) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Glycine Degradation (Creatine Biosynthesis)	N/A	N/A	1.12	0.11	0.50	0.11
Thyroid Hormone Metabolism I (via Deiodination)	N/A	N/A	0.95	0.08	0.36	0.08
Methylglyoxal Degradation VI	N/A	N/A	1.41	0.08	0.76	0.08
Arginine Degradation I (Arginase Pathway)	N/A	N/A	N/A	N/A	0.28	0.08
1D-myo-inositol Hexakisphosphate Biosynthesis V (from Ins(1,3,4)P3)	N/A	N/A	0.95	0.10	0.36	0.10
Trans, trans-farnesyl Diphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.28	0.10
Citrulline-Nitric Oxide Cycle	N/A	N/A	N/A	N/A	0.21	0.06
Asparagine Biosynthesis I	N/A	N/A	N/A	N/A	0.76	0.13
Glucocorticoid Biosynthesis	N/A	N/A	N/A	N/A	0.38	0.09
Galactose Degradation I (Leloir Pathway)	N/A	N/A	0.75	0.06	0.21	0.06
Mineralocorticoid Biosynthesis	N/A	N/A	N/A	N/A	0.46	0.09
dTMP De Novo Biosynthesis	N/A	N/A	N/A	N/A	0.21	0.07
Oxidative Ethanol Degradation III	N/A	N/A	0.35	0.03	N/A	N/A
Ethanol Degradation IV	N/A	N/A	0.31	0.03	N/A	N/A
N-acetylglucosamine Degradation II	N/A	N/A	N/A	N/A	0.28	0.08
Phenylalanine Degradation I (Aerobic)	N/A	N/A	N/A	N/A	0.28	0.08
4-hydroxybenzoate Biosynthesis	N/A	N/A	N/A	N/A	0.76	0.05
GDP-mannose Biosynthesis	N/A	N/A	N/A	N/A	0.56	0.15
D-mannose Degradation	N/A	N/A	N/A	N/A	0.76	0.33
Tyrosine Biosynthesis IV	N/A	N/A	N/A	N/A	0.36	0.13
DNA damage-induced 14-3-3 Sigma Signaling	N/A	N/A	N/A	N/A	0.38	0.19
UDP-N-acetyl-D-galactosamine Biosynthesis I	N/A	N/A	1.41	0.33	0.76	0.33
L-serine Degradation	N/A	N/A	N/A	N/A	0.36	0.17
4-hydroxyphenylpyruvate Biosynthesis	N/A	N/A	N/A	N/A	0.76	0.20
Acetate Conversion to Acetyl-CoA	N/A	N/A	0.75	0.09	0.21	0.09
Fatty Acid Beta-oxidation III (Unsaturated, Odd Number)	N/A	N/A	N/A	N/A	1.10	0.40
Glutamine Degradation I	N/A	N/A	N/A	N/A	0.50	0.20
N-acetylglucosamine Degradation I	N/A	N/A	N/A	N/A	0.36	0.13
Vitamin-C Transport	N/A	N/A	0.37	0.05	0.68	0.18
Parkinson's Signaling	N/A	N/A	N/A	N/A	0.31	0.19
Antigen Presentation Pathway	N/A	N/A	0.45	0.05	N/A	N/A
Glutamate Receptor Signaling	N/A	N/A	0.77	0.06	N/A	N/A

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	3.85	0.25	2.27	0.29	3.41	0.21
Mismatch Repair in Eukaryotes	3.01	0.25	3.79	0.38	3.61	0.25
Mitotic Roles of Polo-Like Kinase	2.71	0.19	2.43	0.27	4.40	0.20
Coagulation System	2.66	0.24	2.13	0.32	2.15	0.18
Hereditary Breast Cancer Signaling	2.63	0.15	5.18	0.29	2.68	0.13
Complement System	2.43	0.23	5.20	0.46	1.84	0.17
Role of JAK family kinases in IL-6-type Cytokine Signaling	2.40	0.26	1.00	0.26	N/A	N/A
Cell Cycle Control of Chromosomal Replication	2.17	0.19	3.81	0.36	5.48	0.29
Extrinsic Prothrombin Activation Pathway	2.05	0.25	1.46	0.30	1.74	0.20
Hepatic Fibrosis / Hepatic Stellate Cell Activation	2.00	0.14	2.87	0.25	2.15	0.12
DNA damage-induced 14-3-3 Sigma Signaling	1.72	0.24	2.15	0.38	2.98	0.29
cAMP-mediated signaling	1.67	0.12	0.32	0.16	1.67	0.10
DNA Methylation and Transcriptional Repression Signaling	1.62	0.22	0.66	0.22	0.85	0.13
ATM Signaling	1.57	0.16	2.30	0.30	2.83	0.18
Intrinsic Prothrombin Activation Pathway	1.55	0.17	0.52	0.17	0.55	0.09
LXR/RXR Activation	1.48	0.12	0.79	0.17	0.31	0.06
Acute Phase Response Signaling	1.47	0.12	0.87	0.18	0.42	0.07
Inhibition of Matrix Metalloproteases	1.46	0.18	2.37	0.33	1.03	0.13
Prostanoid Biosynthesis	1.45	0.20	2.08	0.33	0.94	0.13
Uracil Degradation II (Reductive)	1.41	0.18	0.89	0.18	0.62	0.09
Thymine Degradation	1.41	0.18	0.89	0.18	0.62	0.09
L-cysteine Degradation I	1.41	0.18	0.89	0.18	0.62	0.09
G-protein alpha-i Signaling	1.39	0.12	N/A	N/A	0.82	0.08
Granulocyte Adhesion and Diapedesis	1.38	0.11	2.01	0.21	0.84	0.08
MIF-mediated Glucocorticoid Regulation	1.35	0.14	0.91	0.19	N/A	N/A
IL-22 Signaling	1.31	0.20	0.73	0.24	N/A	N/A
Role of JAK2 in Hormone-like Cytokine Signaling	1.29	0.17	0.37	0.17	N/A	N/A
Inhibition of Angiogenesis by TSP1	1.24	0.15	1.11	0.23	0.77	0.10
Purine Nucleotides De Novo Biosynthesis II	1.21	0.07	0.25	0.05	0.28	0.02
Glycerol Degradation I	1.21	0.17	0.23	0.08	0.54	0.08
IL-6 Signaling	1.18	0.12	1.10	0.20	NA	NA
GADD45 Signaling	1.13	0.18	2.15	0.36	2.98	0.27
Sorbitol Degradation I	1.07	0.20	0.79	0.20	NA	NA
Salvage Pathways of Pyrimidine Deoxyribonucleotides	1.06	0.11	0.59	0.11	1.26	0.11

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Glycogen Biosynthesis II (from UDP-D-Glucose)	1.06	0.17	1.23	0.25	0.47	0.08
p38 MAPK Signaling	1.04	0.12	0.88	0.20	NA	NA
PPAR-alpha/RXR-alpha Activation	1.01	0.10	0.31	0.14	0.57	0.07
Angiopoietin Signaling	1.00	0.12	1.84	0.24	0.59	0.08
Agranulocyte Adhesion and Diapedesis	0.99	0.10	1.88	0.20	1.14	0.09
Atherosclerosis Signaling	0.95	0.10	0.76	0.17	0.64	0.07
Factors Promoting Cardiogenesis in Vertebrates	0.94	0.12	1.46	0.22	2.39	0.14
Leukocyte Extravasation Signaling	0.92	0.10	1.95	0.21	0.59	0.07
Mechanisms of Viral Exit from Host Cells	0.91	0.13	0.49	0.18	0.30	0.07
Colorectal Cancer Metastasis Signaling	0.90	0.10	1.54	0.19	0.58	0.07
RAR Activation	0.90	0.10	2.34	0.22	0.83	0.08
The Visual Cycle	0.88	0.11	0.34	0.11	0.19	0.04
Retinol Biosynthesis	0.87	0.09	0.58	0.12	0.45	0.05
Role of BRCA1 in DNA Damage Response	0.86	0.12	6.14	0.40	3.33	0.19
Sertoli Cell-Sertoli Cell Junction Signaling	0.86	0.10	0.92	0.17	0.63	0.07
Estrogen-mediated S-phase Entry	0.84	0.14	1.98	0.32	4.00	0.29
PPAR Signaling	0.84	0.11	0.40	0.15	0.61	0.08
Triacylglycerol Biosynthesis	0.83	0.11	N/A	N/A	0.43	0.07
Granzyme B Signaling	0.82	0.19	0.30	0.19	0.54	0.13
CCR3 Signaling in Eosinophils	0.82	0.10	0.57	0.17	N/A	N/A
IL-9 Signaling	0.79	0.13	0.74	0.20	N/A	N/A
Oncostatin M Signaling	0.79	0.14	0.31	0.17	N/A	N/A
Epoxyqualene Biosynthesis	0.79	0.11	0.52	0.11	N/A	N/A
All-trans-decaprenyl Diphosphate Biosynthesis	0.79	0.17	0.52	0.17	0.89	0.17
Taurine Biosynthesis	0.79	0.11	0.52	0.11	0.89	0.11
Flavin Biosynthesis IV (Mammalian)	0.79	0.13	0.52	0.13	0.89	0.13
Glycerol-3-phosphate Shuttle	0.79	0.11	0.52	0.11	0.89	0.11
GDP-L-fucose Biosynthesis I (from GDP-D-mannose)	0.79	0.14	0.52	0.14	NA	NA
Formaldehyde Oxidation II (Glutathione-dependent)	0.79	0.10	0.52	0.10	0.89	0.10
eNOS Signaling	0.78	0.09	1.01	0.17	1.81	0.10
tRNA Splicing	0.76	0.11	0.46	0.15	1.59	0.13
Assembly of RNA Polymerase I Complex	0.75	0.15	0.77	0.23	0.34	0.08
Glycogen Degradation II	0.75	0.13	0.35	0.13	0.94	0.13
Antiproliferative Role of TOB in T Cell Signaling	0.75	0.15	1.30	0.31	1.59	0.19

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
NF- κ B Signaling	0.75	0.10	0.49	0.16	N/A	N/A
RhoA Signaling	0.73	0.10	0.89	0.18	0.59	0.08
IGF-1 Signaling	0.73	0.11	1.27	0.21	N/A	N/A
Alpha-Adrenergic Signaling	0.72	0.10	0.51	0.15	0.48	0.07
Protein Kinase A Signaling	0.72	0.09	0.32	0.15	0.28	0.06
Cyclins and Cell Cycle Regulation	0.68	0.10	1.40	0.21	1.53	0.11
JAK/Stat Signaling	0.67	0.11	0.53	0.19	N/A	N/A
Role of NFAT in Cardiac Hypertrophy	0.66	0.09	0.62	0.16	N/A	N/A
Ephrin Receptor Signaling	0.66	0.09	0.51	0.15	N/A	N/A
IL-10 Signaling	0.65	0.10	0.67	0.18	N/A	N/A
Cardiac beta-adrenergic Signaling	0.64	0.09	N/A	N/A	0.81	0.08
Ethanol Degradation II	0.63	0.09	1.43	0.21	2.63	0.16
Creatine-phosphate Biosynthesis	0.63	0.11	N/A	N/A	N/A	N/A
5-aminoimidazole Ribonucleotide Biosynthesis I	0.63	0.06	N/A	N/A	N/A	N/A
Methionine Salvage II (Mammalian)	0.63	0.11	0.38	0.11	N/A	N/A
Glutamate Degradation II	0.63	0.10	0.38	0.10	N/A	N/A
Aspartate Biosynthesis	0.63	0.14	0.38	0.14	N/A	N/A
Eicosanoid Signaling	0.62	0.09	1.30	0.19	0.47	0.06
MIF Regulation of Innate Immunity	0.62	0.10	1.03	0.20	N/A	N/A
G-Protein Coupled Receptor Signaling	0.62	0.09	N/A	N/A	0.97	0.08
Glycogen Degradation III	0.62	0.12	0.25	0.12	0.79	0.12
ERK5 Signaling	0.60	0.11	N/A	N/A	N/A	N/A
Thyroid Cancer Signaling	0.59	0.12	N/A	N/A	N/A	N/A
Nicotine Degradation II	0.59	0.06	0.71	0.11	0.57	0.05
PEDF Signaling	0.59	0.10	0.30	0.15	0.29	0.06
CCR5 Signaling in Macrophages	0.58	0.07	0.38	0.12	N/A	N/A
Antiproliferative Role of Somatostatin Receptor 2	0.58	0.10	0.38	0.16	N/A	N/A
Estrogen-Dependent Breast Cancer Signaling	0.58	0.10	1.48	0.22	N/A	N/A
TCA Cycle II (Eukaryotic)	0.58	0.07	N/A	N/A	N/A	N/A
HMGB1 Signaling	0.57	0.10	1.61	0.23	N/A	N/A
G Protein Signaling Mediated by Tubby	0.57	0.10	N/A	N/A	N/A	N/A
Noradrenaline and Adrenaline Degradation	0.57	0.08	1.26	0.17	2.46	0.14
Gamma-glutamyl Cycle	0.56	0.07	0.51	0.11	N/A	N/A
TGF-beta Signaling	0.56	0.10	NA	NA	0.33	0.07

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Pyridoxal 5'-phosphate Salvage Pathway	0.56	0.10	0.36	0.15	2.15	0.14
Prolactin Signaling	0.55	0.10	0.69	0.19	N/A	N/A
Ephrin B Signaling	0.55	0.10	N/A	N/A	N/A	N/A
AMPK Signaling	0.54	0.08	0.29	0.13	0.33	0.05
Galpha (s) Signaling	0.53	0.09	N/A	N/A	N/A	N/A
VEGF Family Ligand-Receptor Interactions	0.53	0.10	0.66	0.18	0.27	0.06
Nitric Oxide Signaling in the Cardiovascular System	0.53	0.08	1.30	0.18	1.27	0.09
Retinoate Biosynthesis II	0.52	0.11	0.29	0.11	N/A	N/A
2-ketoglutarate Dehydrogenase Complex	0.52	0.11	0.29	0.11	N/A	N/A
Heme Degradation	0.52	0.09	N/A	N/A	N/A	N/A
Phenylethylamine Degradation I	0.52	0.09	0.29	0.09	1.62	0.18
Eumelanin Biosynthesis	0.52	0.09	0.29	0.09	N/A	N/A
Geranylgeranyldiphosphate Biosynthesis	0.52	0.13	0.29	0.13	N/A	N/A
Biotin-carboxyl Carrier Protein Assembly	0.52	0.07	0.29	0.07	0.62	0.07
Trans, trans-farnesyl Diphosphate Biosynthesis	0.52	0.10	0.29	0.10	N/A	N/A
iNOS Signaling	0.52	0.09	0.39	0.15	N/A	N/A
Cholesterol Biosynthesis I	0.51	0.05	0.82	0.10	N/A	N/A
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)	0.51	0.05	0.82	0.10	N/A	N/A
Cholesterol Biosynthesis III (via Desmosterol)	0.51	0.05	0.82	0.10	N/A	N/A
Role of CHK Proteins in Cell Cycle Checkpoint Control	0.48	0.11	1.56	0.26	3.09	0.19
Growth Hormone Signaling	0.48	0.09	1.77	0.24	N/A	N/A
Triacylglycerol Degradation	0.47	0.09	0.73	0.19	0.68	0.09
DNA Double-Strand Break Repair by Homologous Recombination	0.47	0.12	1.76	0.35	1.22	0.18
DNA Double-Strand Break Repair by Non-Homologous End Joining	0.47	0.11	0.39	0.16	N/A	N/A
nNOS Signaling in Skeletal Muscle Cells	0.47	0.06	N/A	N/A	0.21	0.03
Vitamin-C Transport	0.47	0.09	N/A	N/A	0.21	0.05
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	0.47	0.11	0.97	0.24	0.79	0.11
ErbB2-ErbB3 Signaling	0.46	0.10	0.36	0.17	N/A	N/A
Neurotrophin/TRK Signaling	0.46	0.09	0.26	0.15	N/A	N/A
Macropinocytosis Signaling	0.46	0.09	0.70	0.18	N/A	N/A
Hepatic Cholestasis	0.46	0.07	0.48	0.14	N/A	N/A
Relaxin Signaling	0.46	0.08	0.48	0.15	0.58	0.07
LPS/IL-1 Mediated Inhibition of RXR Function	0.45	0.08	N/A	N/A	0.74	0.07
Tetrahydrofolate Salvage from 5,10-methenyltetrahydrofolate	0.44	0.10	N/A	N/A	0.54	0.10

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Telomere Extension by Telomerase	0.43	0.12	N/A	N/A	N/A	N/A
CDP-diacylglycerol Biosynthesis I	0.43	0.07	N/A	N/A	0.19	0.04
Parkinson's Signaling	0.43	0.13	N/A	N/A	N/A	N/A
Myc Mediated Apoptosis Signaling	0.42	0.10	N/A	N/A	N/A	N/A
PTEN Signaling	0.42	0.08	0.51	0.16	N/A	N/A
Antioxidant Action of Vitamin C	0.41	0.08	N/A	N/A	N/A	N/A
Notch Signaling	0.41	0.09	N/A	N/A	N/A	N/A
IL-3 Signaling	0.41	0.09	1.25	0.23	N/A	N/A
RhoGDI Signaling	0.41	0.08	0.90	0.17	N/A	N/A
Ephrin A Signaling	0.41	0.10	0.60	0.19	N/A	N/A
G-alpha-12/13 Signaling	0.40	0.09	N/A	N/A	0.31	0.06
Aldosterone Signaling in Epithelial Cells	0.40	0.08	0.62	0.17	N/A	N/A
Mouse Embryonic Stem Cell Pluripotency	0.40	0.09	0.34	0.16	N/A	N/A
RAN Signaling	0.40	0.08	0.30	0.13	0.58	0.08
Phosphatidylglycerol Biosynthesis II (Non-plastidic)	0.40	0.06	N/A	N/A	N/A	N/A
TR/RXR Activation	0.39	0.08	1.16	0.20	0.53	0.07
Salvage Pathways of Pyrimidine Ribonucleotides	0.39	0.08	N/A	N/A	2.13	0.12
FLT3 Signaling in Hematopoietic Progenitor Cells	0.39	0.09	0.30	0.16	N/A	N/A
Superpathway of Cholesterol Biosynthesis	0.39	0.03	0.56	0.07	N/A	N/A
Serotonin Degradation	0.39	0.05	1.09	0.13	1.95	0.09
Chondroitin and Dermatan Biosynthesis	0.38	0.08	0.59	0.15	N/A	N/A
Thioredoxin Pathway	0.38	0.13	N/A	N/A	N/A	N/A
Superoxide Radicals Degradation	0.38	0.13	0.18	0.13	0.47	0.13
UDP-N-acetyl-D-glucosamine Biosynthesis II	0.38	0.06	0.59	0.12	N/A	N/A
Pregnenolone Biosynthesis	0.38	0.08	N/A	N/A	N/A	N/A
GDP-glucose Biosynthesis	0.38	0.06	0.18	0.06	0.47	0.06
IL-15 Signaling	0.37	0.09	0.26	0.15	N/A	N/A
Retinoate Biosynthesis I	0.36	0.08	0.79	0.19	1.46	0.14
Ethanol Degradation IV	0.36	0.07	0.52	0.14	2.40	0.17
LPS-stimulated MAPK Signaling	0.36	0.09	0.69	0.18	N/A	N/A
Leptin Signaling in Obesity	0.36	0.08	0.52	0.17	0.45	0.07
Glucose and Glucose-1-phosphate Degradation	0.33	0.05	N/A	N/A	0.42	0.05
Aspartate Degradation II	0.33	0.07	N/A	N/A	N/A	N/A
UVC-Induced MAPK Signaling	0.33	0.10	0.45	0.19	N/A	N/A

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
HIF1-alpha Signaling	0.32	0.08	0.59	0.18	N/A	N/A
HER-2 Signaling in Breast Cancer	0.32	0.09	0.59	0.19	N/A	N/A
Superpathway of Methionine Degradation	0.32	0.05	0.44	0.09	0.22	0.03
Type II Diabetes Mellitus Signaling	0.32	0.06	0.45	0.12	0.51	0.06
Virus Entry via Endocytic Pathways	0.32	0.08	0.92	0.19	N/A	N/A
G Beta Gamma Signaling	0.32	0.07	N/A	N/A	NA	NA
Cardiac Hypertrophy Signaling	0.32	0.08	N/A	N/A	NA	NA
Estrogen Receptor Signaling	0.31	0.08	N/A	N/A	NA	NA
Melanoma Signaling	0.31	0.09	0.42	0.17	0.28	0.07
Toll-like Receptor Signaling	0.31	0.08	0.58	0.18	N/A	N/A
Tight Junction Signaling	0.30	0.08	1.25	0.20	0.29	0.06
Signaling by Rho Family GTPases	0.29	0.08	1.73	0.19	N/A	N/A
Phosphatidylethanolamine Biosynthesis II	0.29	0.06	0.41	0.11	0.38	0.06
Thrombopoietin Signaling	0.29	0.08	0.55	0.18	N/A	N/A
Erythropoietin Signaling	0.29	0.08	0.70	0.18	N/A	N/A
Regulation of the Epithelial-Mesenchymal Transition Pathway	0.29	0.08	0.50	0.16	N/A	N/A
D-myo-inositol-5-phosphate Metabolism	0.29	0.07	0.30	0.13	N/A	N/A
IL-1 Signaling	0.28	0.07	N/A	N/A	N/A	N/A
Circadian Rhythm Signaling	0.28	0.08	N/A	N/A	0.45	0.08
Glutamate Receptor Signaling	0.28	0.07	N/A	N/A	N/A	N/A
Glioma Signaling	0.27	0.07	0.62	0.16	N/A	N/A
NRF2-mediated Oxidative Stress Response	0.27	0.08	N/A	N/A	N/A	N/A
MSP-RON Signaling Pathway	0.26	0.08	1.27	0.24	N/A	N/A
Glioma Invasiveness Signaling	0.26	0.08	2.48	0.30	1.09	0.12
Nicotine Degradation III	0.26	0.04	N/A	N/A	NA	NA
FXR/RXR Activation	0.26	0.07	N/A	N/A	NA	NA
Polyamine Regulation in Colon Cancer	0.26	0.07	N/A	N/A	0.39	0.07
Glutathione-mediated Detoxification	0.26	0.05	N/A	N/A	N/A	N/A
fMLP Signaling in Neutrophils	0.26	0.07	0.45	0.15	N/A	N/A
Histidine Degradation VI	0.26	0.05	N/A	N/A	N/A	N/A
Caveolar-mediated Endocytosis Signaling	0.25	0.07	0.61	0.17	N/A	N/A
Nucleotide Excision Repair Pathway	0.25	0.09	N/A	N/A	N/A	N/A
IL-17A Signaling in Fibroblasts	0.23	0.08	0.28	0.15	N/A	N/A
Glycine Betaine Degradation	0.23	0.04	0.30	0.09	N/A	N/A

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Ubiquinol-10 Biosynthesis (Eukaryotic)	0.20	0.03	N/A	N/A	N/A	N/A
Methylglyoxal Degradation III	0.20	0.04	0.25	0.09	0.28	0.04
Glucocorticoid Receptor Signaling	N/A	N/A	0.49	0.15	N/A	N/A
Natural Killer Cell Signaling	N/A	N/A	0.56	0.16	N/A	N/A
Neuregulin Signaling	N/A	N/A	0.51	0.16	N/A	N/A
Axonal Guidance Signaling	N/A	N/A	0.37	0.15	0.31	0.06
Amyotrophic Lateral Sclerosis Signaling	N/A	N/A	N/A	N/A	0.34	0.06
Actin Cytoskeleton Signaling	N/A	N/A	0.38	0.15	N/A	N/A
Aryl Hydrocarbon Receptor Signaling	N/A	N/A	0.64	0.16	1.29	0.09
p53 Signaling	N/A	N/A	0.78	0.20	1.09	0.10
Ceramide Signaling	N/A	N/A	0.40	0.16	N/A	N/A
PXR/RXR Activation	N/A	N/A	N/A	N/A	0.28	0.05
Regulation of Actin-based Motility by Rho	N/A	N/A	0.98	0.20	N/A	N/A
14-3-3-mediated Signaling	N/A	N/A	0.30	0.16	N/A	N/A
Clathrin-mediated Endocytosis Signaling	N/A	N/A	1.03	0.19	0.30	0.06
Fc-gamma Receptor-mediated Phagocytosis in Macrophages and Monocytes	N/A	N/A	0.29	0.15	N/A	N/A
IL-8 Signaling	N/A	N/A	1.04	0.18	N/A	N/A
IL-12 Signaling and Production in Macrophages	N/A	N/A	0.46	0.15	N/A	N/A
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	N/A	N/A	2.12	0.23	N/A	N/A
TREM1 Signaling	N/A	N/A	0.79	0.17	N/A	N/A
Role of NFAT in Regulation of the Immune Response	N/A	N/A	0.61	0.15	N/A	N/A
NF-kappaB Activation by Viruses	N/A	N/A	0.40	0.16	N/A	N/A
IL-17 Signaling	N/A	N/A	0.28	0.16	N/A	N/A
CXCR4 Signaling	N/A	N/A	1.15	0.19	N/A	N/A
CTLA4 Signaling in Cytotoxic T Lymphocytes	N/A	N/A	0.44	0.15	N/A	N/A
B Cell Activating Factor Signaling	N/A	N/A	0.49	0.18	N/A	N/A
CD28 Signaling in T Helper Cells	N/A	N/A	0.36	0.14	N/A	N/A
Dendritic Cell Maturation	N/A	N/A	0.61	0.14	N/A	N/A
Reelin Signaling in Neurons	N/A	N/A	1.98	0.26	0.41	0.07
Endothelin-1 Signaling	N/A	N/A	0.42	0.16	N/A	N/A
CNTF Signaling	N/A	N/A	0.29	0.15	N/A	N/A
Aggrin Interactions at Neuromuscular Junction	N/A	N/A	0.95	0.22	N/A	N/A
Renin-Angiotensin Signaling	N/A	N/A	0.65	0.17	N/A	N/A
Docosahexaenoic Acid (DHA) Signaling	N/A	N/A	0.34	0.14	0.32	0.06

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Semaphorin Signaling in Neurons	N/A	N/A	1.44	0.27	0.59	0.10
Thrombin Signaling	N/A	N/A	0.81	0.18	N/A	N/A
Molecular Mechanisms of Cancer	N/A	N/A	1.12	0.17	N/A	N/A
Lipid Antigen Presentation by CD1	N/A	N/A	0.73	0.18	N/A	N/A
Cell Cycle Regulation by BTG Family Proteins	N/A	N/A	0.46	0.19	1.59	0.17
Corticotropin Releasing Hormone Signaling	N/A	N/A	0.55	0.15	N/A	N/A
HGF Signaling	N/A	N/A	0.74	0.19	N/A	N/A
Cholecystokinin/Gastrin-mediated Signaling	N/A	N/A	0.45	0.17	N/A	N/A
Human Embryonic Stem Cell Pluripotency	N/A	N/A	0.41	0.15	N/A	N/A
Germ Cell-Sertoli Cell Junction Signaling	N/A	N/A	0.56	0.17	0.37	0.07
Prostate Cancer Signaling	N/A	N/A	N/A	N/A	0.36	0.06
Renal Cell Carcinoma Signaling	N/A	N/A	0.36	0.16	N/A	N/A
Small Cell Lung Cancer Signaling	N/A	N/A	0.96	0.18	0.73	0.08
Acute Myeloid Leukemia Signaling	N/A	N/A	0.32	0.16	N/A	N/A
Bladder Cancer Signaling	N/A	N/A	0.53	0.18	0.50	0.08
Chronic Myeloid Leukemia Signaling	N/A	N/A	0.36	0.15	N/A	N/A
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	N/A	N/A	0.78	0.16	N/A	N/A
Cleavage and Polyadenylation of Pre-mRNA	N/A	N/A	0.22	0.17	0.25	0.08
Pancreatic Adenocarcinoma Signaling	N/A	N/A	1.04	0.19	1.04	0.09
Sphingosine-1-phosphate Signaling	N/A	N/A	1.51	0.21	N/A	N/A
Crosstalk between Dendritic Cells and Natural Killer Cells	N/A	N/A	0.38	0.15	N/A	N/A
Systemic Lupus Erythematosus Signaling	N/A	N/A	0.51	0.12	0.35	0.05
Cdc42 Signaling	N/A	N/A	0.31	0.12	N/A	N/A
ILK Signaling	N/A	N/A	1.32	0.20	N/A	N/A
FAK Signaling	N/A	N/A	0.63	0.17	N/A	N/A
April Mediated Signaling	N/A	N/A	0.56	0.19	N/A	N/A
PAK Signaling	N/A	N/A	0.58	0.16	N/A	N/A
Rac Signaling	N/A	N/A	0.38	0.15	N/A	N/A
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	N/A	N/A	0.42	0.16	0.35	0.06
Phospholipase C Signaling	N/A	N/A	0.89	0.16	N/A	N/A
Ovarian Cancer Signaling	N/A	N/A	0.36	0.16	N/A	N/A
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	N/A	N/A	0.51	0.15	N/A	N/A
Breast Cancer Regulation by Stathmin1	N/A	N/A	0.38	0.16	1.39	0.09
RANK Signaling in Osteoclasts	N/A	N/A	0.66	0.18	N/A	N/A

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Glioblastoma Multiforme Signaling	N/A	N/A	0.76	0.17	0.82	0.08
Neuroprotective Role of THOP1 in Alzheimer's Disease	N/A	N/A	N/A	N/A	0.32	0.06
PI3K Signaling in B Lymphocytes	N/A	N/A	0.38	0.15	N/A	N/A
P2Y Purigenic Receptor Signaling Pathway	N/A	N/A	0.33	0.15	N/A	N/A
Assembly of RNA Polymerase III Complex	N/A	N/A	1.32	0.31	N/A	N/A
Role of Tissue Factor in Cancer	N/A	N/A	0.86	0.19	N/A	N/A
Actin Nucleation by ARP-WASP Complex	N/A	N/A	0.36	0.15	N/A	N/A
Paxillin Signaling	N/A	N/A	0.50	0.16	N/A	N/A
Gap Junction Signaling	N/A	N/A	0.39	0.15	0.72	0.07
ErbB Signaling	N/A	N/A	0.66	0.20	N/A	N/A
GDNF Family Ligand-Receptor Interactions	N/A	N/A	0.50	0.18	N/A	N/A
Fatty Acid Activation	N/A	N/A	N/A	N/A	0.23	0.05
Dopamine Degradation	N/A	N/A	N/A	N/A	1.48	0.11
Chondroitin Sulfate Degradation (Metazoa)	N/A	N/A	0.51	0.13	N/A	N/A
Glutathione Redox Reactions I	N/A	N/A	N/A	N/A	0.54	0.08
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I	N/A	N/A	0.44	0.09	2.08	0.12
D-myo-inositol (1,4,5)-Trisphosphate Biosynthesis	N/A	N/A	0.37	0.13	N/A	N/A
Estrogen Biosynthesis	N/A	N/A	0.28	0.12	N/A	N/A
Tryptophan Degradation X (Mammalian, via Tryptamine)	N/A	N/A	0.30	0.10	1.74	0.14
Leukotriene Biosynthesis	N/A	N/A	0.22	0.08	N/A	N/A
tRNA Charging	N/A	N/A	N/A	N/A	0.35	0.04
Urate Biosynthesis/Inosine 5'-phosphate Degradation	N/A	N/A	N/A	N/A	0.23	0.05
Dermatan Sulfate Degradation (Metazoa)	N/A	N/A	0.44	0.13	N/A	N/A
Purine Nucleotides Degradation II (Aerobic)	N/A	N/A	0.23	0.09	N/A	N/A
Phenylalanine Degradation IV (Mammalian, via Side Chain)	N/A	N/A	N/A	N/A	0.63	0.05
Bile Acid Biosynthesis, Neutral Pathway	N/A	N/A	N/A	N/A	0.23	0.02
3-phosphoinositide Biosynthesis	N/A	N/A	0.51	0.14	N/A	N/A
Colanic Acid Building Blocks Biosynthesis	N/A	N/A	N/A	N/A	0.63	0.06
Histamine Degradation	N/A	N/A	0.51	0.10	2.21	0.14
Guanosine Nucleotides Degradation III	N/A	N/A	0.22	0.09	0.25	0.05
Adenosine Nucleotides Degradation II	N/A	N/A	0.34	0.12	0.19	0.04
Putrescine Degradation III	N/A	N/A	0.30	0.10	1.74	0.13
Fatty Acid alpha-oxidation	N/A	N/A	0.44	0.14	1.30	0.14
Oxidative Ethanol Degradation III	N/A	N/A	0.34	0.08	1.84	0.10

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Epithelial Adherens Junction Signaling	N/A	N/A	N/A	N/A	1.10	0.10
G-alpha-q Signaling	N/A	N/A	0.90	0.17	N/A	N/A
Regulation of Cellular Mechanics by Calpain Protease	N/A	N/A	N/A	N/A	0.55	0.07
Remodeling of Epithelial Adherens Junctions	N/A	N/A	N/A	N/A	0.61	0.09
Role of p14/p19ARF in Tumor Suppression	N/A	N/A	0.68	0.22	0.22	0.06
Tec Kinase Signaling	N/A	N/A	1.65	0.19	N/A	N/A
UVA-Induced MAPK Signaling	N/A	N/A	0.63	0.19	N/A	N/A
UVB-Induced MAPK Signaling	N/A	N/A	0.69	0.20	N/A	N/A
EGF Signaling	N/A	N/A	0.93	0.21	N/A	N/A
Cell Cycle: G1/S Checkpoint Regulation	N/A	N/A	1.04	0.21	0.71	0.09
SAPK/JNK Signaling	N/A	N/A	0.58	0.17	0.29	0.06
IL-2 Signaling	N/A	N/A	0.83	0.21	N/A	N/A
IL-4 Signaling	N/A	N/A	0.36	0.15	N/A	N/A
Wnt/Beta-catenin Signaling	N/A	N/A	0.64	0.18	0.90	0.09
Sonic Hedgehog Signaling	N/A	N/A	N/A	N/A	0.24	0.06
Integrin Signaling	N/A	N/A	0.68	0.17	N/A	N/A
PDGF Signaling	N/A	N/A	0.57	0.18	N/A	N/A
Airway Pathology in Chronic Obstructive Pulmonary Disease	N/A	N/A	0.49	0.22	0.38	0.11
Spliceosomal Cycle	N/A	N/A	0.52	0.11	N/A	N/A
Sphingosine and Sphingosine-1-phosphate Metabolism	N/A	N/A	0.59	0.10	N/A	N/A
Arginine Biosynthesis IV	N/A	N/A	0.18	0.04	N/A	N/A
Pyrimidine Ribonucleotides De Novo Biosynthesis	N/A	N/A	0.66	0.10	1.41	0.08
UDP-D-xylose and UDP-D-glucuronate Biosynthesis	N/A	N/A	0.52	0.14	N/A	N/A
Glutaryl-CoA Degradation	N/A	N/A	0.25	0.08	N/A	N/A
Androgen Biosynthesis	N/A	N/A	0.51	0.12	0.25	0.04
Proline Biosynthesis II (from Arginine)	N/A	N/A	0.72	0.10	0.54	0.05
Ketogenesis	N/A	N/A	0.67	0.14	N/A	N/A
Sucrose Degradation V (Mammalian)	N/A	N/A	N/A	N/A	0.42	0.05
NADH Repair	N/A	N/A	0.38	0.11	N/A	N/A
Ceramide Biosynthesis	N/A	N/A	0.18	0.06	N/A	N/A
Guanine and Guanosine Salvage I	N/A	N/A	0.52	0.11	N/A	N/A
Serotonin and Melatonin Biosynthesis	N/A	N/A	0.23	0.06	N/A	N/A
Tetrapyrrole Biosynthesis II	N/A	N/A	0.72	0.15	N/A	N/A
Spermine Biosynthesis	N/A	N/A	0.52	0.14	N/A	N/A

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Arginine Degradation VI (Arginase 2 Pathway)	N/A	N/A	0.59	0.13	0.47	0.06
Histidine Degradation III	N/A	N/A	N/A	N/A	0.38	0.06
Choline Degradation I	N/A	N/A	0.52	0.14	N/A	N/A
Alanine Degradation III	N/A	N/A	0.52	0.17	N/A	N/A
Thiamin Salvage III	N/A	N/A	0.79	0.20	N/A	N/A
Acetyl-CoA Biosynthesis I (Pyruvate Dehydrogenase Complex)	N/A	N/A	0.18	0.09	N/A	N/A
Selenocysteine Biosynthesis II (Archaea and Eukaryotes)	N/A	N/A	0.23	0.06	N/A	N/A
Inositol Pyrophosphates Biosynthesis	N/A	N/A	N/A	N/A	0.42	0.06
Alanine Biosynthesis II	N/A	N/A	0.52	0.17	N/A	N/A
Lysine Degradation II	N/A	N/A	N/A	N/A	0.54	0.05
D-glucuronate Degradation I	N/A	N/A	0.38	0.08	0.73	0.08
Adenine and Adenosine Salvage III	N/A	N/A	0.59	0.13	N/A	N/A
Inosine-5'-phosphate Biosynthesis II	N/A	N/A	0.38	0.06	N/A	N/A
Uridine-5'-phosphate Biosynthesis	N/A	N/A	0.52	0.05	0.89	0.05
Heme Biosynthesis II	N/A	N/A	0.35	0.09	N/A	N/A
Hypusine Biosynthesis	N/A	N/A	0.38	0.20	N/A	N/A
Spermidine Biosynthesis I	N/A	N/A	0.38	0.13	N/A	N/A
Purine Ribonucleosides Degradation to Ribose-1-phosphate	N/A	N/A	0.18	0.06	N/A	N/A
Ketolysis	N/A	N/A	0.89	0.16	N/A	N/A
Anandamide Degradation	N/A	N/A	0.52	0.20	N/A	N/A
Ceramide Degradation	N/A	N/A	0.29	0.07	N/A	N/A
Pyrimidine Ribonucleotides Interconversion	N/A	N/A	0.47	0.12	0.95	0.09
Glycolysis I	N/A	N/A	N/A	N/A	0.76	0.08
Proline Biosynthesis I	N/A	N/A	0.89	0.14	0.62	0.07
Melatonin Degradation II	N/A	N/A	0.29	0.08	0.62	0.08
Dolichyl-diphosphooligosaccharide Biosynthesis	N/A	N/A	0.30	0.05	N/A	N/A
Zymosterol Biosynthesis	N/A	N/A	0.18	0.05	N/A	N/A
Threonine Degradation II	N/A	N/A	0.52	0.11	N/A	N/A
1D-myo-inositol Hexakisphosphate Biosynthesis V (from Ins(1,3,4)P3)	N/A	N/A	N/A	N/A	0.73	0.10
Oxidized GTP and dGTP Detoxification	N/A	N/A	0.38	0.09	0.73	0.09
Asparagine Biosynthesis I	N/A	N/A	0.79	0.13	N/A	N/A
NAD Biosynthesis III	N/A	N/A	0.29	0.10	N/A	N/A
Sphingomyelin Metabolism	N/A	N/A	1.23	0.19	N/A	N/A
dTMP De Novo Biosynthesis	N/A	N/A	0.72	0.14	0.54	0.07

Table S26. Subtype 2 (MES) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
UDP-N-acetyl-D-galactosamine Biosynthesis II	N/A	N/A	N/A	N/A	0.34	0.04
N-acetylglucosamine Degradation II	N/A	N/A	0.29	0.08	N/A	N/A
Methionine Degradation I (to Homocysteine)	N/A	N/A	0.34	0.13	0.19	0.04
Folate Transformations I	N/A	N/A	N/A	N/A	0.34	0.03
GDP-mannose Biosynthesis	N/A	N/A	N/A	N/A	1.26	0.15
Cysteine Biosynthesis III (mammalia)	N/A	N/A	0.27	0.10	N/A	N/A
Acetate Conversion to Acetyl-CoA	N/A	N/A	0.23	0.09	0.54	0.09
Glutamate Biosynthesis II	N/A	N/A	0.52	0.14	N/A	N/A
N-acetylglucosamine Degradation I	N/A	N/A	0.38	0.13	N/A	N/A
Glutamate Degradation X	N/A	N/A	0.52	0.14	N/A	N/A
Serotonin Receptor Signaling	N/A	N/A	N/A	N/A	0.22	0.04

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	3.77	0.06	6.87	0.20	9.23	0.23
Antigen Presentation Pathway	3.06	0.10	4.06	0.28	8.07	0.40
Allograft Rejection Signaling	2.96	0.04	5.28	0.14	9.54	0.20
Ephrin B Signaling	2.51	0.06	0.28	0.09	N/A	N/A
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	2.49	0.05	2.53	0.16	5.89	0.24
Calcium-induced T Lymphocyte Apoptosis	2.34	0.06	3.31	0.19	5.58	0.24
Autoimmune Thyroid Disease Signaling	2.08	0.05	2.81	0.15	6.44	0.23
T Helper Cell Differentiation	2.06	0.06	4.09	0.22	8.48	0.32
Fatty Acid Activation	1.89	0.11	N/A	N/A	0.43	0.11
Graft-versus-Host Disease Signaling	1.87	0.06	2.81	0.20	4.72	0.26
Thiamin Salvage III	1.87	0.20	1.03	0.20	1.01	0.20
Glutamate Removal from Folates	1.87	0.33	N/A	N/A	1.01	0.33
Mitochondrial L-carnitine Shuttle Pathway	1.71	0.09	N/A	N/A	0.33	0.09
Nur77 Signaling in T Lymphocytes	1.69	0.05	2.82	0.18	2.64	0.18
OX40 Signaling Pathway	1.67	0.03	3.30	0.13	5.01	0.17
Gamma-linolenate Biosynthesis II (Animals)	1.66	0.08	0.32	0.08	0.64	0.13
Cdc42 Signaling	1.64	0.03	2.52	0.12	3.75	0.14
Spermine Biosynthesis	1.57	0.14	2.06	0.29	0.73	0.14
Sulfate Activation for Sulfonation	1.57	0.13	0.75	0.13	0.73	0.13
B Cell Development	1.53	0.06	2.81	0.21	7.36	0.36
Polyamine Regulation in Colon Cancer	1.49	0.07	0.51	0.10	0.47	0.10
iCOS-iCOSL Signaling in T Helper Cells	1.41	0.03	3.47	0.16	8.61	0.24
Spermidine Biosynthesis I	1.40	0.13	1.61	0.25	0.58	0.13
Actin Nucleation by ARP-WASP Complex	1.40	0.05	N/A	N/A	0.33	0.09
Tumoricidal Function of Hepatic Natural Killer Cells	1.38	0.08	2.30	0.29	2.84	0.33
Leukocyte Extravasation Signaling	1.38	0.03	1.39	0.12	1.83	0.14
Retinoic acid Mediated Apoptosis Signaling	1.38	0.04	1.10	0.13	1.68	0.16
Type I Diabetes Mellitus Signaling	1.34	0.03	4.06	0.18	4.19	0.19
Eicosanoid Signaling	1.34	0.04	2.59	0.16	0.69	0.10
Natural Killer Cell Signaling	1.33	0.03	3.99	0.19	3.49	0.18
CD28 Signaling in T Helper Cells	1.28	0.03	2.51	0.14	5.27	0.20
PKC-delta Signaling in T Lymphocytes	1.28	0.03	2.15	0.13	3.01	0.15
Uracil Degradation II (Reductive)	1.28	0.09	0.49	0.09	0.47	0.09
2-ketoglutarate Dehydrogenase Complex	1.28	0.11	N/A	N/A	N/A	N/A

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Heme Degradation	1.28	0.09	0.49	0.09	0.47	0.09
Serine Biosynthesis	1.28	0.08	0.49	0.08	0.47	0.08
Thymine Degradation	1.28	0.09	0.49	0.09	0.47	0.09
Fatty Acid Beta-oxidation I	1.23	0.04	N/A	N/A	0.26	0.07
JAK/Stat Signaling	1.21	0.04	1.05	0.14	1.56	0.17
Interferon Signaling	1.18	0.06	1.20	0.17	1.56	0.19
Stearate Biosynthesis I (Animals)	1.16	0.04	N/A	N/A	N/A	N/A
Sphingosine and Sphingosine-1-phosphate Metabolism	1.10	0.05	1.00	0.10	0.96	0.10
Superpathway of Serine and Glycine Biosynthesis I	1.10	0.06	0.35	0.06	0.34	0.06
Thioredoxin Pathway	1.10	0.13	N/A	N/A	N/A	N/A
Ephrin Receptor Signaling	1.07	0.02	0.61	0.09	0.38	0.09
Netrin Signaling	1.03	0.04	N/A	N/A	0.79	0.11
Regulation of Actin-based Motility by Rho	1.01	0.03	N/A	N/A	N/A	N/A
Docosahexaenoic Acid (DHA) Signaling	1.01	0.04	0.30	0.08	0.27	0.08
Neuroprotective Role of THOP1 in Alzheimer's Disease	1.01	0.04	N/A	N/A	1.95	0.17
Alpha-Adrenergic Signaling	0.97	0.03	N/A	N/A	N/A	N/A
NAD Phosphorylation and Dephosphorylation	0.94	0.06	0.23	0.06	0.22	0.06
Glycogen Degradation II	0.94	0.07	0.23	0.07	0.22	0.07
Integrin Signaling	0.92	0.02	N/A	N/A	N/A	N/A
Fc-gamma Receptor-mediated Phagocytosis in Macrophages and Monocytes	0.91	0.03	0.67	0.11	1.04	0.13
Glycogen Degradation III	0.86	0.06	N/A	N/A	N/A	N/A
Sphingosine-1-phosphate Signaling	0.77	0.03	0.97	0.12	1.06	0.13
Vitamin-C Transport	0.76	0.05	N/A	N/A	N/A	N/A
ErbB2-ErbB3 Signaling	0.76	0.03	N/A	N/A	N/A	N/A
Mismatch Repair in Eukaryotes	0.73	0.04	0.38	0.08	N/A	N/A
CDP-diacylglycerol Biosynthesis I	0.73	0.04	N/A	N/A	N/A	N/A
Death Receptor Signaling	0.73	0.03	1.40	0.16	0.69	0.13
Endothelin-1 Signaling	0.73	0.02	0.86	0.11	N/A	N/A
Cell Cycle: G1/S Checkpoint Regulation	0.72	0.03	1.73	0.17	0.93	0.14
Type II Diabetes Mellitus Signaling	0.72	0.02	0.47	0.07	N/A	N/A
Granzyme B Signaling	0.71	0.06	0.74	0.19	0.70	0.19
Glutathione Redox Reactions I	0.71	0.04	0.74	0.13	N/A	N/A
Phosphatidylglycerol Biosynthesis II (Non-plastidic)	0.71	0.03	N/A	N/A	N/A	N/A
Atherosclerosis Signaling	0.69	0.02	3.09	0.16	1.80	0.14

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Hypoxia Signaling in the Cardiovascular System	0.69	0.03	N/A	N/A	N/A	N/A
Granzyme A Signaling	0.68	0.05	0.32	0.10	0.30	0.10
Communication between Innate and Adaptive Immune Cells	0.67	0.02	4.28	0.16	6.45	0.19
Endoplasmic Reticulum Stress Pathway	0.66	0.06	1.10	0.22	0.27	0.11
Angiopoietin Signaling	0.66	0.03	0.40	0.09	N/A	N/A
IL-10 Signaling	0.63	0.03	0.53	0.10	N/A	N/A
GDNF Family Ligand-Receptor Interactions	0.63	0.03	0.53	0.11	1.19	0.15
IL-4 Signaling	0.63	0.03	0.75	0.11	1.87	0.17
DNA Methylation and Transcriptional Repression Signaling	0.62	0.04	0.55	0.13	N/A	N/A
NAD Salvage Pathway II	0.60	0.03	0.23	0.06	N/A	N/A
Glutathione-mediated Detoxification	0.60	0.02	1.40	0.11	N/A	N/A
TCA Cycle II (Eukaryotic)	0.60	0.02	N/A	N/A	N/A	N/A
Glycolysis I	0.59	0.03	N/A	N/A	N/A	N/A
Gluconeogenesis I	0.57	0.02	N/A	N/A	N/A	N/A
VDR/RXR Activation	0.55	0.02	0.98	0.14	0.45	0.11
LPS/IL-1 Mediated Inhibition of RXR Function	0.54	0.02	1.48	0.11	N/A	N/A
FXR/RXR Activation	0.52	0.02	0.32	0.08	N/A	N/A
Molecular Mechanisms of Cancer	0.52	0.02	0.70	0.10	1.00	0.11
CTLA4 Signaling in Cytotoxic T Lymphocytes	0.52	0.02	3.36	0.18	4.55	0.21
Glioblastoma Multiforme Signaling	0.52	0.02	N/A	N/A	1.19	0.12
ErbB Signaling	0.50	0.02	N/A	N/A	N/A	N/A
Huntington's Disease Signaling	0.49	0.02	N/A	N/A	N/A	N/A
Tec Kinase Signaling	0.49	0.02	1.74	0.12	1.74	0.13
UVA-Induced MAPK Signaling	0.49	0.02	0.39	0.10	0.88	0.13
PAK Signaling	0.48	0.02	N/A	N/A	N/A	N/A
Apoptosis Signaling	0.48	0.02	N/A	N/A	N/A	N/A
Germ Cell-Sertoli Cell Junction Signaling	0.47	0.02	0.47	0.10	0.64	0.11
Complement System	0.46	0.03	4.20	0.31	1.12	0.17
Role of NFAT in Regulation of the Immune Response	0.46	0.02	3.34	0.14	2.44	0.13
Dendritic Cell Maturation	0.46	0.01	2.99	0.13	3.43	0.14
B Cell Receptor Signaling	0.46	0.02	0.43	0.09	0.59	0.11
Role of JAK2 in Hormone-like Cytokine Signaling	0.45	0.03	0.77	0.14	1.12	0.17
p53 Signaling	0.45	0.02	1.35	0.15	1.20	0.15
Antioxidant Action of Vitamin C	0.45	0.02	0.31	0.08	N/A	N/A

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
HMGB1 Signaling	0.44	0.02	0.44	0.10	0.52	0.11
TWEAK Signaling	0.44	0.03	N/A	N/A	N/A	N/A
Triacylglycerol Biosynthesis	0.44	0.02	N/A	N/A	N/A	N/A
IGF-1 Signaling	0.43	0.02	0.28	0.09	N/A	N/A
IL-9 Signaling	0.43	0.03	1.04	0.15	2.36	0.23
Nucleotide Excision Repair Pathway	0.43	0.03	N/A	N/A	N/A	N/A
Telomerase Signaling	0.43	0.02	0.56	0.11	0.47	0.11
Calcium Signaling	0.42	0.01	N/A	N/A	N/A	N/A
tRNA Splicing	0.42	0.02	0.39	0.09	N/A	N/A
Neuropathic Pain Signaling In Dorsal Horn Neurons	0.42	0.02	N/A	N/A	0.61	0.11
Cholecystokinin/Gastrin-mediated Signaling	0.41	0.02	N/A	N/A	N/A	N/A
April Mediated Signaling	0.39	0.02	N/A	N/A	N/A	N/A
Fc Epsilon RI Signaling	0.39	0.02	0.78	0.11	0.52	0.10
Role of NFAT in Cardiac Hypertrophy	0.39	0.01	0.27	0.08	0.28	0.08
Role of RIG1-like Receptors in Antiviral Innate Immunity	0.38	0.02	N/A	N/A	0.45	0.10
Transcriptional Regulatory Network in Embryonic Stem Cells	0.38	0.03	0.29	0.10	0.27	0.10
Nicotine Degradation II	0.38	0.01	0.29	0.05	N/A	N/A
Protein Ubiquitination Pathway	0.37	0.01	N/A	N/A	N/A	N/A
ILK Signaling	0.36	0.02	N/A	N/A	N/A	N/A
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	0.36	0.02	1.04	0.15	0.62	0.13
Hereditary Breast Cancer Signaling	0.36	0.02	0.35	0.09	0.57	0.10
Sperm Motility	0.36	0.01	N/A	N/A	0.75	0.10
GABA Receptor Signaling	0.35	0.02	N/A	N/A	N/A	N/A
LXR/RXR Activation	0.34	0.01	2.40	0.15	N/A	N/A
PTEN Signaling	0.34	0.02	N/A	N/A	0.49	0.10
TNFR1 Signaling	0.33	0.02	N/A	N/A	N/A	N/A
Ephrin A Signaling	0.32	0.02	0.81	0.14	1.39	0.17
PI3K Signaling in B Lymphocytes	0.31	0.01	N/A	N/A	1.33	0.13
Amyloid Processing	0.31	0.02	N/A	N/A	N/A	N/A
Cellular Effects of Sildenafil (Viagra)	0.30	0.01	N/A	N/A	N/A	N/A
Semaphorin Signaling in Neurons	0.29	0.02	N/A	N/A	N/A	N/A
3-phosphoinositide Degradation	0.29	0.01	0.41	0.08	0.78	0.10
Phospholipases	0.29	0.02	0.66	0.11	0.88	0.12
TREM1 Signaling	0.28	0.01	1.59	0.14	1.11	0.13

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Toll-like Receptor Signaling	0.28	0.02	0.63	0.11	0.56	0.11
Role of CHK Proteins in Cell Cycle Checkpoint Control	0.28	0.02	0.39	0.11	N/A	N/A
Cardiac Beta-adrenergic Signaling	0.27	0.01	N/A	N/A	N/A	N/A
EGF Signaling	0.27	0.02	N/A	N/A	0.33	0.10
PXR/RXR Activation	0.27	0.01	N/A	N/A	N/A	N/A
Glioma Invasiveness Signaling	0.27	0.02	N/A	N/A	0.31	0.10
Synaptic Long Term Depression	0.26	0.01	0.32	0.08	N/A	N/A
Role of BRCA1 in DNA Damage Response	0.25	0.02	0.99	0.14	1.19	0.15
Phospholipase C Signaling	0.25	0.01	1.16	0.10	1.15	0.11
GM-CSF Signaling	0.24	0.01	0.45	0.10	0.39	0.10
IL-17A Signaling in Airway Cells	0.24	0.01	N/A	N/A	N/A	N/A
G-alpha-q Signaling	0.24	0.01	0.46	0.09	0.63	0.10
Non-Small Cell Lung Cancer Signaling	0.23	0.01	0.42	0.09	0.36	0.09
Role of MAPK Signaling in the Pathogenesis of Influenza	0.23	0.01	0.26	0.09	N/A	N/A
Agrin Interactions at Neuromuscular Junction	0.23	0.01	N/A	N/A	N/A	N/A
Growth Hormone Signaling	0.23	0.01	1.08	0.13	1.00	0.13
Macropinocytosis Signaling	0.22	0.01	0.78	0.12	0.48	0.11
IL-3 Signaling	0.21	0.01	0.70	0.12	0.85	0.14
FLT3 Signaling in Hematopoietic Progenitor Cells	0.21	0.01	N/A	N/A	0.41	0.11
Small Cell Lung Cancer Signaling	0.21	0.01	0.31	0.08	0.26	0.08
PEDF Signaling	0.21	0.01	0.47	0.10	0.26	0.09
NF-kappaB Activation by Viruses	0.20	0.01	0.65	0.11	1.05	0.13
IL-17 Signaling	0.20	0.01	N/A	N/A	N/A	N/A
Prolactin Signaling	0.20	0.01	1.13	0.14	0.55	0.11
Leptin Signaling in Obesity	0.20	0.01	N/A	N/A	N/A	N/A
Glucocorticoid Receptor Signaling	N/A	N/A	N/A	N/A	0.32	0.09
Amyotrophic Lateral Sclerosis Signaling	N/A	N/A	0.38	0.09	N/A	N/A
Hepatic Fibrosis / Hepatic Stellate Cell Activation	N/A	N/A	2.22	0.15	1.70	0.14
RAR Activation	N/A	N/A	0.53	0.10	N/A	N/A
IL-8 Signaling	N/A	N/A	0.28	0.08	N/A	N/A
IL-12 Signaling and Production in Macrophages	N/A	N/A	2.14	0.14	1.37	0.12
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	N/A	N/A	3.35	0.18	3.08	0.18
fMLP Signaling in Neutrophils	N/A	N/A	0.57	0.09	N/A	N/A
Virus Entry via Endocytic Pathways	N/A	N/A	0.94	0.12	1.64	0.15

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Reelin Signaling in Neurons	N/A	N/A	1.61	0.16	1.84	0.17
Renin-Angiotensin Signaling	N/A	N/A	N/A	N/A	0.31	0.09
HGF Signaling	N/A	N/A	0.68	0.11	N/A	N/A
Human Embryonic Stem Cell Pluripotency	N/A	N/A	0.48	0.09	1.83	0.14
Prostate Cancer Signaling	N/A	N/A	N/A	N/A	0.42	0.09
Chronic Myeloid Leukemia Signaling	N/A	N/A	0.84	0.11	0.54	0.11
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	N/A	N/A	1.67	0.12	0.86	0.10
Colorectal Cancer Metastasis Signaling	N/A	N/A	0.41	0.09	1.80	0.13
Crosstalk between Dendritic Cells and Natural Killer Cells	N/A	N/A	6.98	0.25	11.70	0.33
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	N/A	N/A	0.58	0.10	0.84	0.11
HER-2 Signaling in Breast Cancer	N/A	N/A	N/A	N/A	0.49	0.11
Protein Kinase A Signaling	N/A	N/A	N/A	N/A	0.64	0.10
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	N/A	N/A	1.23	0.10	1.11	0.11
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	N/A	N/A	0.42	0.09	1.58	0.15
Cyclins and Cell Cycle Regulation	N/A	N/A	0.54	0.10	0.32	0.09
Paxillin Signaling	N/A	N/A	N/A	N/A	0.63	0.11
Signaling by Rho Family GTPases	N/A	N/A	0.32	0.08	N/A	N/A
RhoGDI Signaling	N/A	N/A	0.28	0.08	N/A	N/A
D-myo-inositol-5-phosphate Metabolism	N/A	N/A	0.55	0.09	0.62	0.10
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	N/A	N/A	0.49	0.09	0.57	0.09
Superpathway of Inositol Phosphate Compounds	N/A	N/A	0.35	0.07	0.61	0.09
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	N/A	N/A	0.49	0.09	0.57	0.09
3-phosphoinositide Biosynthesis	N/A	N/A	0.69	0.09	0.60	0.09
G-alpha (s) Signaling	N/A	N/A	N/A	N/A	0.47	0.10
Agranulocyte Adhesion and Diapedesis	N/A	N/A	0.46	0.09	N/A	N/A
Granulocyte Adhesion and Diapedesis	N/A	N/A	1.08	0.11	0.35	0.09
ERK/MAPK Signaling	N/A	N/A	0.28	0.08	N/A	N/A
SAPK/JNK Signaling	N/A	N/A	0.52	0.10	N/A	N/A
FGF Signaling	N/A	N/A	N/A	N/A	0.36	0.10
Xenobiotic Metabolism Signaling	N/A	N/A	0.50	0.08	N/A	N/A
Wnt/Beta-catenin Signaling	N/A	N/A	1.27	0.13	1.10	0.13
cAMP-mediated signaling	N/A	N/A	0.63	0.10	0.91	0.12
p38 MAPK Signaling	N/A	N/A	0.83	0.12	1.16	0.14
NF-kappaB Signaling	N/A	N/A	0.87	0.11	2.07	0.14

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
T Cell Receptor Signaling	N/A	N/A	1.62	0.14	4.16	0.20
G-Protein Coupled Receptor Signaling	N/A	N/A	0.89	0.11	0.59	0.10
Aryl Hydrocarbon Receptor Signaling	N/A	N/A	1.47	0.12	0.28	0.08
Coagulation System	N/A	N/A	1.00	0.16	N/A	N/A
Hepatic Cholestasis	N/A	N/A	0.33	0.07	N/A	N/A
TR/RXR Activation	N/A	N/A	N/A	N/A	0.56	0.10
Erythropoietin Signaling	N/A	N/A	0.36	0.09	N/A	N/A
Activation of IRF by Cytosolic Pattern Recognition Receptors	N/A	N/A	N/A	N/A	0.45	0.10
Caveolar-mediated Endocytosis Signaling	N/A	N/A	N/A	N/A	1.77	0.16
Clathrin-mediated Endocytosis Signaling	N/A	N/A	0.32	0.09	N/A	N/A
Role of PKR in Interferon Induction and Antiviral Response	N/A	N/A	0.30	0.09	0.48	0.11
MIF Regulation of Innate Immunity	N/A	N/A	0.83	0.12	0.51	0.10
Fc-gamma-RIIB Signaling in B Lymphocytes	N/A	N/A	0.75	0.10	1.37	0.14
LPS-stimulated MAPK Signaling	N/A	N/A	0.44	0.10	N/A	N/A
CCR5 Signaling in Macrophages	N/A	N/A	1.63	0.12	1.86	0.13
Thrombopoietin Signaling	N/A	N/A	0.61	0.11	0.54	0.11
IL-15 Production	N/A	N/A	0.66	0.13	0.98	0.16
Oncostatin M Signaling	N/A	N/A	0.41	0.11	NA	NA
IL-15 Signaling	N/A	N/A	0.69	0.12	0.61	0.12
Melatonin Signaling	N/A	N/A	N/A	N/A	0.31	0.09
Factors Promoting Cardiogenesis in Vertebrates	N/A	N/A	0.39	0.10	2.07	0.17
CNTF Signaling	N/A	N/A	0.57	0.11	0.31	0.09
Lipid Antigen Presentation by CD1	N/A	N/A	1.58	0.18	0.97	0.14
Cell Cycle Regulation by BTG Family Proteins	N/A	N/A	0.39	0.11	N/A	N/A
RAN Signaling	N/A	N/A	0.35	0.08	N/A	N/A
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	N/A	N/A	0.39	0.11	N/A	N/A
Role of NANOG in Mammalian Embryonic Stem Cell Pluripotency	N/A	N/A	N/A	N/A	0.80	0.12
Melanoma Signaling	N/A	N/A	0.45	0.11	0.41	0.11
Endometrial Cancer Signaling	N/A	N/A	N/A	N/A	0.25	0.09
Basal Cell Carcinoma Signaling	N/A	N/A	N/A	N/A	0.44	0.11
Primary Immunodeficiency Signaling	N/A	N/A	1.47	0.11	10.60	0.31
Glioma Signaling	N/A	N/A	0.63	0.10	0.54	0.10
Acute Myeloid Leukemia Signaling	N/A	N/A	0.78	0.12	0.69	0.12
Thyroid Cancer Signaling	N/A	N/A	0.79	0.14	0.72	0.14

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Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Myc Mediated Apoptosis Signaling	N/A	N/A	0.34	0.10	N/A	N/A
Pancreatic Adenocarcinoma Signaling	N/A	N/A	0.40	0.09	0.82	0.12
Systemic Lupus Erythematosus Signaling	N/A	N/A	0.61	0.08	1.37	0.10
Rac Signaling	N/A	N/A	0.44	0.09	N/A	N/A
Ovarian Cancer Signaling	N/A	N/A	N/A	N/A	0.74	0.11
Estrogen-Dependent Breast Cancer Signaling	N/A	N/A	0.30	0.08	N/A	N/A
Pathogenesis of Multiple Sclerosis	N/A	N/A	2.42	0.44	2.34	0.44
Role of Wnt/GSK3-beta Signaling in the Pathogenesis of Influenza	N/A	N/A	N/A	N/A	0.59	0.11
TNFR2 Signaling	N/A	N/A	0.31	0.09	0.28	0.09
Role of PI3K/AKT Signaling in the Pathogenesis of Influenza	N/A	N/A	0.33	0.08	0.45	0.09
Role of Hypercytokinemia/hyperchemokine in the Pathogenesis of Influenza	N/A	N/A	0.83	0.14	N/A	N/A
Antiproliferative Role of TOB in T Cell Signaling	N/A	N/A	0.66	0.15	0.98	0.19
MSP-RON Signaling Pathway	N/A	N/A	1.27	0.16	1.17	0.16
Extrinsic Prothrombin Activation Pathway	N/A	N/A	1.26	0.20	N/A	N/A
MIF-mediated Glucocorticoid Regulation	N/A	N/A	1.67	0.17	0.79	0.12
Cell Cycle Control of Chromosomal Replication	N/A	N/A	1.40	0.16	1.89	0.19
Assembly of RNA Polymerase III Complex	N/A	N/A	0.46	0.13	N/A	N/A
Role of Tissue Factor in Cancer	N/A	N/A	0.40	0.10	N/A	N/A
Assembly of RNA Polymerase I Complex	N/A	N/A	0.23	0.08	0.22	0.08
Differential Regulation of Cytokine Production in Macrophages & T Helper Cells by IL-17A & IL-17F	N/A	N/A	0.32	0.11	N/A	N/A
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	N/A	N/A	N/A	N/A	0.41	0.11
Role of JAK family kinases in IL-6-type Cytokine Signaling	N/A	N/A	0.38	0.11	N/A	N/A
Role of JAK1 and JAK3 in Gamma chain-binding Cytokine Signaling	N/A	N/A	1.68	0.16	2.80	0.21
Mouse Embryonic Stem Cell Pluripotency	N/A	N/A	0.82	0.12	1.52	0.15
Hematopoiesis from Pluripotent Stem Cells	N/A	N/A	1.46	0.10	1.89	0.11
Hematopoiesis from Multipotent Stem Cells	N/A	N/A	0.51	0.17	N/A	N/A
iNOS Signaling	N/A	N/A	1.00	0.13	1.27	0.15
nNOS Signaling in Skeletal Muscle Cells	N/A	N/A	N/A	N/A	0.82	0.10
VEGF Family Ligand-Receptor Interactions	N/A	N/A	0.42	0.10	N/A	N/A
ErbB4 Signaling	N/A	N/A	0.34	0.09	0.30	0.09
Estrogen-mediated S-phase Entry	N/A	N/A	1.18	0.18	1.10	0.18
GADD45 Signaling	N/A	N/A	0.27	0.09	N/A	N/A
Heparan Sulfate Biosynthesis	N/A	N/A	0.27	0.07	1.16	0.12
L-carnitine Biosynthesis	N/A	N/A	N/A	N/A	0.58	0.08

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Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Bupropion Degradation	N/A	N/A	0.41	0.09	N/A	N/A
Retinoate Biosynthesis I	N/A	N/A	0.31	0.08	0.54	0.11
NAD biosynthesis II (from tryptophan)	N/A	N/A	0.46	0.06	N/A	N/A
Prostanoid Biosynthesis	N/A	N/A	0.70	0.13	0.66	0.13
Dopamine Degradation	N/A	N/A	1.58	0.13	0.97	0.11
Heparan Sulfate Biosynthesis (Late Stages)	N/A	N/A	0.39	0.08	1.50	0.15
Pyrimidine Ribonucleotides De Novo Biosynthesis	N/A	N/A	0.55	0.06	0.51	0.06
UDP-D-xylose and UDP-D-glucuronate Biosynthesis	N/A	N/A	0.75	0.14	N/A	N/A
Retinoate Biosynthesis II	N/A	N/A	N/A	N/A	0.47	0.11
Beta-alanine Degradation I	N/A	N/A	N/A	N/A	0.73	0.10
Ubiquinol-10 Biosynthesis (Eukaryotic)	N/A	N/A	0.56	0.07	N/A	N/A
Superpathway of Citrulline Metabolism	N/A	N/A	N/A	N/A	0.39	0.05
Urea Cycle	N/A	N/A	N/A	N/A	0.34	0.05
The Visual Cycle	N/A	N/A	N/A	N/A	0.36	0.07
Sucrose Degradation V (Mammalian)	N/A	N/A	0.31	0.05	0.29	0.05
Tetrahydrofolate Salvage from 5,10-methenyltetrahydrofolate	N/A	N/A	N/A	N/A	0.40	0.10
Ceramide Biosynthesis	N/A	N/A	N/A	N/A	0.34	0.06
Phosphatidylethanolamine Biosynthesis II	N/A	N/A	0.27	0.06	N/A	N/A
Triacylglycerol Degradation	N/A	N/A	0.41	0.09	N/A	N/A
Estrogen Biosynthesis	N/A	N/A	0.39	0.08	N/A	N/A
Oleate Biosynthesis II (Animals)	N/A	N/A	0.23	0.06	0.22	0.06
Spermine and Spermidine Degradation I	N/A	N/A	0.49	0.07	0.47	0.07
Arginine Degradation VI (Arginase 2 Pathway)	N/A	N/A	N/A	N/A	0.34	0.06
Tryptophan Degradation X (Mammalian, via Tryptamine)	N/A	N/A	1.90	0.17	0.70	0.10
Leukotriene Biosynthesis	N/A	N/A	1.03	0.12	N/A	N/A
CMP-N-acetylneuraminate Biosynthesis I (Eukaryotes)	N/A	N/A	0.41	0.06	N/A	N/A
All-trans-decaprenyl Diphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.73	0.17
Histidine Degradation III	N/A	N/A	N/A	N/A	0.25	0.06
Chondroitin Sulfate Biosynthesis	N/A	N/A	N/A	N/A	0.44	0.09
S-methyl-5'-thioadenosine Degradation II	N/A	N/A	1.03	0.17	N/A	N/A
Proline Degradation	N/A	N/A	N/A	N/A	0.73	0.14
Choline Degradation I	N/A	N/A	N/A	N/A	0.73	0.14
Dermatan Sulfate Biosynthesis	N/A	N/A	N/A	N/A	0.40	0.08
Alanine Degradation III	N/A	N/A	0.75	0.17	N/A	N/A

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
1D-myo-inositol Hexakisphosphate Biosynthesis II (Mammalian)	N/A	N/A	N/A	N/A	0.25	0.07
Phenylethylamine Degradation I	N/A	N/A	0.49	0.09	0.47	0.09
Phosphatidylcholine Biosynthesis I	N/A	N/A	0.31	0.06	N/A	N/A
Calcium Transport I	N/A	N/A	N/A	N/A	0.22	0.08
Glutamine Biosynthesis I	N/A	N/A	0.75	0.13	N/A	N/A
Dermatan Sulfate Biosynthesis (Late Stages)	N/A	N/A	0.32	0.09	0.75	0.13
NAD Salvage Pathway III	N/A	N/A	0.41	0.09	N/A	N/A
Glycine Cleavage Complex	N/A	N/A	0.41	0.07	N/A	N/A
Dermatan Sulfate Degradation (Metazoa)	N/A	N/A	N/A	N/A	0.43	0.09
Citrulline Biosynthesis	N/A	N/A	N/A	N/A	0.74	0.08
Alanine Biosynthesis II	N/A	N/A	0.75	0.17	N/A	N/A
Superpathway of D-myo-inositol (1,4,5)-trisphosphate Metabolism	N/A	N/A	N/A	N/A	0.38	0.09
Purine Nucleotides Degradation II (Aerobic)	N/A	N/A	N/A	N/A	0.27	0.06
Tetrahydrobiopterin Biosynthesis I	N/A	N/A	0.60	0.09	0.58	0.09
D-myo-inositol (1,3,4)-trisphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.25	0.08
Serotonin Degradation	N/A	N/A	0.87	0.08	0.79	0.08
Leucine Degradation I	N/A	N/A	N/A	N/A	0.22	0.04
D-glucuronate Degradation I	N/A	N/A	0.60	0.08	N/A	N/A
Phenylalanine Degradation IV (Mammalian, via Side Chain)	N/A	N/A	0.87	0.08	0.82	0.08
Bile Acid Biosynthesis, Neutral Pathway	N/A	N/A	0.95	0.05	N/A	N/A
Adenine and Adenosine Salvage III	N/A	N/A	N/A	N/A	0.34	0.06
D-myo-inositol (1,4,5)-trisphosphate Degradation	N/A	N/A	N/A	N/A	0.59	0.13
Inosine-5'-phosphate Biosynthesis II	N/A	N/A	N/A	N/A	0.58	0.06
Uridine-5'-phosphate Biosynthesis	N/A	N/A	N/A	N/A	0.73	0.05
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	N/A	N/A	0.88	0.11	0.29	0.06
Myo-inositol Biosynthesis	N/A	N/A	N/A	N/A	0.47	0.13
Purine Ribonucleosides Degradation to Ribose-1-phosphate	N/A	N/A	N/A	N/A	0.34	0.06
Tryptophan Degradation III (Eukaryotic)	N/A	N/A	0.27	0.04	N/A	N/A
Anandamide Degradation	N/A	N/A	N/A	N/A	0.73	0.20
Ceramide Degradation	N/A	N/A	0.49	0.07	0.47	0.07
Pyrimidine Ribonucleotides Interconversion	N/A	N/A	0.64	0.09	0.27	0.06
Histamine Degradation	N/A	N/A	1.70	0.14	0.98	0.10
Melatonin Degradation II	N/A	N/A	1.34	0.17	0.47	0.08
Chondroitin Sulfate Biosynthesis (Late Stages)	N/A	N/A	0.27	0.07	0.65	0.11

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Salvage Pathways of Pyrimidine Deoxyribonucleotides	N/A	N/A	0.35	0.06	0.34	0.06
Cysteine Biosynthesis/Homocysteine Degradation	N/A	N/A	0.75	0.13	0.73	0.13
Adenosine Nucleotides Degradation II	N/A	N/A	N/A	N/A	0.36	0.08
Superpathway of Melatonin Degradation	N/A	N/A	0.53	0.06	N/A	N/A
Threonine Degradation II	N/A	N/A	0.75	0.11	N/A	N/A
Histidine Degradation VI	N/A	N/A	0.23	0.05	0.22	0.05
Noradrenaline and Adrenaline Degradation	N/A	N/A	1.20	0.12	0.74	0.10
Arginine Degradation I (Arginase Pathway)	N/A	N/A	N/A	N/A	0.47	0.08
Pregnenolone Biosynthesis	N/A	N/A	0.35	0.08	0.34	0.08
Acetone Degradation I (to Methylglyoxal)	N/A	N/A	0.38	0.08	N/A	N/A
Putrescine Degradation III	N/A	N/A	1.90	0.17	0.70	0.10
Tetrahydrobiopterin Biosynthesis II	N/A	N/A	0.60	0.08	0.58	0.08
Sphingomyelin Metabolism	N/A	N/A	0.35	0.06	N/A	N/A
Galactose Degradation I (Leloir Pathway)	N/A	N/A	0.41	0.06	0.40	0.06
Fatty Acid Alpha-oxidation	N/A	N/A	0.95	0.14	0.43	0.10
Sulfite Oxidation IV	N/A	N/A	N/A	N/A	1.01	0.25
dTMP De Novo Biosynthesis	N/A	N/A	0.41	0.07	N/A	N/A
Glycine Betaine Degradation	N/A	N/A	0.21	0.04	N/A	N/A
UDP-N-acetyl-D-galactosamine Biosynthesis II	N/A	N/A	0.23	0.04	N/A	N/A
Oxidative Ethanol Degradation III	N/A	N/A	0.80	0.08	0.36	0.05
Ethanol Degradation IV	N/A	N/A	0.69	0.10	0.30	0.07
Ethanol Degradation II	N/A	N/A	0.55	0.09	0.50	0.09
N-acetylglucosamine Degradation II	N/A	N/A	1.34	0.17	N/A	N/A
Tyrosine Degradation I	N/A	N/A	N/A	N/A	0.40	0.07
Glutamate Degradation III (via 4-aminobutyrate)	N/A	N/A	N/A	N/A	0.40	0.08
Methionine Degradation I (to Homocysteine)	N/A	N/A	N/A	N/A	0.36	0.09
Superpathway of Methionine Degradation	N/A	N/A	N/A	N/A	0.47	0.06
Folate Polyglutamylation	N/A	N/A	N/A	N/A	0.40	0.06
Folate Transformations I	N/A	N/A	N/A	N/A	0.66	0.06
S-adenosyl-L-methionine Biosynthesis	N/A	N/A	N/A	N/A	0.58	0.13
G-alpha(i) Signaling	N/A	N/A	0.39	0.09	N/A	N/A
Cysteine Biosynthesis III (mammalia)	N/A	N/A	N/A	N/A	0.64	0.10
4-aminobutyrate Degradation I	N/A	N/A	N/A	N/A	0.58	0.10
L-serine Degradation	N/A	N/A	0.60	0.17	N/A	N/A

Table S27. Subtype 3 (BLIS) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Fatty Acid beta-oxidation III (Unsaturated, Odd Number)	N/A	N/A	N/A	N/A	0.58	0.20
N-acetylglucosamine Degradation I	N/A	N/A	0.60	0.13	N/A	N/A
Regulation of the Epithelial-Mesenchymal Transition Pathway	N/A	N/A	0.46	0.09	0.77	0.11
Role of p14/p19ARF in Tumor Suppression	N/A	N/A	1.75	0.22	0.79	0.16
UVB-Induced MAPK Signaling	N/A	N/A	0.28	0.09	0.25	0.09
IL-2 Signaling	N/A	N/A	0.43	0.10	1.16	0.16
Serotonin Receptor Signaling	N/A	N/A	0.85	0.11	N/A	N/A
Chemokine Signaling	N/A	N/A	0.55	0.11	0.31	0.10
Notch Signaling	N/A	N/A	0.91	0.14	1.19	0.16
IL-6 Signaling	N/A	N/A	0.30	0.09	N/A	N/A
PDGF Signaling	N/A	N/A	N/A	N/A	0.47	0.11

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Pathogenesis of Multiple Sclerosis	11.90	0.78	9.85	0.78	7.65	0.89
Primary Immunodeficiency Signaling	7.50	0.13	11.30	0.21	14.10	0.37
Antigen Presentation Pathway	6.39	0.18	7.80	0.25	17.80	0.63
Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells	5.77	0.09	3.91	0.09	15.60	0.32
Granulocyte Adhesion and Diapedesis	5.38	0.07	4.87	0.09	7.15	0.23
T Cell Receptor Signaling	4.94	0.08	4.76	0.11	12.90	0.35
iCOS-iCOSL Signaling in T Helper Cells	4.90	0.07	6.22	0.11	15.90	0.34
Type I Diabetes Mellitus Signaling	4.72	0.08	6.72	0.13	16.50	0.37
CCR5 Signaling in Macrophages	4.44	0.07	4.99	0.11	4.15	0.19
Agranulocyte Adhesion and Diapedesis	4.42	0.06	5.20	0.09	5.63	0.21
Interferon Signaling	4.03	0.14	5.64	0.22	7.55	0.44
Allograft Rejection Signaling	3.83	0.05	3.38	0.07	19.50	0.29
CD28 Signaling in T Helper Cells	3.74	0.06	4.95	0.10	16.30	0.34
Crosstalk between Dendritic Cells and Natural Killer Cells	3.72	0.07	8.09	0.16	22.80	0.47
Graft-versus-Host Disease Signaling	3.65	0.10	3.17	0.12	13.30	0.46
Role of Hypercytokinemia/hyperchemokine in the Pathogenesis of Influenza	3.54	0.11	3.05	0.14	3.13	0.27
Communication between Innate and Adaptive Immune Cells	3.39	0.06	3.26	0.07	21.10	0.36
Tumoricidal Function of Hepatic Natural Killer Cells	3.37	0.17	4.27	0.25	4.72	0.46
Hematopoiesis from Pluripotent Stem Cells	3.16	0.06	2.12	0.06	4.14	0.18
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	3.05	0.07	4.23	0.11	19.90	0.45
Calcium-induced T Lymphocyte Apoptosis	3.03	0.07	3.21	0.10	4.84	0.24
Hepatic Fibrosis / Hepatic Stellate Cell Activation	3.00	0.05	4.39	0.10	8.07	0.27
Autoimmune Thyroid Disease Signaling	2.93	0.07	2.71	0.08	12.90	0.34
CTLA4 Signaling in Cytotoxic T Lymphocytes	2.82	0.06	2.55	0.08	8.93	0.31
Granzyme B Signaling	2.78	0.19	1.10	0.13	1.03	0.25
Retinoic acid Mediated Apoptosis Signaling	2.77	0.07	1.59	0.07	1.34	0.16
Inhibition of Matrix Metalloproteases	2.64	0.10	0.53	0.05	0.96	0.18
Cell Cycle: G2/M DNA Damage Checkpoint Regulation	2.44	0.08	N/A	N/A	0.47	0.13
Natural Killer Cell Signaling	2.38	0.05	7.48	0.14	8.94	0.28
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A & IL-17F	2.37	0.13	1.59	0.13	1.54	0.26
NF-kappaB Activation by Viruses	2.33	0.06	2.91	0.10	6.40	0.29
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	2.31	0.11	1.54	0.11	3.32	0.33
Prolactin Signaling	2.30	0.06	2.88	0.10	2.26	0.20
PKC-delta Signaling in T Lymphocytes	2.30	0.04	4.95	0.09	11.80	0.27
IL-17A Signaling in Gastric Cells	2.21	0.12	2.24	0.16	1.79	0.28
Tec Kinase Signaling	2.13	0.04	2.36	0.06	7.18	0.22
Role of NFAT in Regulation of the Immune Response	2.03	0.04	4.27	0.08	10.50	0.24
Glioma Invasiveness Signaling	1.96	0.07	0.30	0.03	2.08	0.22
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	1.94	0.05	5.72	0.12	15.30	0.38
Role of PI3K/AKT Signaling in the Pathogenesis of Influenza	1.91	0.05	1.53	0.07	1.95	0.18
T Helper Cell Differentiation	1.89	0.06	4.23	0.13	10.50	0.38

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Role of JAK1 and JAK3 in Gamma Chain-binding Cytokine Signaling	1.89	0.06	4.23	0.13	6.74	0.33
Protein Ubiquitination Pathway	1.88	0.03	1.83	0.05	1.64	0.14
IL-12 Signaling and Production in Macrophages	1.88	0.04	2.34	0.06	6.08	0.22
IL-15 Signaling	1.86	0.06	2.05	0.09	3.12	0.24
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	1.75	0.03	2.67	0.06	5.98	0.20
Role of PKR in Interferon Induction and Antiviral Response	1.68	0.07	2.26	0.11	4.39	0.30
Leukocyte Extravasation Signaling	1.62	0.03	3.37	0.07	7.35	0.23
Granzyme A Signaling	1.57	0.10	1.06	0.10	0.54	0.15
Differential Regulation of Cytokine Production in Macrophages & T Helper Cells by IL-17A & IL-17F	1.57	0.11	1.06	0.11	1.48	0.28
Nur77 Signaling in T Lymphocytes	1.56	0.05	2.08	0.08	5.16	0.25
iNOS Signaling	1.56	0.06	4.51	0.15	4.49	0.28
OX40 Signaling Pathway	1.54	0.03	2.04	0.05	16.00	0.31
VDR/RXR Activation	1.51	0.05	1.56	0.07	0.44	0.12
Glucocorticoid Receptor Signaling	1.43	0.03	1.18	0.04	2.90	0.15
UVA-Induced MAPK Signaling	1.38	0.04	0.96	0.05	1.59	0.17
Semaphorin Signaling in Neurons	1.35	0.06	0.34	0.04	0.45	0.14
Apoptosis Signaling	1.35	0.04	2.36	0.08	3.30	0.22
IL-2 Signaling	1.33	0.05	1.71	0.09	2.83	0.24
Thrombopoietin Signaling	1.29	0.05	1.11	0.06	1.44	0.18
p53 Signaling	1.29	0.04	N/A	N/A	N/A	N/A
HMGB1 Signaling	1.28	0.04	0.29	0.03	2.97	0.21
IL-15 Production	1.23	0.06	2.18	0.13	3.57	0.32
Antiproliferative Role of TOB in T Cell Signaling	1.23	0.08	0.75	0.08	0.81	0.19
Melatonin Degradation II	1.23	0.08	0.95	0.08	0.43	0.08
Induction of Apoptosis by HIV1	1.22	0.05	1.53	0.08	3.81	0.26
ATM Signaling	1.22	0.05	0.28	0.03	0.31	0.12
Colorectal Cancer Metastasis Signaling	1.21	0.03	N/A	N/A	2.59	0.16
Role of BRCA1 in DNA Damage Response	1.20	0.05	0.59	0.05	N/A	N/A
Mitotic Roles of Polo-Like Kinase	1.17	0.04	N/A	N/A	0.27	0.10
Role of MAPK Signaling in the Pathogenesis of Influenza	1.14	0.04	0.54	0.04	1.07	0.16
Growth Hormone Signaling	1.10	0.04	1.89	0.08	2.37	0.20
Chemokine Signaling	1.09	0.04	1.33	0.07	1.86	0.19
Macropinocytosis Signaling	1.09	0.04	1.33	0.07	2.65	0.21
Renin-Angiotensin Signaling	1.09	0.03	1.00	0.05	3.20	0.19
Superoxide Radicals Degradation	1.06	0.13	0.79	0.13	0.30	0.13
Salvage Pathways of Pyrimidine Deoxyribonucleotides	1.06	0.06	0.79	0.06	0.87	0.11
IL-3 Signaling	1.04	0.04	0.47	0.04	1.37	0.18
PEDF Signaling	1.03	0.04	0.81	0.05	1.65	0.18
IL-9 Signaling	1.03	0.05	1.77	0.10	3.12	0.28
Oncostatin M Signaling	1.03	0.06	0.58	0.06	1.12	0.20
IL-17 Signaling	1.02	0.04	N/A	N/A	1.01	0.16

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Tryptophan Degradation to 2-amino-3-carboxymuconate Semialdehyde	0.99	0.06	0.72	0.06	1.47	0.17
Cdc42 Signaling	0.97	0.02	0.86	0.03	4.09	0.16
HER-2 Signaling in Breast Cancer	0.96	0.04	1.14	0.06	1.42	0.18
Phospholipase C Signaling	0.95	0.02	2.32	0.05	5.46	0.18
Cyclins and Cell Cycle Regulation	0.95	0.03	N/A	N/A	0.46	0.11
Role of IL-17F in Allergic Inflammatory Airway Diseases	0.89	0.04	0.47	0.04	1.11	0.17
Salvage Pathways of Pyrimidine Ribonucleotides	0.89	0.03	0.36	0.03	0.53	0.11
Aryl Hydrocarbon Receptor Signaling	0.86	0.02	0.27	0.02	0.42	0.10
Hepatic Cholestasis	0.84	0.02	1.37	0.05	3.97	0.17
MSP-RON Signaling Pathway	0.83	0.04	0.84	0.06	6.28	0.36
Virus Entry via Endocytic Pathways	0.83	0.03	2.95	0.09	3.74	0.22
Purine Nucleotides De Novo Biosynthesis II	0.81	0.02	N/A	N/A	N/A	N/A
CNTF Signaling	0.80	0.04	N/A	N/A	1.15	0.16
Leukotriene Biosynthesis	0.78	0.04	N/A	N/A	N/A	N/A
Gamma-glutamyl Cycle	0.78	0.04	N/A	N/A	N/A	N/A
Assembly of RNA Polymerase II Complex	0.77	0.04	N/A	N/A	N/A	N/A
NAD biosynthesis II (from tryptophan)	0.74	0.03	0.49	0.03	0.78	0.09
Pyrimidine Deoxyribonucleotides De Novo Biosynthesis I	0.74	0.03	N/A	N/A	2.80	0.18
UVB-Induced MAPK Signaling	0.74	0.04	0.35	0.04	0.70	0.15
HIF1-alpha Signaling	0.72	0.03	N/A	N/A	0.38	0.11
Phenylalanine Degradation IV (Mammalian, via Side Chain)	0.72	0.03	0.47	0.03	0.33	0.05
Lymphotoxin-beta Receptor Signaling	0.70	0.03	1.68	0.08	4.95	0.30
Role of IL-17A in Arthritis	0.70	0.03	0.67	0.05	2.75	0.22
EGF Signaling	0.68	0.03	N/A	N/A	N/A	N/A
Dendritic Cell Maturation	0.68	0.02	3.71	0.07	18.20	0.29
Tryptophan Degradation X (Mammalian, via Tryptamine)	0.66	0.03	0.42	0.03	0.59	0.10
Putrescine Degradation III	0.66	0.03	0.42	0.03	0.59	0.10
Role of Tissue Factor in Cancer	0.66	0.03	0.42	0.03	2.24	0.18
Myc Mediated Apoptosis Signaling	0.66	0.03	N/A	N/A	1.63	0.20
ErbB4 Signaling	0.66	0.03	0.61	0.04	0.99	0.15
Death Receptor Signaling	0.66	0.03	1.04	0.06	2.89	0.23
Activation of IRF by Cytosolic Pattern Recognition Receptors	0.65	0.03	3.50	0.11	6.21	0.29
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	0.65	0.02	0.35	0.03	1.32	0.13
Hereditary Breast Cancer Signaling	0.63	0.02	N/A	N/A	N/A	N/A
p38 MAPK Signaling	0.62	0.03	0.64	0.04	1.48	0.16
Role of Lipids/Lipid Rafts in the Pathogenesis of Influenza	0.62	0.04	0.38	0.04	0.22	0.07
GM-CSF Signaling	0.62	0.03	0.96	0.06	2.58	0.22
Molecular Mechanisms of Cancer	0.61	0.02	0.55	0.03	0.91	0.12
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	0.61	0.02	2.82	0.05	7.60	0.19
Dopamine Degradation	0.60	0.03	0.36	0.03	0.82	0.11
Tryptophan Degradation III (Eukaryotic)	0.60	0.02	0.36	0.02	0.45	0.06

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
DNA damage-induced 14-3-3 Sigma Signaling	0.60	0.05	0.36	0.05	0.45	0.14
B Cell Development	0.58	0.03	1.70	0.09	10.40	0.46
Systemic Lupus Erythematosus Signaling	0.58	0.02	1.89	0.04	9.81	0.20
Erythropoietin Signaling	0.57	0.03	1.33	0.06	2.65	0.21
JAK/Stat Signaling	0.57	0.03	0.50	0.04	1.86	0.20
Polyamine Regulation in Colon Cancer	0.56	0.03	0.90	0.07	0.70	0.14
Cell Cycle Control of Chromosomal Replication	0.56	0.03	N/A	N/A	0.70	0.13
NRF2-mediated Oxidative Stress Response	0.56	0.02	N/A	N/A	N/A	N/A
IL-10 Signaling	0.56	0.03	0.85	0.05	3.02	0.22
IL-4 Signaling	0.56	0.03	2.42	0.09	5.08	0.27
Clathrin-mediated Endocytosis Signaling	0.55	0.02	0.38	0.03	1.27	0.14
ILK Signaling	0.55	0.02	0.81	0.04	0.90	0.13
FLT3 Signaling in Hematopoietic Progenitor Cells	0.53	0.03	NA	NA	1.05	0.16
Small Cell Lung Cancer Signaling	0.53	0.02	1.24	0.06	1.33	0.15
IL-8 Signaling	0.53	0.02	1.37	0.05	1.77	0.15
LPS-stimulated MAPK Signaling	0.52	0.02	0.78	0.05	1.89	0.18
IL-22 Signaling	0.51	0.04	0.29	0.04	0.30	0.12
Estrogen-mediated S-phase Entry	0.51	0.04	0.81	0.07	0.57	0.14
Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes	0.51	0.02	3.51	0.10	6.15	0.27
VEGF Family Ligand-Receptor Interactions	0.51	0.02	0.43	0.04	0.74	0.13
Role of JAK family kinases in IL-6-type Cytokine Signaling	0.50	0.04	0.78	0.07	1.29	0.22
Acute Myeloid Leukemia Signaling	0.49	0.02	N/A	N/A	2.08	0.20
Reelin Signaling in Neurons	0.49	0.02	2.13	0.09	2.87	0.22
PDGF Signaling	0.49	0.02	0.72	0.05	2.40	0.20
TNFR2 Signaling	0.46	0.03	2.92	0.15	5.56	0.39
LPS/IL-1 Mediated Inhibition of RXR Function	0.44	0.02	0.26	0.03	1.42	0.13
Bladder Cancer Signaling	0.44	0.02	N/A	N/A	N/A	N/A
Role of p14/p19ARF in Tumor Suppression	0.43	0.03	N/A	N/A	0.37	0.13
Serotonin Receptor Signaling	0.43	0.02	0.66	0.04	N/A	N/A
G-alpha-q Signaling	0.43	0.02	0.89	0.04	1.37	0.14
RANK Signaling in Osteoclasts	0.43	0.02	0.34	0.03	1.63	0.17
ErbB Signaling	0.43	0.02	0.62	0.05	1.08	0.16
Factors Promoting Cardiogenesis in Vertebrates	0.43	0.02	0.33	0.03	N/A	N/A
4-1BB Signaling in T Lymphocytes	0.42	0.03	1.91	0.11	2.87	0.28
G Protein Signaling Mediated by Tubby	0.42	0.02	0.64	0.05	0.92	0.14
Noradrenaline and Adrenaline Degradation	0.42	0.02	0.22	0.02	0.34	0.08
SAPK/JNK Signaling	0.41	0.02	0.93	0.05	1.86	0.17
Role of JAK2 in Hormone-like Cytokine Signaling	0.41	0.03	1.17	0.08	1.31	0.19
Retinol Biosynthesis	0.41	0.02	N/A	N/A	N/A	N/A
Aldosterone Signaling in Epithelial Cells	0.40	0.02	N/A	N/A	0.67	0.12
TWEAK Signaling	0.40	0.03	1.81	0.11	3.24	0.29

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
CXCR4 Signaling	0.40	0.02	0.54	0.04	0.79	0.13
Glioma Signaling	0.39	0.02	0.29	0.03	1.35	0.14
Coagulation System	0.38	0.03	N/A	N/A	N/A	N/A
NF-kappaB Signaling	0.37	0.02	2.19	0.06	12.60	0.29
Telomerase Signaling	0.37	0.02	0.27	0.03	0.30	0.11
tRNA Charging	0.36	0.01	N/A	N/A	N/A	N/A
Notch Signaling	0.36	0.02	N/A	N/A	N/A	N/A
Amyotrophic Lateral Sclerosis Signaling	0.36	0.02	N/A	N/A	0.41	0.10
Paxillin Signaling	0.36	0.02	1.18	0.05	2.72	0.19
Neuropathic Pain Signaling In Dorsal Horn Neurons	0.36	0.02	0.49	0.04	0.28	0.10
Serotonin Degradation	0.36	0.01	N/A	N/A	N/A	N/A
HGF Signaling	0.35	0.02	0.78	0.05	0.38	0.11
Cholecystokinin/Gastrin-mediated Signaling	0.35	0.02	0.48	0.04	0.71	0.13
Docosahexaenoic Acid (DHA) Signaling	0.35	0.02	N/A	N/A	0.59	0.12
Neuroprotective Role of THOP1 in Alzheimer's Disease	0.35	0.02	N/A	N/A	2.58	0.20
Superpathway of Melatonin Degradation	0.35	0.01	N/A	N/A	N/A	N/A
Role of RIG1-like Receptors in Antiviral Innate Immunity	0.34	0.02	1.53	0.08	3.61	0.27
Mechanisms of Viral Exit from Host Cells	0.34	0.02	0.95	0.07	N/A	N/A
Thyroid Cancer Signaling	0.34	0.02	N/A	N/A	N/A	N/A
Transcriptional Regulatory Network in Embryonic Stem Cells	0.34	0.03	N/A	N/A	N/A	N/A
Wnt/Beta-catenin Signaling	0.34	0.02	N/A	N/A	N/A	N/A
Fc-gamma-RIIB Signaling in B Lymphocytes	0.33	0.02	0.92	0.05	5.48	0.27
UVC-Induced MAPK Signaling	0.33	0.02	0.47	0.05	N/A	N/A
Fc Epsilon RI Signaling	0.33	0.02	0.72	0.04	3.12	0.20
RAR Activation	0.33	0.02	N/A	N/A	0.62	0.12
Melanoma Signaling	0.32	0.02	N/A	N/A	0.30	0.11
fMLP Signaling in Neutrophils	0.32	0.02	0.70	0.04	2.63	0.17
Sphingosine-1-phosphate Signaling	0.32	0.02	N/A	N/A	4.23	0.22
Corticotropin Releasing Hormone Signaling	0.32	0.01	0.42	0.03	N/A	N/A
Pancreatic Adenocarcinoma Signaling	0.32	0.02	N/A	N/A	0.91	0.13
Androgen Signaling	0.31	0.01	N/A	N/A	N/A	N/A
Role of Oct4 in Mammalian Embryonic Stem Cell Pluripotency	0.30	0.02	N/A	N/A	0.26	0.11
nNOS Signaling in Neurons	0.30	0.02	0.84	0.06	0.25	0.10
mTOR Signaling	0.30	0.01	N/A	N/A	N/A	N/A
Xenobiotic Metabolism Signaling	0.30	0.01	N/A	N/A	N/A	N/A
CCR3 Signaling in Eosinophils	0.30	0.02	N/A	N/A	N/A	N/A
Type II Diabetes Mellitus Signaling	0.30	0.01	1.34	0.04	2.01	0.13
TNFR1 Signaling	0.29	0.02	1.31	0.08	2.37	0.23
LXR/RXR Activation	0.29	0.01	N/A	N/A	2.80	0.18
14-3-3-mediated Signaling	0.29	0.02	N/A	N/A	0.42	0.12
PTEN Signaling	0.29	0.02	0.36	0.03	1.88	0.16

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Ephrin A Signaling	0.28	0.02	N/A	N/A	0.55	0.14
Atherosclerosis Signaling	0.28	0.01	N/A	N/A	7.86	0.26
IL-6 Signaling	0.28	0.02	0.60	0.04	2.80	0.19
p70S6K Signaling	0.27	0.02	1.22	0.05	1.72	0.16
P2Y Purigenic Receptor Signaling Pathway	0.27	0.01	N/A	N/A	1.00	0.13
Thrombin Signaling	0.27	0.01	0.33	0.03	0.39	0.11
Role of Cytokines in Mediating Communication between Immune Cells	0.27	0.02	0.72	0.05	0.48	0.13
Endometrial Cancer Signaling	0.27	0.02	N/A	N/A	0.48	0.12
eNOS Signaling	0.25	0.01	0.53	0.03	1.07	0.13
Estrogen Receptor Signaling	0.25	0.01	N/A	N/A	N/A	N/A
Integrin Signaling	0.25	0.01	1.24	0.05	1.54	0.15
TREM1 Signaling	0.25	0.01	1.68	0.07	15.80	0.44
Regulation of Cellular Mechanics by Calpain Protease	0.25	0.01	0.32	0.03	0.61	0.11
Role of CHK Proteins in Cell Cycle Checkpoint Control	0.25	0.02	N/A	N/A	N/A	N/A
3-phosphoinositide Degradation	0.24	0.01	N/A	N/A	0.64	0.11
Actin Nucleation by ARP-WASP Complex	0.24	0.02	0.31	0.03	1.74	0.18
ErbB2-ErbB3 Signaling	0.24	0.02	N/A	N/A	0.79	0.15
Ovarian Cancer Signaling	0.24	0.01	N/A	N/A	N/A	N/A
PXR/RXR Activation	0.24	0.01	N/A	N/A	N/A	N/A
Cell Cycle: G1/S Checkpoint Regulation	0.23	0.02	N/A	N/A	0.31	0.11
Antiproliferative Role of Somatostatin Receptor 2	0.22	0.01	N/A	N/A	0.28	0.10
Estrogen-Dependent Breast Cancer Signaling	0.22	0.01	N/A	N/A	0.64	0.13
CD40 Signaling	0.21	0.01	2.02	0.09	4.60	0.27
Pyridoxal 5'-phosphate Salvage Pathway	0.21	0.01	N/A	N/A	N/A	N/A
Hypoxia Signaling in the Cardiovascular System	0.21	0.02	0.26	0.03	N/A	N/A
IL-17A Signaling in Airway Cells	0.21	0.01	0.94	0.06	2.09	0.19
Non-Small Cell Lung Cancer Signaling	0.20	0.01	N/A	N/A	0.56	0.11
Angiopoietin Signaling	0.20	0.01	0.52	0.04	1.61	0.18
Neuregulin Signaling	N/A	N/A	0.34	0.03	0.33	0.10
Circadian Rhythm Signaling	N/A	N/A	0.21	0.03	0.32	0.11
Synaptic Long Term Potentiation	N/A	N/A	0.60	0.04	0.29	0.10
Axonal Guidance Signaling	N/A	N/A	0.34	0.03	0.53	0.11
Actin Cytoskeleton Signaling	N/A	N/A	N/A	N/A	0.47	0.11
Synaptic Long Term Depression	N/A	N/A	0.44	0.03	N/A	N/A
PPAR-alpha/RXR-alpha Activation	N/A	N/A	0.70	0.04	1.73	0.14
Acute Phase Response Signaling	N/A	N/A	0.47	0.03	1.47	0.15
FXR/RXR Activation	N/A	N/A	N/A	N/A	0.39	0.10
Ceramide Signaling	N/A	N/A	N/A	N/A	0.44	0.11
Regulation of Actin-based Motility by Rho	N/A	N/A	0.67	0.04	0.74	0.14
Alpha-Adrenergic Signaling	N/A	N/A	0.34	0.03	0.47	0.11
Caveolar-mediated Endocytosis Signaling	N/A	N/A	1.26	0.06	2.45	0.19

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

Ingenuity Canonical Pathways	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Fc-gamma Receptor-mediated Phagocytosis in Macrophages and Monocytes	N/A	N/A	2.30	0.08	3.66	0.22
Melatonin Signaling	N/A	N/A	0.50	0.04	N/A	N/A
Endothelin-1 Signaling	N/A	N/A	N/A	N/A	1.61	0.14
Relaxin Signaling	N/A	N/A	N/A	N/A	0.39	0.10
Cardiac Hypertrophy Signaling	N/A	N/A	N/A	N/A	0.55	0.11
Melanocyte Development and Pigmentation Signaling	N/A	N/A	N/A	N/A	0.87	0.14
Germ Cell-Sertoli Cell Junction Signaling	N/A	N/A	N/A	N/A	0.62	0.12
Prostate Cancer Signaling	N/A	N/A	0.38	0.03	0.99	0.13
Chronic Myeloid Leukemia Signaling	N/A	N/A	N/A	N/A	0.67	0.12
G-alpha-12/13 Signaling	N/A	N/A	N/A	N/A	1.08	0.14
G Beta Gamma Signaling	N/A	N/A	0.32	0.03	N/A	N/A
FAK Signaling	N/A	N/A	0.33	0.03	1.59	0.16
PAK Signaling	N/A	N/A	N/A	N/A	1.50	0.15
Rac Signaling	N/A	N/A	N/A	N/A	1.47	0.15
RhoA Signaling	N/A	N/A	0.43	0.03	0.57	0.12
Protein Kinase A Signaling	N/A	N/A	0.57	0.03	N/A	N/A
Leptin Signaling in Obesity	N/A	N/A	N/A	N/A	0.74	0.13
Role of NFAT in Cardiac Hypertrophy	N/A	N/A	N/A	N/A	0.57	0.11
Glioblastoma Multiforme Signaling	N/A	N/A	N/A	N/A	0.79	0.12
PI3K Signaling in B Lymphocytes	N/A	N/A	1.58	0.06	8.33	0.26
Dopamine-DARPP32 Feedback in cAMP Signaling	N/A	N/A	1.03	0.04	N/A	N/A
NGF Signaling	N/A	N/A	N/A	N/A	0.57	0.12
Signaling by Rho Family GTPases	N/A	N/A	N/A	N/A	0.75	0.12
RhoGDI Signaling	N/A	N/A	0.41	0.03	0.47	0.11
Gap Junction Signaling	N/A	N/A	0.34	0.03	N/A	N/A
Mouse Embryonic Stem Cell Pluripotency	N/A	N/A	N/A	N/A	0.37	0.11
GDNF Family Ligand-Receptor Interactions	N/A	N/A	0.85	0.05	1.46	0.18
D-myo-inositol-5-phosphate Metabolism	N/A	N/A	0.29	0.03	0.66	0.11
D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.49	0.10
Superpathway of Inositol Phosphate Compounds	N/A	N/A	N/A	N/A	1.00	0.11
D-myo-inositol (3,4,5,6)-tetrakisphosphate Biosynthesis	N/A	N/A	N/A	N/A	0.49	0.10
3-phosphoinositide Biosynthesis	N/A	N/A	N/A	N/A	1.14	0.12
Sperm Motility	N/A	N/A	0.39	0.03	0.36	0.09
ERK/MAPK Signaling	N/A	N/A	0.77	0.04	0.45	0.11
PI3K/AKT Signaling	N/A	N/A	0.33	0.03	0.49	0.10
Nitric Oxide Signaling in the Cardiovascular System	N/A	N/A	N/A	N/A	0.72	0.11
B Cell Receptor Signaling	N/A	N/A	1.78	0.06	8.13	0.25
Insulin Receptor Signaling	N/A	N/A	N/A	N/A	0.37	0.11
PPAR Signaling	N/A	N/A	0.30	0.03	4.04	0.22
IGF-1 Signaling	N/A	N/A	0.51	0.04	0.44	0.11
Dopamine Receptor Signaling	N/A	N/A	0.42	0.03	N/A	N/A

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
TGF-beta Signaling	N/A	N/A	N/A	N/A	0.51	0.12
VEGF Signaling	N/A	N/A	0.60	0.04	0.60	0.12
G-Protein Coupled Receptor Signaling	N/A	N/A	N/A	N/A	0.65	0.12
MIF Regulation of Innate Immunity	N/A	N/A	N/A	N/A	2.15	0.20
CD27 Signaling in Lymphocytes	N/A	N/A	0.72	0.05	2.07	0.21
Airway Pathology in Chronic Obstructive Pulmonary Disease	N/A	N/A	N/A	N/A	1.30	0.33
B Cell Activating Factor Signaling	N/A	N/A	1.53	0.09	3.61	0.29
Airway Inflammation in Asthma	N/A	N/A	N/A	N/A	0.43	0.17
Cellular Effects of Sildenafil (Viagra)	N/A	N/A	0.53	0.03	0.41	0.10
Agrin Interactions at Neuromuscular Junction	N/A	N/A	0.51	0.04	0.96	0.16
Lipid Antigen Presentation by CD1	N/A	N/A	N/A	N/A	0.82	0.14
Maturity Onset Diabetes of Young (MODY) Signaling	N/A	N/A	N/A	N/A	0.41	0.10
RAN Signaling	N/A	N/A	0.42	0.04	N/A	N/A
April Mediated Signaling	N/A	N/A	1.60	0.09	3.25	0.28
IL-1 Signaling	N/A	N/A	0.55	0.04	0.89	0.13
Inhibition of Angiogenesis by TSP1	N/A	N/A	N/A	N/A	0.52	0.13
MIF-mediated Glucocorticoid Regulation	N/A	N/A	0.22	0.02	2.39	0.21
Mismatch Repair in Eukaryotes	N/A	N/A	0.44	0.04	N/A	N/A
DNA Double-Strand Break Repair by Homologous Recombination	N/A	N/A	0.47	0.06	0.33	0.12
DNA Double-Strand Break Repair by Non-Homologous End Joining	N/A	N/A	0.47	0.05	N/A	N/A
IL-17A Signaling in Fibroblasts	N/A	N/A	0.56	0.05	1.46	0.20
Role of IL-17A in Psoriasis	N/A	N/A	0.49	0.08	0.37	0.15
Hematopoiesis from Multipotent Stem Cells	N/A	N/A	0.52	0.08	0.85	0.25
GADD45 Signaling	N/A	N/A	0.36	0.05	N/A	N/A
Netrin Signaling	N/A	N/A	1.60	0.07	0.38	0.09
Arsenate Detoxification I (Glutaredoxin)	N/A	N/A	N/A	N/A	0.43	0.05
Heparan Sulfate Biosynthesis	N/A	N/A	N/A	N/A	0.27	0.08
Uracil Degradation II (Reductive)	N/A	N/A	N/A	N/A	0.43	0.09
Fatty Acid Activation	N/A	N/A	0.49	0.05	0.37	0.11
Sphingosine and Sphingosine-1-phosphate Metabolism	N/A	N/A	N/A	N/A	0.30	0.05
Heparan Sulfate Biosynthesis (Late Stages)	N/A	N/A	N/A	N/A	0.40	0.10
Pyrimidine Ribonucleotides De Novo Biosynthesis	N/A	N/A	0.35	0.02	2.37	0.15
UDP-D-xylose and UDP-D-glucuronate Biosynthesis	N/A	N/A	N/A	N/A	0.68	0.14
Androgen Biosynthesis	N/A	N/A	0.52	0.04	N/A	N/A
Beta-alanine Degradation I	N/A	N/A	N/A	N/A	0.68	0.10
Pyruvate Fermentation to Lactate	N/A	N/A	N/A	N/A	0.35	0.11
Pentose Phosphate Pathway (Oxidative Branch)	N/A	N/A	N/A	N/A	0.43	0.09
Superpathway of Serine and Glycine Biosynthesis I	N/A	N/A	N/A	N/A	0.30	0.06
PRPP Biosynthesis I	N/A	N/A	N/A	N/A	0.53	0.14
Sucrose Degradation V (Mammalian)	N/A	N/A	N/A	N/A	0.25	0.05
Ceramide Biosynthesis	N/A	N/A	N/A	N/A	0.30	0.06

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Gamma-linolenate Biosynthesis II (Animals)	N/A	N/A	0.40	0.04	0.24	0.08
NAD Salvage Pathway II	N/A	N/A	0.33	0.03	0.70	0.13
Phosphatidylethanolamine Biosynthesis II	N/A	N/A	N/A	N/A	0.22	0.06
Triacylglycerol Degradation	N/A	N/A	N/A	N/A	0.30	0.09
Serine Biosynthesis	N/A	N/A	N/A	N/A	0.43	0.08
D-myo-inositol (1,4,5)-Trisphosphate Biosynthesis	N/A	N/A	0.27	0.03	0.81	0.13
Guanine and Guanosine Salvage I	N/A	N/A	N/A	N/A	1.91	0.22
Phospholipases	N/A	N/A	N/A	N/A	0.45	0.11
Oleate Biosynthesis II (Animals)	N/A	N/A	N/A	N/A	0.58	0.11
Thioredoxin Pathway	N/A	N/A	N/A	N/A	0.30	0.13
Chondroitin Sulfate Biosynthesis	N/A	N/A	N/A	N/A	0.32	0.09
Proline Degradation	N/A	N/A	N/A	N/A	0.68	0.14
Dermatan Sulfate Biosynthesis	N/A	N/A	N/A	N/A	0.28	0.08
L-DOPA Degradation	N/A	N/A	N/A	N/A	0.68	0.08
Cholesterol Biosynthesis I	N/A	N/A	0.49	0.03	0.37	0.05
Glutathione-mediated Detoxification	N/A	N/A	0.33	0.02	N/A	N/A
1D-myo-inositol Hexakisphosphate Biosynthesis II (Mammalian)	N/A	N/A	0.36	0.04	N/A	N/A
Phenylethylamine Degradation I	N/A	N/A	N/A	N/A	1.20	0.18
Glycerol Degradation I	N/A	N/A	N/A	N/A	0.35	0.08
Urate Biosynthesis/Inosine 5'-phosphate Degradation	N/A	N/A	0.49	0.05	0.37	0.09
NAD Phosphorylation and Dephosphorylation	N/A	N/A	N/A	N/A	1.16	0.18
Dermatan Sulfate Biosynthesis (Late Stages)	N/A	N/A	N/A	N/A	0.59	0.13
Glycogen Degradation II	N/A	N/A	N/A	N/A	0.19	0.07
Valine Degradation I	N/A	N/A	N/A	N/A	0.22	0.06
Ascorbate Recycling (Cytosolic)	N/A	N/A	N/A	N/A	0.53	0.08
Superpathway of D-myo-inositol (1,4,5)-trisphosphate Metabolism	N/A	N/A	0.29	0.03	N/A	N/A
Purine Nucleotides Degradation II (Aerobic)	N/A	N/A	1.01	0.06	0.88	0.11
Mitochondrial L-carnitine Shuttle Pathway	N/A	N/A	0.42	0.05	0.27	0.09
Tetrahydrobiopterin Biosynthesis I	N/A	N/A	1.07	0.09	0.53	0.09
Glutathione Redox Reactions II	N/A	N/A	N/A	N/A	0.53	0.14
D-myo-inositol (1,3,4)-trisphosphate Biosynthesis	N/A	N/A	0.36	0.04	N/A	N/A
Adenine and Adenosine Salvage III	N/A	N/A	0.79	0.06	2.73	0.25
D-myo-inositol (1,4,5)-trisphosphate Degradation	N/A	N/A	0.38	0.04	0.22	0.09
4-hydroxyproline Degradation I	N/A	N/A	N/A	N/A	0.96	0.07
Thymine Degradation	N/A	N/A	N/A	N/A	0.43	0.09
Purine Ribonucleosides Degradation to Ribose-1-phosphate	N/A	N/A	0.79	0.06	1.68	0.17
Anandamide Degradation	N/A	N/A	N/A	N/A	0.68	0.20
Pyrimidine Ribonucleotides Interconversion	N/A	N/A	0.38	0.03	2.67	0.21
Xanthine and Xanthosine Salvage	N/A	N/A	N/A	N/A	0.96	0.11
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)	N/A	N/A	0.49	0.03	0.37	0.05
Histamine Degradation	N/A	N/A	N/A	N/A	0.41	0.07

Table S28. Subtype 4 (BLIA) Pathways with Differentially Expressed Members in Either the Discovery, Validation, or External Sets

	Discovery		Validation		External	
	-log(p-value)	Ratio	-log(p-value)	Ratio	-log(p-value)	Ratio
Ingenuity Canonical Pathways						
Chondroitin Sulfate Biosynthesis (Late Stages)	N/A	N/A	N/A	N/A	0.50	0.11
Guanosine Nucleotides Degradation III	N/A	N/A	0.52	0.05	0.41	0.09
Zymosterol Biosynthesis	N/A	N/A	0.79	0.05	0.87	0.09
Cholesterol Biosynthesis III (via Desmosterol)	N/A	N/A	0.49	0.03	0.37	0.05
Adenosine Nucleotides Degradation II	N/A	N/A	1.15	0.08	1.12	0.15
Threonine Degradation II	N/A	N/A	N/A	N/A	0.68	0.11
Histidine Degradation VI	N/A	N/A	N/A	N/A	0.19	0.05
Stearate Biosynthesis I (Animals)	N/A	N/A	0.21	0.02	N/A	N/A
Glycogen Biosynthesis II (from UDP-D-Glucose)	N/A	N/A	N/A	N/A	0.30	0.08
Adenine and Adenosine Salvage I	N/A	N/A	N/A	N/A	0.68	0.11
Arginine Degradation I (Arginase Pathway)	N/A	N/A	N/A	N/A	0.43	0.08
Pregnenolone Biosynthesis	N/A	N/A	N/A	N/A	0.30	0.08
Tetrahydrobiopterin Biosynthesis II	N/A	N/A	1.07	0.08	0.53	0.08
Galactose Degradation I (Leloir Pathway)	N/A	N/A	N/A	N/A	0.35	0.06
Fatty Acid Alpha-oxidation	N/A	N/A	N/A	N/A	0.37	0.10
Sulfite Oxidation IV	N/A	N/A	N/A	N/A	0.96	0.25
Putrescine Biosynthesis III	N/A	N/A	N/A	N/A	0.68	0.25
dTMP De Novo Biosynthesis	N/A	N/A	N/A	N/A	0.35	0.07
Oxidative Ethanol Degradation III	N/A	N/A	N/A	N/A	0.64	0.08
Ethanol Degradation IV	N/A	N/A	N/A	N/A	0.54	0.10
Fatty Acid β -oxidation I	N/A	N/A	0.24	0.02	N/A	N/A
S-adenosyl-L-methionine Biosynthesis	N/A	N/A	N/A	N/A	0.53	0.13
Superpathway of Cholesterol Biosynthesis	N/A	N/A	0.26	0.01	N/A	N/A
Antioxidant Action of Vitamin C	N/A	N/A	0.29	0.03	1.99	0.17
Remodeling of Epithelial Adherens Junctions	N/A	N/A	0.25	0.03	N/A	N/A
Acetate Conversion to Acetyl-CoA	N/A	N/A	N/A	N/A	0.35	0.09
Vitamin-C Transport	N/A	N/A	N/A	N/A	0.33	0.09
Toll-like Receptor Signaling	N/A	N/A	1.68	0.08	5.59	0.31
Endoplasmic Reticulum Stress Pathway	N/A	N/A	N/A	N/A	0.49	0.17
BMP signaling pathway	N/A	N/A	N/A	N/A	0.39	0.11
Complement System	N/A	N/A	0.22	0.03	1.31	0.20
Eicosanoid Signaling	N/A	N/A	N/A	N/A	0.51	0.10
Ephrin Receptor Signaling	N/A	N/A	N/A	N/A	1.02	0.12

Table S29. Pathway Overlap Between Sets by Subtypes.

<i>Subtype 1 (LAR)</i>						
Set Significance	Validation Set			External Set		
	All Validation Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test	All External Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test
> 0.05	259	22	1.2657E-08	281	23	1.3521E-02
≤ 0.05	55	29		170	28	

<i>Subtype 2 (MES)</i>						
Set Significance	Validation Set			External Set		
	All Validation Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test	All External Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test
> 0.05	291	30	4.7827E-06	204	29	9.1458E-05
≤ 0.05	65	27		60	28	

<i>Subtype 3 (BLIS)</i>						
Set Significance	Validation Set			External Set		
	All Validation Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test	All External Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test
> 0.05	229	6	6.4517E-04	218	6	3.3239E-03
≤ 0.05	115	15		138	15	

<i>Subtype 4 (BLIA)</i>						
Set Significance	Validation Set			External Set		
	All Validation Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test	All External Set tests	Only Sig Hits in Discovery Set	Fisher's Exact Test
> 0.05	201	19	9.2375E-10	229	12	2.7549E-08
≤ 0.05	78	44		182	51	