INGENUITY PATHWAY ANALYSIS

Analysis Name: MM.pink
Analysis Creation Date: 2022-04-26
Build version: exported
Content version: 73620684 (Release Date: 2022-03-12)

Experiment Metadata

Name	Value

Analysis Settings

Reference set: User Dataset
Relationship to include: Direct and Indirect
Includes Endogenous Chemicals
Optional Analyses: My Pathways My List

Filter Summary:
Consider only molecules and/or relationships where
(species = Rat OR Human OR Uncategorized OR Mouse) AND
(confidence = Experimentally Observed) AND
(tissues/cell lines = Activated helper T cells OR Activated Vd1 Gamma-delta T cells OR SF-539 OR Amygdala OR Effector memory cytotoxic T cells OR MDA-N OR Endothelial cells not otherwise specified OR Other Neurons OR Esophagus OR Salivary Gland OR Pheochromocytoma cell lines not otherwise specified OR Peritoneal macrophages OR Lung Cancer Cell Lines not otherwise specified OR Kidney Cancer Cell Lines not

otherwise specified OR CD56dim NK cells OR Mesenchymal stem cells OR Keratinocytes OR Subventricular Zone OR Cells not otherwise specified OR HepG2 OR TK-10 OR Ovary OR Neurons not otherwise specified OR HS 578T OR Fibroblasts OR Other Cells OR Smooth muscle cells not otherwise specified OR Monocytes not otherwise specified OR 3T3-L1 cells OR Other Ovarian Cancer Cell Lines OR Other Organ Systems OR SF-295 OR Other Smooth muscle cells OR Peripheral blood lymphocytes OR RKO OR Prostate Gland OR Other Cell Line OR Central memory helper T cells OR Effector memory helper T cells OR Cos-7 cells OR RAW 264.7 OR Other Bone marrow cells OR Microvascular endothelial cells OR Neutrophils OR Intraepithelial T lymphocytes OR SN12C OR Vd2 Gamma-delta T cells OR Other B lymphocytes OR Stromal cells OR RPMI-8266 OR OVCAR-5 OR Chondrocytes OR Forestomach OR Mononuclear leukocytes not otherwise specified OR Other Lymphocytes OR Other Prostate Cancer Cell Lines OR SW-620 OR Min6 OR Pre-B lymphocytes OR Other Melanoma Cell Lines OR Central memory cytotoxic T cells OR Megakaryocytes OR Plasma cells OR Hematopoietic progenitor cells OR Other Dendritic cells OR OVCAR-3 OR A375 OR SW-480 OR Dendritic cells not otherwise specified OR SK-MEL-28 OR Stomach OR Thalamus OR Activated CD56bright NK cells OR NCI-H23 OR PANC-1 OR J-774A.1 OR Other Lymphoma Cell Lines OR Other Tissues and Primary Cells OR Eosinophils OR SK-N-SH OR Purkinje cells OR Striatum OR P19 OR Activated CD56dim NK cells OR Langerhans cells OR NK cells not otherwise specified OR Other Teratocarcinoma Cell Lines OR PC-3 OR Granulocytes not otherwise specified OR Nucleus Accumbens OR UACC-257 OR Osteoblasts OR MCF7 OR Colon Cancer Cell Lines not otherwise specified OR Thymocytes OR K-562 OR Pyramidal neurons OR Epidermis OR Other Memory T lymphocytes OR Stem cells not otherwise specified OR UACC-62 OR Cell Line not otherwise specified OR Lymph node OR Placenta OR Bone marrow-derived macrophages OR Kidney cell lines not otherwise specified OR Cerebral Cortex OR INS-1 OR Cerebral Ventricles OR Corpus Callosum OR Pituitary Gland OR Large Intestine OR HeLa OR Myeloma Cell Lines not otherwise specified OR Vascular smooth muscle cells OR Sertoli cells OR Other Kidney cell lines OR BDCA-1+ dendritic cells OR Other Epithelial cells OR Murine NKT cells OR Th1 cells OR Memory T lymphocytes not otherwise specified OR Naive B cells OR Other Macrophages OR Microglia OR Other Mononuclear leukocytes OR Immune cell lines not otherwise specified OR NT2/D1 OR Plasmacytoid dendritic cells OR HOP-62 OR Cervical cancer cell line not otherwise specified OR CCRF-CEM OR CD34+ cells OR Effector T cells OR Pancreas OR Retina OR Immune cells not otherwise specified OR Thymus OR Caudate Nucleus OR Cornea OR A549-ATCC OR PC-12 cells OR Other Stem cells OR Lymphoma Cell Lines not otherwise specified OR Thyroid Gland OR Dermis OR NB4 OR Smooth Muscle OR Fibroblast cell lines not otherwise specified OR Other Kidney Cancer Cell Lines OR MDA-MB-361 OR Neuroblastoma Cell Lines not otherwise specified OR Spleen OR Substantia Nigra OR Mature monocyte-derived dendritic cells OR NCI-H332M OR U2OS OR BA/F3 OR Trigeminal Ganglion OR Myeloid dendritic cells OR PBMCs OR Hepatoma Cell Lines not otherwise specified OR Peripheral blood leukocytes not otherwise specified OR BT-474 OR HCC-2998 OR RXF-393 OR Other Cervical cancer cell line OR Epithelial cells not otherwise specified OR Monocyte-derived macrophage OR Other Monocytes OR Adipose OR Other Granulocytes OR Other NK cells OR Adipocytes OR Mast cells OR B lymphocytes not otherwise specified OR Bone marrow-derived dendritic cells OR Pro-B lymphocytes OR A498 OR Immature monocyte-derived dendritic cells OR SNB-75 OR Dorsal Root Ganglion

OR ACHN OR Macrophages not otherwise specified OR Th17 cells OR NIH/3T3 cells OR Putamen OR U266 OR LNCaP cells OR MDA-MB-231 OR Other Immune cells OR Cortical neurons OR T47-D OR Prostate Cancer Cell Lines not otherwise specified OR Small Intestine OR Other Macrophage Cancer Cell Lines OR Trachea OR Testis OR Other Osteosarcoma Cell Lines OR Blood platelets OR Other Immune cell lines OR Astrocytes OR Hep3B OR U87MG OR NCI-ADR-RES OR Other Leukemia Cell Lines OR IGROV1 OR Ventricular Zone OR Hypothalamus OR HEL OR Mammary Gland OR Calvaria OR 786-0 OR NCI-H522 OR U937 OR KM-12 OR Kidney OR Spinal Cord OR Other Fibroblast cell lines OR HUVEC cells OR Lung OR Lymphocytes not otherwise specified OR Caco2 cells OR Cerebellum OR Embryonic stem cells OR Natural T-regulatory cells OR 293 cells OR Bladder OR Ovarian Cancer Cell Lines not otherwise specified OR Gray Matter OR Memory B cells OR Splenocytes OR Liver OR Organ Systems not otherwise specified OR MG-63 OR Teratocarcinoma Cell Lines not otherwise specified OR Effector memory RA+ cytotoxic T cells OR Adrenal Gland OR HCT-15 OR Other T lymphocytes OR SK-MEL-5 OR Hepatocytes OR Nervous System not otherwise specified OR HMC-1 OR Hippocampus OR A2780 OR UO-31 OR Choroid Plexus OR NCI-H226 OR Granule cells OR Medulla Oblongata OR Brainstem OR SK-OV-3 OR Other Endothelial cells OR Olfactory Bulb OR Other Monocyte-derived dendritic cells OR HOP-92 OR Cytotoxic T cells OR Oocytes OR Other Pancreatic Cancer Cell Lines OR Other Neuroblastoma Cell Lines OR CAKI-1 OR SR OR Skeletal Muscle OR H460 OR MDA-MB-435 OR RBL-2H3 OR J774 OR Other Lung Cancer Cell Lines OR T lymphocytes not otherwise specified OR MOLT-4 OR Granulosa cells OR EKVX OR Melanoma Cell Lines not otherwise specified OR Swiss 3T3 cells OR Sciatic Nerve OR Melanocytes OR Bone marrow cells not otherwise specified OR Cartilage Tissue OR Lens OR White Matter OR COLO205 OR Macrophage Cancer Cell Lines not otherwise specified OR LOX IMVI OR MEF cells OR Crypt OR Vd1 Gamma-delta T cells OR Other Hepatoma Cell Lines OR Naive helper T cells OR Breast Cancer Cell Lines not otherwise specified OR HCT-116 OR Other Myeloma Cell Lines OR MALME-3M OR MDA-MB-468 OR Osteosarcoma Cell Lines not otherwise specified OR BDCA-3+ dendritic cells OR Pancreatic Cancer Cell Lines not otherwise specified OR Other Peripheral blood leukocytes OR BT-549 OR Granule Cell Layer OR Tissues and Primary Cells not otherwise specified OR Jurkat OR U251 OR Th2 cells OR HL-60 OR Activated Vd2 Gamma-delta T cells OR Other CNS Cell Lines OR Uterus OR CD4+ T-lymphocytes OR HuH7 OR OVCAR-4 OR OVCAR-8 OR Skin OR SK-MEL-2 OR Monocyte-derived dendritic cells not otherwise specified OR CNS Cell Lines not otherwise specified OR Leukemia Cell Lines not otherwise specified OR Heart OR THP-1 OR Beta islet cells OR DU-145 OR Other Breast Cancer Cell Lines OR Brain OR CD56bright NK cells OR Parietal Lobe OR Other Pheochromocytoma cell lines OR HT29 OR Other Colon Cancer Cell Lines OR Cardiomyocytes OR Peripheral blood monocytes OR M14 OR WEHI-231 OR Other Nervous System OR SF-268) AND (mol. types = biologic drug OR canonical pathway OR chemical - endogenous mammalian OR chemical - endogenous non-mammalian OR chemical - kinase inhibitor OR chemical - other OR chemical - protease inhibitor OR chemical drug OR chemical reagent OR chemical toxicant OR complex OR cytokine OR disease OR enzyme OR function OR fusion gene/product OR G-protein coupled receptor OR group OR growth factor OR ion channel OR kinase OR ligand-dependent nuclear receptor OR mature microRNA OR microRNA OR other OR peptidase OR phosphatase OR transcription regulator OR translation regulator OR transmembrane receptor OR transporter) AND

(data sources = An Open Access Database of Genome-wide Association Results OR BIND OR BioGRID OR Catalogue Of Somatic Mutations In Cancer (COSMIC) OR Chemical Carcinogenesis Research Information System (CCRIS) OR Clinical Genome Resource (ClinGen) OR ClinicalTrials.gov OR ClinVar OR Cognia OR DIP OR DrugBank OR Gene Ontology (GO) OR GVK Biosciences OR Hazardous Substances Data Bank (HSDB) OR HumanCyc OR Ingenuity Expert Findings OR Ingenuity ExpertAssist Findings OR IntAct OR Interactome studies OR MIPS OR miRBase OR miRecords OR Mouse Genome Database (MGD) OR Obesity Gene Map Database OR Online Mendelian Inheritance in Man (OMIM) OR TarBase OR TargetScan Human)

Top Canonical Pathways

Name	p-value	Overlap
Oxidative Phosphorylation	5.00E-06	94.1 % 32/34
LPS/IL-1 Mediated Inhibition of RXR Function	2.74E-05	81.0 % 64/79
Sirtuin Signaling Pathway	1.74E-04	75.9 % 82/108
Mitochondrial Dysfunction	2.33E-04	81.4 % 48/59
Fatty Acid -oxidation I	1.05E-03	94.4 % 17/18

Top Upstream Regulators

Upstream Regulators

Name	p-value	Predicted Activation
torin1	2.57E-10	Inhibited
RICTOR	4.87E-10	Inhibited
metribolone	4.85E-09	Activated

CLPP	9.75E-09	Inhibited
pirinixic acid	1.20E-08	Activated

Causal Network

Name	p-value	Predicted Activation
RICTOR	4.87E-10	Inhibited
desmosterol	6.83E-10	Inhibited
LG100268	9.07E-10	Activated
INSR	1.02E-09	Activated
antimycin A	1.45E-09	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value range	# Molecules
Cancer	4.28E-02 - 1.81E-05	3093
Organismal Injury and Abnormalities	4.29E-02 - 1.81E-05	3135
Tumor Morphology	4.16E-02 - 1.81E-05	193
Metabolic Disease	3.71E-02 - 3.20E-05	801
Developmental Disorder	2.80E-02 - 6.28E-05	290

Molecular and Cellular Functions

Name	p-value range	# Molecules
Cell Death and Survival	4.29E-02 - 1.81E-05	1220
Cell Signaling	3.12E-02 - 4.62E-05	108
Post-Translational Modification	1.42E-02 - 4.62E-05	92
Protein Synthesis	1.42E-02 - 4.62E-05	113
Vitamin and Mineral Metabolism	4.16E-02 - 5.04E-05	132

Physiological System Development and Function

Name	p-value range	# Molecules
Nervous System Development and Function	4.29E-02 - 3.79E-04	368
Digestive System Development and Function	4.29E-02 - 4.99E-04	193
Hepatic System Development and Function	3.48E-02 - 4.99E-04	138
Organ Development	4.16E-02 - 4.99E-04	307
Tissue Development	4.16E-02 - 1.02E-03	300

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value range	# Molecules
Increased Levels of Red Blood Cells	9.80E-02 - 9.80E-02	23
Increased Levels of Hematocrit	1.62E-01 - 1.62E-01	19

Increased Levels of ALT	1.00E00 - 2.07E-01	5
Decreased Levels of Albumin	1.00E00 - 3.50E-01	8
Increased Levels of Bilirubin	3.50E-01 - 3.50E-01	2

Cardiotoxicity

Name	p-value range	# Molecules
Cardiac Necrosis/Cell Death	5.92E-01 - 1.08E-02	68
Cardiac Dilation	1.00E00 - 2.67E-02	86
Cardiac Enlargement	1.00E00 - 2.67E-02	174
Cardiac Infarction	1.00E00 - 4.29E-02	70
Cardiac Arteriopathy	1.00E00 - 7.26E-02	90

Hepatotoxicity

Name	p-value range	# Molecules
Liver Inflammation/Hepatitis	1.00E00 - 4.99E-04	100
Liver Hyperplasia/Hyperproliferation	1.00E00 - 1.20E-02	1610
Hepatocellular carcinoma	1.00E00 - 2.04E-02	439
Liver Steatosis	1.00E00 - 4.57E-02	113
Liver Fibrosis	1.00E00 - 1.05E-01	83

Nephrotoxicity

Name	p-value range	# Molecules
Nephrosis	1.00E00 - 2.34E-02	51
Glomerular Injury	1.00E00 - 6.04E-02	85
Renal Damage	1.00E00 - 6.15E-02	71
Renal Necrosis/Cell Death	1.00E00 - 7.26E-02	126
Renal Tubule Injury	1.00E00 - 8.13E-02	26

Top Regulator Effect Networks

ID	Regulators	Disease & Functions	Consistency Score
1	DDX3X,FAAH,HSF2,LARP1,Lh,MLXIPL,MYC,MYCN,NFE2L2 (+2 more)	Cell death of osteosarcoma cells (+2 more)	13.752
2	BACH1,CLPP,HBA1/HBA2,Hbb-b1,KDM5A (+4 more)	Biosynthesis of purine ribonucleotide (+1 more)	8.944
3	CLPP,GSR,KDM5A (+6 more)	Biosynthesis of purine ribonucleotide (+4 more)	8.262
4	NR1I3,PPARGC1A,PXR ligand-PXR-Retinoic acid-RXR	Metabolism of vitamin,Metabolism of xenobiotic	6.102
5	ESRRA,ESRRG,INSR,MAP4K4,NR4A1,PKM,SLC27A2	Microvesicular hepatic steatosis	4.543

Top Networks

ID	Associated Network Functions	Score
1	Cellular Assembly and Organization, Cellular Function and Maintenance, Developmental Disorder	36

2	Cancer, Cell Death and Survival, Organismal Injury and Abnormalities	36
3	Metabolic Disease, Organismal Injury and Abnormalities, Developmental Disorder	36
4	RNA Post-Transcriptional Modification, Cancer, Cell Death and Survival	36
5	Developmental Disorder, Hereditary Disorder, Metabolic Disease	34

Top Tox Lists

Name	p-value	Overlap
LPS/IL-1 Mediated Inhibition of RXR Function	2.23E-05	80.7 % 67/83
Fatty Acid Metabolism	2.67E-05	87.2 % 41/47
Mitochondrial Dysfunction	2.33E-04	81.4 % 48/59
Cardiac Hypertrophy	2.19E-02	67.6 % 98/145
Glutathione Depletion - CYP Induction and Reactive Metabolites	2.54E-02	100.0 % 7/7

Top My Lists

Name	p-value	Overlap
DevBloodVesselSelectionGraph	4.31E-03	93.3 % 14/15
Vasculogenesis	5.15E-03	72.2 % 70/97
MuscleCellProliferation	1.61E-02	76.2 % 32/42
FAO	1.87E-02	79.3 % 23/29
MuscleDevelopment	3.16E-02	71.9 % 41/57

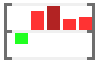
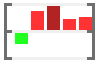
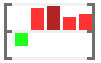
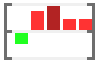
Top My Pathways

Name	p-value	Overlap
BloodVesselDevelop	4.31E-03	93.3 % 14/15
FAO	4.69E-02	76.9 % 20/26
MuscleCellProliferation	4.61E-01	64.3 % 9/14
quantity of photoreceptors 2	6.36E-01	66.7 % 2/3
ANGPT	1.00E00	50.0 % 1/2

Top Analysis-Ready Molecules

Expr Log Ratio

Molecules	Expr. Value	Chart
FH	↑ 0.964	

PGK1	0.955	
NDUFA9	0.948	
ATP5F1B*	0.947	
SUCLG1	0.946	
GATD3A/GATD3B	0.945	
ATP5PB	0.944	
SOD2*	0.940	
ATP5F1C	0.940	
SLC25A3	0.934	

Expr Log Ratio

Molecules	Expr. Value	Chart
CCDC15	-0.886	
LIN28B	-0.838	
BAHD1	-0.834	
TBC1D15	-0.832	
UBR3*	-0.832	
NEURL4*	-0.827	
MOB2	-0.823	

TECPR1	-0.822	
UBR1*	-0.819	
XPO7*	-0.817