INGENUITY
PATHWAY ANALYSIS

Analysis Name: Kidney - 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 | 1.15E-46 | 35.7 % 61/171 |
| Oxidative Phosphorylation | 4.75E-34 | 38.5 % 42/109 |
| TCA Cycle II (Eukaryotic) | 1.04E-09 | 43.5 % 10/23 |
| Fatty Acid -oxidation | 1.40E-08 | 40.9 % 9/22 |
| Ethanol Degradation II | 1.70E-08 | 29.7 % 11/37 |

## Top Upstream Regulators

| Upstream Regulator | p-value of overlap | Predicted Activation |
|---|---|---|
| HNF4A | 1.21E-24 | |
| LONP1 | 3.51E-24 | |
| RICTOR | 1.42E-23 | |
| KDM5A | 4.09E-21 | |
| mono-(2-ethylhexyl)phthalate | 1.82E-20 | |

## Top Diseases and Bio Functions

### Diseases and Disorders

| Name | p-value | #Molecules |
|---|---|---|
| Metabolic Disease | 6.15E-03 - 3.28E-53 | 206 |
| Developmental Disorder | 6.15E-03 - 1.62E-29 | 124 |
| Hereditary Disorder | 6.15E-03 - 1.62E-29 | 245 |
| Organismal Injury and Abnormalities | 6.16E-03 - 1.62E-29 | 399 |
| Neurological Disease | 6.15E-03 - 2.74E-22 | 202 |

### Molecular and Cellular Functions

| Name | p-value | #Molecules |
|---|---|---|
| Nucleic Acid Metabolism | 6.15E-03 - 7.30E-21 | 78 |
| Small Molecule Biochemistry | 6.17E-03 - 7.30E-21 | 242 |
| Energy Production | 4.14E-03 - 3.12E-14 | 80 |
| Lipid Metabolism | 6.17E-03 - 1.78E-10 | 142 |
| Cell Morphology | 6.15E-03 - 6.39E-10 | 171 |

### Physiological System Development and Function

| Name | p-value | #Molecules |
|---|---|---|
| Hematological System Development and Function | 6.15E-03 - 2.05E-05 | 14 |
| Tissue Development | 6.15E-03 - 2.05E-05 | 25 |
| Organ Morphology | 5.74E-03 - 2.09E-05 | 57 |
| Organismal Development | 5.74E-03 - 2.09E-05 | 99 |
| Renal and Urological System Development and Function | 5.22E-03 - 2.09E-05 | 33 |

## Top Tox Functions

### Assays: Clinical Chemistry and Hematology

| Name | p-value | #Molecules |
|---|---|---|
| Decreased Levels of Albumin | 1.81E-01 - 4.71E-03 | 5 |
| Increased Levels of Bilirubin | 7.52E-02 - 6.45E-02 | 2 |
| Increased Levels of Creatinine | 2.51E-01 - 7.52E-02 | 3 |
| Increased Levels of ALT | 1.81E-01 - 1.81E-01 | 1 |
| Increased Levels of Hematocrit | 2.07E-01 - 2.07E-01 | 5 |

### Cardiotoxicity

| Name | p-value | #Molecules |
|---|---|---|
| Cardiac Dilation | 3.79E-01 - 4.14E-05 | 23 |
| Heart Failure | 5.93E-01 - 6.15E-03 | 16 |
| Cardiac Arrythmia | 1.00E00 - 7.83E-03 | 4 |
| Cardiac Necrosis/Cell Death | 2.82E-01 - 3.21E-02 | 13 |
| Cardiac Damage | 4.56E-01 - 3.28E-02 | 6 |

**Hepatotoxicity**

| Name | p-value | #Molecules |
|---|---|---|
| Liver Steatosis | 3.79E-01 - 3.48E-08 | 24 |
| Liver Necrosis/Cell Death | 1.16E-01 - 3.75E-04 | 22 |
| Liver Cholestasis | 2.59E-01 - 6.47E-04 | 11 |
| Hepatocellular Carcinoma | 6.32E-01 - 2.77E-03 | 39 |
| Liver Hyperplasia/Hyperproliferation | 1.00E00 - 2.77E-03 | 205 |

**Nephrotoxicity**

| Name | p-value | #Molecules |
|---|---|---|
| Nephrosis | 4.87E-01 - 1.45E-05 | 14 |
| Renal Necrosis/Cell Death | 5.35E-01 - 5.72E-04 | 33 |
| Renal Inflammation | 1.00E00 - 7.66E-04 | 16 |
| Renal Nephritis | 1.00E00 - 7.66E-04 | 16 |
| Renal Damage | 3.78E-01 - 9.34E-04 | 20 |

## Top Networks

| ID | Associated Network Functions | Score |
|---|---|---|
| 1 | Metabolic Disease, Hereditary Disorder, Organismal Injury and Abnormalities | 53 |

| | | |
|---|---|---|
| 2 | Cell-To-Cell Signaling and Interaction, Hematological System Development and Function, Inflammatory Response | 51 |
| 3 | Gene Expression, Protein Synthesis, Cellular Function and Maintenance | 48 |
| 4 | Metabolic Disease, Small Molecule Biochemistry, Gastrointestinal Disease | 45 |
| 5 | Developmental Disorder, Hereditary Disorder, Metabolic Disease | 41 |

## Top Tox Lists

| Name | p-value | Overlap |
|---|---|---|
| Mitochondrial Dysfunction | 8.53E-46 | 34.7 % 61/176 |
| Fatty Acid Metabolism | 4.98E-13 | 20.5 % 24/117 |
| LPS/IL-1 Mediated Inhibition of RXR Function | 9.21E-05 | 8.3 % 21/252 |
| Increases Transmembrane Potential of Mitochondria and Mitochondrial Membrane | 2.03E-04 | 16.0 % 8/50 |
| Liver Necrosis/Cell Death | 4.49E-04 | 7.3 % 22/303 |

## Top My Lists

| Name | p-value | Overlap |
|---|---|---|
| Changed only in WT - IUB288 Effect | 8.08E-13 | 7.7 % 80/1036 |
| Mitochondrial Dysfunction | 2.06E-10 | 16.3 % 23/141 |
| C57_only - p<0.01, FC > 1.5 | 5.48E-04 | 7.0 % 23/328 |
| Fatty Acid Synthesis | 4.30E-03 | 5.1 % 38/739 |
| Bile Acid Synthesis | 3.55E-01 | 5.3 % 2/38 |

## Top My Pathways

| Name | p-value | Overlap |
|---|---|---|
| Metabolism Summary - DMRs with DEGs | 1.97E-05 | 25.9 % 7/27 |
| UHRF1 - CGIs - Pathway | 5.80E-01 | 3.8 % 1/26 |

## Top Analysis-Ready Molecules

### Expr Log Ratio up-regulated

| Molecules | Expr. Value | Expr. Chart |
|---|---|---|
| ABCA3 | 100.000 |  |
| ABCB6 | 100.000 |  |
| ACAD11* | 100.000 |  |
| ACOT11 | 100.000 |  |
| AGA | 100.000 |  |
| ALDH18A1 | 100.000 |  |
| ALPL | 100.000 |  |
| ARL1 | 100.000 |  |
| ASH1L | 100.000 |  |
| ATP6V0C* | 100.000 |  |

### Expr Log Ratio down-regulated

| Molecules | Expr. Value | Expr. Chart |
|---|---|---|
| WEE2 | -100.000 |  |
| Uox | -100.000 |  |
| SLC37A4 | -100.000 |  |
| SLC25A11* | -100.000 |  |
| RPL8 | -100.000 |  |

| | | |
|---|---|---|
| **RNF17** | -100.000 |  |
| **RCC1L** | -100.000 |  |
| **RB1CC1** | -100.000 |  |
| **RAB4A** | -100.000 |  |
| **RAB11A** | -100.000 |  |