INGENUITY
PATHWAY ANALYSIS

Analysis Name: mega_dataset_nov16
Analysis Creation Date: 2016-11-16
Build version: 400896M
Content version: 28820210 (Release Date: 2016-09-24)

Analysis Settings

Reference set: Ingenuity Knowledge Base (Genes Only)
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 = Mouse OR Rat OR Human) AND
(confidence = High (predicted) OR Experimentally Observed)

(c) 2000-2016 QIAGEN. All rights reserved.

Top Canonical Pathways

Name	p-value	Overlap
Oxidative Phosphorylation	1.88E-16	35.4 % 35/99
Mitochondrial Dysfunction	5.72E-13	25.2 % 40/159
TCA Cycle II (Eukaryotic)	7.19E-05	36.4 % 8/22
Methylglyoxal Degradation III	1.92E-03	35.7 % 5/14
RhoA Signaling	3.04E-03	14.5 % 17/117

Top Upstream Regulators

Upstream Regulator	p-value of overlap	Predicted Activation
TCF7L2	9.07E-20	Inhibited
RICTOR	5.95E-12	Activated
KDM5A	1.35E-09	Activated
RB1	3.89E-07	Inhibited
MAP4K4	1.24E-06	Activated

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value	#Molecules
Neurological Disease	1.69E-02 - 5.63E-10	181
Organismal Injury and Abnormalities	1.85E-02 - 5.64E-09	275
Developmental Disorder	1.78E-02 - 1.37E-05	150
Cancer	1.85E-02 - 1.03E-04	80
Hematological Disease	1.45E-02 - 1.28E-04	31

Molecular and Cellular Functions

(c) 2000-2016 QIAGEN. All rights reserved.

INGENUITY PATHWAY ANALYSIS

Name	p-value	#Molecules
Cell Morphology	1.90E-02 - 2.47E-10	293
Cellular Assembly and Organization	1.72E-02 - 2.47E-10	178
Cellular Function and Maintenance	1.73E-02 - 2.47E-10	170
Cellular Development	1.67E-02 - 2.60E-10	278
Cellular Growth and Proliferation	1.67E-02 - 2.60E-10	326

Physiological System Development and Function

Name	p-value	#Molecules
Nervous System Development and Function	1.73E-02 - 2.55E-10	279
Tissue Development	1.83E-02 - 1.92E-09	302
Organ Morphology	1.83E-02 - 1.96E-09	165
Organismal Development	1.83E-02 - 1.96E-09	312
Tissue Morphology	1.85E-02 - 1.09E-08	304

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value	#Molecules
Increased Levels of LDH	6.97E-02 - 6.97E-02	1
Increased Levels of Red Blood Cells	1.95E-01 - 1.51E-01	10
Increased Levels of Hematocrit	3.43E-01 - 3.43E-01	8
Increased Levels of Alkaline Phosphatase	3.84E-01 - 3.84E-01	4
Decreased Levels of Hematocrit	4.39E-01 - 4.39E-01	1

Cardiotoxicity

(c) 2000-2016 QIAGEN. All rights reserved.

INGENUITY PATHWAY ANALYSIS

Name	p-value	#Molecules
Cardiac Hypoplasia	2.51E-01 - 3.41E-03	10
Congenital Heart Anomaly	1.00E00 - 3.97E-03	15
Cardiac Hypertrophy	4.22E-01 - 2.69E-02	29
Cardiac Enlargement	8.06E-02 - 3.65E-02	4
Cardiac Stress Response	6.97E-02 - 6.97E-02	1

Hepatotoxicity

Name	p-value	#Molecules
Liver Hyperplasia/Hyperproliferation	5.48E-01 - 4.70E-03	23
Hepatocellular Carcinoma	3.23E-01 - 7.17E-03	16
Liver Damage	1.00E00 - 2.80E-02	8
Liver Dysplasia	4.21E-02 - 4.21E-02	2
Glutathione Depletion In Liver	3.03E-01 - 5.70E-02	5

Nephrotoxicity

Name	p-value	#Molecules
Renal Hypertrophy	2.32E-01 - 4.21E-02	4
Renal Damage	5.48E-01 - 6.84E-02	7
Renal Tubule Injury	5.48E-01 - 6.84E-02	5
Glomerular Injury	5.80E-01 - 6.97E-02	13
Kidney Failure	4.96E-01 - 6.97E-02	7

Top Regulator Effect Networks

ID	Regulators	Diseases & Functions	Consistency Score
1	TSC1	apoptosis of neurons,development of body axis (+2 more)	5.367

(c) 2000-2016 QIAGEN. All rights reserved.

INGENUITY PATHWAY ANALYSIS

2	TCF7L2	astrocytosis,demyelination of nerves	4.333
3	PAX6	migration of neurons	-7.0
4	PAX6	myelination	-7.506
5	PAX6	transactivation of RNA	-7.506

Top Networks

ID	Associated Network Functions	Score
1	Tissue Morphology, Cellular Development, Nervous System Development and Function	32
2	Amino Acid Metabolism, Drug Metabolism, Endocrine System Development and Function	32
3	Nervous System Development and Function, Neurological Disease, Cell Morphology	32
4	Cellular Development, Cellular Growth and Proliferation, Embryonic Development	30
5	Free Radical Scavenging, Small Molecule Biochemistry, Molecular Transport	28

Top Tox Lists

Name	p-value	Overlap
Mitochondrial Dysfunction	7.12E-13	25.0 % 40/160
Increases Liver Hyperplasia/Hyperproliferation	2.48E-02	12.7 % 13/102
RAR Activation	3.52E-02	10.8 % 20/186
Decreases Depolarization of Mitochondria and Mitochondrial Membrane	4.19E-02	17.9 % 5/28
Renal Necrosis/Cell Death	6.06E-02	8.8 % 45/510

Top My Lists

Name	p-value	Overlap
103pt01Found93	9.80E-08	27.0 % 20/74
AS3MT-d2d3corrDLPFC-top132becomes128byENSG	6.77E-06	19.3 % 23/119
pipe-oldCONTeqtlDLPFC-11-67-sum78	1.13E-01	11.4 % 8/70
PGC_DiffExp_40	1.43E-01	12.5 % 5/40
eqtl287_v003-removeHLA	1.76E-01	9.1 % 15/165

(c) 2000-2016 QIAGEN. All rights reserved.

INGENUITY PATHWAY ANALYSIS

Top My Pathways

Name	p-value	Overlap
103-93	9.80E-08	27.0 % 20/74
AS3MT-d2d3corrDLPFC-top132-128	6.77E-06	19.3 % 23/119
0405-2107-214-overlay-on-Axonal Guidance Signaling	2.00E-02	9.7 % 42/435
0405-2107-214-overlay-on-Axonal Guidance Signaling-2	2.00E-02	9.7 % 42/435
AS3MT-d2d3-top40	5.13E-02	15.4 % 6/39

Top Analysis-Ready Molecules

Exp Log Ratio up-regulated

Molecules	Exp. Value	Exp. Chart
AKR1C3	↑ 0.471	
KLHL14	↑ 0.374	
MC4R	↑ 0.333	
ATP2B4	↑ 0.320	
TCERG1L	↑ 0.299	
CFAP44	↑ 0.285	
TGM3	↑ 0.283	
SDK2	↑ 0.283	
COL23A1	↑ 0.282	
ZBTB7C	↑ 0.278	

Exp Log Ratio down-regulated

Molecules	Exp. Value	Exp. Chart
Cyp2j12	↓ -0.462	
CACNA2D4	↓ -0.446	
ENPP6	↓ -0.441	

(c) 2000-2016 QIAGEN. All rights reserved.

INGENUITY PATHWAY ANALYSIS

PRR5L	-0.376
TBATA	-0.367
MAL	-0.360
PDLIM2	-0.359
GJC2	-0.359
4921539H07Rik	-0.354
ID2	-0.353

(c) 2000-2016 QIAGEN. All rights reserved.

INGENUITY PATHWAY ANALYSIS