

INGENUITY[®]

PATHWAY ANALYSIS



Analysis Name: Liver - proteomics

Analysis Creation Date: 2017-09-22

Build version: 448560M

Content version: 36601845 (Release Date: 2017-06-22)

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 relationships where

confidence = Experimentally Observed

Top Canonical Pathways

Name	p-value	Overlap
Mitochondrial Dysfunction	7.16E-30	27.5 % 47/171
Oxidative Phosphorylation	6.15E-24	31.2 % 34/109
Nicotine Degradation II	1.45E-12	28.6 % 18/63
EIF2 Signaling	1.57E-11	14.0 % 31/221
Nicotine Degradation III	1.68E-10	27.8 % 15/54

Top Upstream Regulators

Upstream Regulator	p-value of overlap	Predicted Activation
HNF4A	1.76E-32	
RICTOR	7.50E-28	
LONP1	5.93E-19	
PPARA	6.08E-19	
pirinixic acid	1.16E-15	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value	#Molecules
Metabolic Disease	3.29E-03 - 3.64E-48	169
Developmental Disorder	3.29E-03 - 3.43E-29	124
Hereditary Disorder	3.77E-03 - 3.43E-29	230
Organismal Injury and Abnormalities	3.77E-03 - 3.43E-29	305
Neurological Disease	3.71E-03 - 2.01E-18	172

Molecular and Cellular Functions

Name	p-value	#Molecules
Amino Acid Metabolism	3.77E-03 - 8.09E-24	54
Small Molecule Biochemistry	3.88E-03 - 8.09E-24	256
Lipid Metabolism	3.77E-03 - 8.11E-19	171
Energy Production	3.29E-03 - 2.93E-13	78
Nucleic Acid Metabolism	3.29E-03 - 3.79E-13	73

Physiological System Development and Function

Name	p-value	#Molecules
Digestive System Development and Function	8.58E-04 - 1.68E-05	29
Hepatic System Development and Function	8.58E-04 - 1.68E-05	29
Organ Morphology	1.12E-03 - 1.68E-05	32
Organismal Development	3.77E-03 - 1.68E-05	40
Endocrine System Development and Function	3.77E-03 - 3.75E-05	18

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value	#Molecules
Increased Levels of Hematocrit	2.20E-01 - 2.20E-01	5
Increased Levels of LDH	3.13E-01 - 3.13E-01	1
Increased Levels of Creatinine	3.80E-01 - 3.80E-01	1
Increased Levels of AST	4.00E-01 - 4.00E-01	1
Increased Levels of ALT	5.28E-01 - 5.28E-01	1

Cardiotoxicity

Name	p-value	#Molecules
Cardiac Dilation	1.49E-01 - 4.14E-04	21
Cardiac Damage	3.36E-01 - 1.15E-02	9
Cardiac Fibrosis	6.15E-01 - 3.35E-02	10
Heart Failure	1.00E00 - 3.35E-02	9
Pulmonary Hypertension	3.35E-02 - 3.35E-02	1

Hepatotoxicity

Name	p-value	#Molecules
Liver Steatosis	3.90E-01 - 9.69E-06	27
Liver Cholestasis	2.64E-01 - 5.70E-04	12
Hepatocellular Peroxisome Proliferation	2.89E-01 - 2.71E-03	4
Liver Cirrhosis	1.00E00 - 6.57E-03	12
Liver Enlargement	1.57E-01 - 1.28E-02	8

Nephrotoxicity

Name	p-value	#Molecules
Renal Damage	2.14E-01 - 2.78E-04	20
Renal Tubule Injury	9.88E-02 - 2.78E-04	14
Renal Dilation	4.22E-02 - 5.06E-03	3
Renal Necrosis/Cell Death	3.87E-01 - 1.33E-02	27
Glomerular Injury	6.02E-01 - 3.35E-02	14

Top Regulator Effect Networks

ID	Regulators	Diseases & Functions	Consistency Score
1	MYCN	cell death of osteosarcoma cells	-.832
2	MYC	cell death of osteosarcoma cells	-5.774

3	EHHADH	concentration of lipid	-16.743
4	HSD17B4	concentration of lipid	-16.743

Top Networks

ID	Associated Network Functions	Score
1	Small Molecule Biochemistry, Hereditary Disorder, Metabolic Disease	56
2	Developmental Disorder, Hereditary Disorder, Metabolic Disease	50
3	Endocrine System Development and Function, Small Molecule Biochemistry, Drug Metabolism	50
4	Vitamin and Mineral Metabolism, Endocrine System Development and Function, Lipid Metabolism	50
5	Developmental Disorder, Hereditary Disorder, Metabolic Disease	48

Top Tox Lists

Name	p-value	Overlap
Mitochondrial Dysfunction	2.96E-29	26.7 % 47/176
Fatty Acid Metabolism	1.43E-16	23.9 % 28/117
LPS/IL-1 Mediated Inhibition of RXR Function	1.93E-09	11.9 % 30/252
Xenobiotic Metabolism Signaling	3.57E-08	9.7 % 34/352
NRF2-mediated Oxidative Stress Response	6.35E-08	11.0 % 27/245

Top My Lists

Name	p-value	Overlap
Changed only in WT - IUB288 Effect	2.62E-12	7.7 % 80/1036
Mitochondrial Dysfunction	1.19E-06	12.8 % 18/141
Bile Acid Synthesis	2.35E-04	18.4 % 7/38
Fatty Acid Synthesis	6.18E-03	5.1 % 38/739
Bile Acid Metabolism	1.51E-02	18.8 % 3/16

Top My Pathways

Name	p-value	Overlap
Metabolism Summary - DMRs with DEGs	8.45E-09	37.0 % 10/27

Top Analysis-Ready Molecules

Expr Log Ratio up-regulated

Molecules	Expr. Value	Expr. Chart
ANXA5	↑ 100.000	
ATP6V0C*	↑ 100.000	
ATP6V1A	↑ 100.000	
CAPZB	↑ 100.000	
CNIH4	↑ 100.000	
CNN3	↑ 100.000	
CYP2A6 (includes others)*	↑ 100.000	
CYP4A22*	↑ 100.000	
Cyp2c40 (includes others)*	↑ 100.000	
DCXR	↑ 100.000	

Expr Log Ratio down-regulated

Molecules	Expr. Value	Expr. Chart
ZNF536	↓ -100.000	
VAMP7	↓ -100.000	

TUBB4A	↓ -100.000	
Spata31d1d	↓ -100.000	
Slc25a48	↓ -100.000	
SLC15A1	↓ -100.000	
RHBDD1	↓ -100.000	
REEP6*	↓ -100.000	
OR5W2	↓ -100.000	
NDUFV2*	↓ -100.000	