

INGENUITY[®]

PATHWAY ANALYSIS



Analysis Name: Heart - 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	9.69E-53	29.2 % 50/171
Oxidative Phosphorylation	7.81E-47	36.7 % 40/109
TCA Cycle II (Eukaryotic)	4.54E-10	34.8 % 8/23
Ethanol Degradation II	6.01E-07	18.9 % 7/37
tRNA Charging	8.76E-07	17.9 % 7/39

Top Upstream Regulators

Upstream Regulator	p-value of overlap	Predicted Activation
RICTOR	1.09E-29	
KDM5A	8.03E-23	
LONP1	9.26E-22	
INSR	3.71E-20	
HNF4A	3.01E-17	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value	#Molecules
Metabolic Disease	2.71E-02 - 4.56E-40	87
Developmental Disorder	2.21E-02 - 1.87E-24	65
Hereditary Disorder	2.71E-02 - 1.87E-24	118
Organismal Injury and Abnormalities	2.71E-02 - 1.87E-24	140
Neurological Disease	2.71E-02 - 9.83E-18	96

Molecular and Cellular Functions

Name	p-value	#Molecules
Nucleic Acid Metabolism	2.71E-02 - 1.12E-13	46
Small Molecule Biochemistry	2.71E-02 - 1.12E-13	80
Energy Production	1.37E-02 - 1.95E-10	42
Cell Morphology	2.71E-02 - 2.36E-10	32
Cellular Assembly and Organization	2.71E-02 - 2.36E-10	44

Physiological System Development and Function

Name	p-value	#Molecules
Embryonic Development	2.71E-02 - 1.86E-04	11
Endocrine System Development and Function	1.02E-03 - 1.02E-03	4
Tissue Development	2.71E-02 - 1.10E-03	11
Cardiovascular System Development and Function	2.71E-02 - 2.69E-03	16
Organismal Development	2.71E-02 - 2.69E-03	16

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value	#Molecules
Increased Levels of Bilirubin	2.71E-02 - 2.71E-02	1
Increased Levels of Blood Urea Nitrogen	2.19E-01 - 2.19E-01	1
Increased Levels of LDH	3.65E-01 - 3.65E-01	1

Cardiotoxicity

Name	p-value	#Molecules
Cardiac Dilation	3.10E-01 - 7.08E-04	11
Cardiac Arrhythmia	5.74E-01 - 1.37E-02	3
Cardiac Dysfunction	1.60E-01 - 1.37E-02	6

Cardiac Enlargement	2.67E-01 - 1.37E-02	9
Congenital Heart Anomaly	1.37E-02 - 1.37E-02	2

Hepatotoxicity

Name	p-value	#Molecules
Glutathione Depletion In Liver	1.37E-02 - 1.37E-02	1
Liver Failure	2.23E-01 - 1.37E-02	2
Liver Inflammation/Hepatitis	1.00E00 - 1.37E-02	5
Liver Steatosis	2.81E-01 - 1.37E-02	8
Liver Fibrosis	5.18E-01 - 2.71E-02	2

Nephrotoxicity

Name	p-value	#Molecules
Glomerular Injury	5.38E-01 - 6.65E-02	4
Nephrosis	4.45E-01 - 1.04E-01	2
Renal Necrosis/Cell Death	1.00E00 - 1.04E-01	7
Renal Damage	1.35E-01 - 1.35E-01	3
Renal Tubule Injury	1.35E-01 - 1.35E-01	3

Top Networks

ID	Associated Network Functions	Score
1	Gene Expression, Protein Synthesis, Cellular Assembly and Organization	67
2	Metabolic Disease, Cellular Function and Maintenance, Lipid Metabolism	55
3	Energy Production, Nucleic Acid Metabolism, Small Molecule Biochemistry	55
4	Metabolic Disease, Developmental Disorder, Hereditary Disorder	55
5	Developmental Disorder, Hereditary Disorder, Metabolic Disease	52

Top Tox Lists

Name	p-value	Overlap
Mitochondrial Dysfunction	4.98E-52	28.4 % 50/176
Fatty Acid Metabolism	7.74E-09	11.1 % 13/117
Biogenesis of Mitochondria	2.42E-03	15.0 % 3/20
LPS/IL-1 Mediated Inhibition of RXR Function	2.56E-03	4.0 % 10/252
Increases Permeability Transition of Mitochondria and Mitochondrial Membrane	4.94E-03	25.0 % 2/8

Top My Lists

Name	p-value	Overlap
Mitochondrial Dysfunction	8.84E-13	12.8 % 18/141
Changed only in WT - IUB288 Effect	2.18E-03	2.5 % 26/1036
C57_only - p<0.01, FC > 1.5	1.00E00	1.2 % 4/328
Fatty Acid Synthesis	1.00E00	0.9 % 7/739



Top My Pathways

Name	p-value	Overlap
Metabolism Summary - DMRs with DEGs	5.56E-11	33.3 % 9/27










Top Analysis-Ready Molecules

Expr Log Ratio up-regulated

Molecules	Expr. Value	Expr. Chart
AGPAT5*	↑ 100.000	
CRYZ	↑ 100.000	

MTHFD1L	↑ 100.000	
OPRM1	↑ 100.000	
SFXN3*	↑ 100.000	
SLMAP	↑ 100.000	
Sf1	↑ 100.000	
TIMM8A	↑ 100.000	
TOMM20	↑ 100.000	
U2AF2	↑ 100.000	

Expr Log Ratio down-regulated

Molecules	Expr. Value	Expr. Chart
TOMM7	↓ -100.000	
TOMM6	↓ -100.000	
NARS2*	↓ -100.000	
MYH7	↓ -100.000	
Cox7c*	↓ -100.000	
CLTC	↓ -100.000	
ADIPOQ	↓ -100.000	
MYH4	↓ -3.282	
ATP5C1*	↓ -2.762	
MYH14	↓ -2.537	