

Supplement 2: DAVID and IPA Analyses

p1. DAVID annotation

p2. NaAsO₂ IPA

p12. DMA IPA

p23. HgCl₂ IPA

p33: meHgCl IPA

DAVID: Functional Annotation Tool

NaAsO₂

Category	Term	Count	PValue
GOTERM_BP_DIRECT	GO:0007186~G-protein coupled receptor signaling pathway	8	0.004895
GOTERM_BP_DIRECT	GO:0050911~detection of chemical stimulus involved in sensory perception of smell	4	0.049165
GOTERM_BP_DIRECT	GO:0042048~olfactory behavior	4	0.05787
GOTERM_CC_DIRECT	GO:0016021~integral component of membrane	30	0.00941
GOTERM_MF_DIRECT	GO:0008528~G-protein coupled peptide receptor activity	4	0.013267

DMA

Category	Term	Count	PValue
GOTERM_BP_DIRECT	GO:0034220~ion transmembrane transport	4	0.026982
GOTERM_CC_DIRECT	GO:0016021~integral component of membrane	42	0.001567
GOTERM_MF_DIRECT	GO:0030246~carbohydrate binding	7	0.001481

HgCl₂

Category	Term	Count	PValue
GOTERM_CC_DIRECT	GO:0016020~membrane	28	0.013239

meHgCl

Category	Term	Count	PValue
GOTERM_CC_DIRECT	GO:0016021~integral component of membrane	25	0.028521
GOTERM_CC_DIRECT	GO:0016020~membrane	25	0.034433
GOTERM_CC_DIRECT	GO:0005887~integral component of plasma membrane	7	0.010891
GOTERM_MF_DIRECT	GO:0030246~carbohydrate binding	7	4.65E-05

INGENUITY[®]

PATHWAY ANALYSIS



Analysis Name: NaASO2xWater_p0.05_FC1.5_CLEAN - 2020-12-23 03:37 PM

Analysis Creation Date: 2020-12-23

Build version: exported

Content version: 60467501 (Release Date: 2020-11-19)

Experiment Metadata

Name	Value
originalColumnNames	GENEBANKACC,GEN_ID_MFR,REFSEQ

Analysis Settings

Reference set: C. elegans (V2)

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 OR Uncategorized) AND

(confidence = Experimentally Observed) AND

(tissues/cell lines = Monocyte-derived macrophage OR Other Monocytes OR Other Breast Cancer Cell Lines OR SF-295 OR Mast cells OR

Other Granulocytes OR HS 578T OR Lung Cancer Cell Lines not otherwise specified OR Lymphoma Cell Lines not otherwise specified OR

Other NK cells OR Adipocytes OR Other Ovarian Cancer Cell Lines OR B lymphocytes not otherwise specified OR Pro-B lymphocytes OR 3T3-

L1 cells OR Adipose OR Kidney Cancer Cell Lines not otherwise specified OR Dorsal Root Ganglion OR OVCAR-3 OR Immature monocyte-derived dendritic cells OR Min6 OR Pheochromocytoma cell lines not otherwise specified OR Epithelial cells not otherwise specified OR Macrophages not otherwise specified OR Th17 cells OR Peripheral blood leukocytes not otherwise specified OR Bladder OR Other CNS Cell Lines OR OVCAR-5 OR Brain OR Heart OR Gray Matter OR Organ Systems not otherwise specified OR Smooth Muscle OR MDA-N OR RKO OR Hepatocytes OR Other Macrophages OR RAW 264.7 OR Adrenal Gland OR Hippocampus OR Microglia OR Cos-7 cells OR Granule Cell Layer OR Mammary Gland OR Spinal Cord OR SF-268 OR Ventricular Zone OR Naive B cells OR HCT-116 OR Activated Vd2 Gamma-delta T cells OR Th1 cells OR Parietal Lobe OR J774 OR OVCAR-4 OR U251 OR Thymus OR Other Mononuclear leukocytes OR HepG2 OR OVCAR-8 OR Caudate Nucleus OR HuH7 OR Lens OR Melanocytes OR NCI-H332M OR U2OS OR HOP-62 OR Jurkat OR Bone marrow-derived macrophages OR MDA-MB-361 OR Bone marrow-derived dendritic cells OR Sciatic Nerve OR Other Immune cells OR HT29 OR Other Colon Cancer Cell Lines OR Naive helper T cells OR Small Intestine OR NCI-H226 OR Astrocytes OR Blood platelets OR WEHI-231 OR Other Peripheral blood leukocytes OR Brainstem OR Kidney cell lines not otherwise specified OR Choroid Plexus OR Medulla Oblongata OR NB4 OR THP-1 OR Oocytes OR INS-1 OR K-562 OR Other Endothelial cells OR CAKI-1 OR RBL-2H3 OR Other Memory T lymphocytes OR T lymphocytes not otherwise specified OR H460 OR A375 OR Monocyte-derived dendritic cells not otherwise specified OR A549-ATCC OR PC-3 OR MALME-3M OR Beta islet cells OR HeLa OR HL-60 OR HOP-92 OR Memory B cells OR CD56bright NK cells OR SR OR Other Myeloma Cell Lines OR Cytotoxic T cells OR Cervical cancer cell line not otherwise specified OR SN12C OR Effector memory RA+ cytotoxic T cells OR BT-549 OR Purkinje cells OR Prostate Cancer Cell Lines not otherwise specified OR Other Macrophage Cancer Cell Lines OR Langerhans cells OR Osteosarcoma Cell Lines not otherwise specified OR T47-D OR Cerebellum OR Microvascular endothelial cells OR Other Cell Line OR Lymphocytes not otherwise specified OR HMC-1 OR Other Fibroblast cell lines OR PANC-1 OR Calvaria OR SW-480 OR Neutrophils OR Other Lymphocytes OR Other Lymphoma Cell Lines OR LNCaP cells OR SK-MEL-28 OR Swiss 3T3 cells OR CD4+ T-lymphocytes OR Crypt OR Other Lung Cancer Cell Lines OR J-774A.1 OR KM-12 OR Megakaryocytes OR Skin OR Kidney OR Other Melanoma Cell Lines OR Natural T-regulatory cells OR Bone marrow cells not otherwise specified OR Cartilage Tissue OR IGROV1 OR SW-620 OR Monocytes not otherwise specified OR Other Leukemia Cell Lines OR Other Teratocarcinoma Cell Lines OR Vd1 Gamma-delta T cells OR Prostate Gland OR Cortical neurons OR Other Smooth muscle cells OR UO-31 OR Trachea OR Olfactory Bulb OR Testis OR Ovarian Cancer Cell Lines not otherwise specified OR SF-539 OR Activated helper T cells OR Activated Vd1 Gamma-delta T cells OR Other Osteosarcoma Cell Lines OR Teratocarcinoma Cell Lines not otherwise specified OR Endothelial cells not otherwise specified OR U266 OR Amygdala OR Effector memory cytotoxic T cells OR Other Neurons OR Esophagus OR Peritoneal macrophages OR Salivary Gland OR SNB-75 OR CD56dim NK cells OR Keratinocytes OR Subventricular Zone OR Mesenchymal stem cells OR Cells not otherwise specified OR A498 OR ACHN OR Other Cervical cancer cell line OR Ovary OR Dendritic cells not otherwise specified OR Stomach OR HEL OR Thalamus OR Activated CD56bright NK cells OR HCC-2998 OR Other Tissues and Primary Cells OR Other Nervous System OR Pancreatic Cancer Cell Lines not otherwise specified OR Spleen

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(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 ClinicalTrials.gov OR ClinVar OR Cogna 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
PXR/RXR Activation	3.48E-04	30.0 % 3/10
Glutathione-mediated Detoxification	1.29E-03	50.0 % 2/4
Melatonin Signaling	3.94E-03	13.6 % 3/22
GPCR-Mediated Nutrient Sensing in Enteroendocrine Cells	3.94E-03	13.6 % 3/22
Neuroprotective Role of THOP1 in Alzheimer's Disease	9.10E-03	20.0 % 2/10

Top Upstream Regulators

Upstream Regulators

Name	p-value	Predicted Activation
MAFG	6.08E-05	
MAFK	6.08E-05	

STIM1	2.19E-04
REST	8.07E-04
EIF2S1	2.13E-03

Causal Network

Name	p-value	Predicted Activation
MAFG	3.07E-05	
MAFK	6.08E-05	
STIM1	2.19E-04	
TFIIH	3.17E-04	
IL1B	8.00E-04	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value range	# Molecules
Neurological Disease	4.42E-02 - 6.49E-04	39
Organismal Injury and Abnormalities	4.55E-02 - 6.49E-04	47
Psychological Disorders	4.42E-02 - 1.01E-03	10
Hereditary Disorder	4.42E-02 - 1.25E-03	19
Gastrointestinal Disease	4.50E-02 - 1.29E-03	42

Molecular and Cellular Functions

Name	p-value range	# Molecules
Carbohydrate Metabolism	4.42E-02 - 1.29E-03	10
Small Molecule Biochemistry	4.42E-02 - 1.29E-03	17
Vitamin and Mineral Metabolism	4.42E-02 - 1.29E-03	7
Molecular Transport	4.42E-02 - 2.12E-03	10
Protein Synthesis	4.42E-02 - 2.12E-03	4

Physiological System Development and Function

Name	p-value range	# Molecules
Endocrine System Development and Function	4.42E-02 - 2.12E-03	2
Connective Tissue Development and Function	4.42E-02 - 3.15E-03	4
Hematological System Development and Function	4.69E-02 - 3.15E-03	9
Lymphoid Tissue Structure and Development	4.69E-02 - 3.15E-03	4
Nervous System Development and Function	4.42E-02 - 3.15E-03	11

Top Tox Functions**Assays: Clinical Chemistry and Hematology**

Name	p-value range	# Molecules
Increased Levels of Potassium	1.00E-01 - 1.00E-01	1

Cardiotoxicity

Name	p-value range	# Molecules
Cardiac Stenosis	5.77E-03 - 5.77E-03	2
Cardiac Dysfunction	1.27E-01 - 4.42E-02	1
Congenital Heart Anomaly	3.31E-01 - 4.42E-02	2
Cardiac Enlargement	1.50E-01 - 5.27E-02	3
Cardiac Infarction	5.84E-02 - 5.84E-02	1

Hepatotoxicity

Name	p-value range	# Molecules
Liver Cholestasis	5.65E-02 - 1.49E-02	2
Liver Hyperbilirubinemia	1.49E-02 - 1.49E-02	1
Glutathione Depletion In Liver	4.42E-02 - 4.42E-02	1
Liver Hyperplasia/Hyperproliferation	2.11E-01 - 6.03E-02	26
Liver Damage	2.14E-01 - 1.00E-01	2

Nephrotoxicity

Name	p-value range	# Molecules
Nephrosis	5.84E-02 - 1.10E-02	2
Kidney Failure	2.03E-01 - 5.84E-02	2

Renal Damage	2.26E-01 - 2.26E-01	1
Glomerular Injury	4.11E-01 - 4.11E-01	1
Renal Inflammation	4.11E-01 - 4.11E-01	1

Top Regulator Effect Networks

Top Networks

ID	Associated Network Functions	Score
1	Cancer, Cell Death and Survival, Organismal Injury and Abnormalities	37
2	Neurological Disease, Organismal Injury and Abnormalities, Nervous System Development and Function	32
3	Drug Metabolism, Endocrine System Development and Function, Energy Production	23
4	Cellular Assembly and Organization, RNA Post-Transcriptional Modification, Auditory and Vestibular System Development and Function	11

Top Tox Lists

Name	p-value	Overlap
PXR/RXR Activation	3.48E-04	30.0 % 3/10
Renal Glomerulus Panel (Human)	1.49E-02	100.0 % 1/1
Hepatic Cholestasis	1.53E-02	15.4 % 2/13
Xenobiotic Metabolism Signaling	1.68E-02	6.0 % 4/67
LPS/IL-1 Mediated Inhibition of RXR Function	2.24E-02	7.3 % 3/41

Top My Lists

Top My Pathways

Top Analysis-Ready Molecules

Expr Fold Change

Molecules	Expr. Value	Chart
HPGDS*	↑ 5.750	
SLC50A1	↑ 5.399	
GSTO1*	↑ 4.079	

DST*	↑ 2.568
DYSF	↑ 2.494
PNPLA7	↑ 2.290
GLRX3	↑ 2.042
GLRA1	↑ 2.035
PDXK	↑ 2.006
AQR	↑ 1.910

Expr Fold Change

Molecules	Expr. Value	Chart
ABCB9	↓ -2.271	
ABHD11	↓ -2.209	
PLCE1	↓ -2.120	
HTR2A	↓ -2.076	
TTC21B	↓ -1.927	
PIGW	↓ -1.849	
COQ2	↓ -1.838	
CYP3A7-CYP3A51P	↓ -1.794	
PRKACB	↓ -1.772	
NIM1K	↓ -1.621	



Analysis Name: DMAxWater_p0.05_FC_1.5_CLEAN - 2020-12-23 03:26 PM

Analysis Creation Date: 2020-12-23

Build version: exported

Content version: 60467501 (Release Date: 2020-11-19)

Experiment Metadata

Name	Value
originalColumnNames	GENEBANKACC,GEN_ID_MFR

Analysis Settings

Reference set: C. elegans (V2)

Relationship to include: Direct and Indirect

Includes Endogenous Chemicals

Optional Analyses: My Pathways My List

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Top Canonical Pathways

Name	p-value	Overlap
Glutathione-mediated Detoxification	1.96E-03	50.0 % 2/4
G-Protein Coupled Receptor Signaling	4.50E-03	8.3 % 5/60
Gustation Pathway	6.24E-03	14.3 % 3/21
cAMP-mediated signaling	6.90E-03	9.5 % 4/42
Gi Signaling	1.40E-02	10.7 % 3/28

Top Upstream Regulators

Upstream Regulators

Name	p-value	Predicted Activation
STIM1	3.47E-04	
FABP5	3.47E-04	
tacrolimus	8.99E-04	
galactosylceramide-alpha	1.03E-03	

ALDH3A2

1.03E-03

Causal Network

Name	p-value	Predicted Activation
RALBP1	2.83E-05	
chlorpropamide	7.06E-05	
glabridin	9.12E-05	
octanoic acid	1.31E-04	
HFE	1.65E-04	

Top Diseases and Bio Functions**Diseases and Disorders**

Name	p-value range	# Molecules
Neurological Disease	1.84E-02 - 3.06E-07	27
Cardiovascular Disease	1.84E-02 - 2.42E-06	21
Organismal Injury and Abnormalities	1.84E-02 - 2.42E-06	57
Respiratory Disease	1.84E-02 - 1.70E-05	15
Skeletal and Muscular Disorders	1.84E-02 - 1.77E-05	22

Molecular and Cellular Functions

Name	p-value range	# Molecules
Cellular Development	1.84E-02 - 5.74E-05	18
Cellular Function and Maintenance	1.84E-02 - 5.74E-05	24
Cellular Growth and Proliferation	1.84E-02 - 5.74E-05	11
Cell Death and Survival	1.84E-02 - 3.12E-04	14
Cell-To-Cell Signaling and Interaction	1.84E-02 - 3.34E-04	11

Physiological System Development and Function

Name	p-value range	# Molecules
Cardiovascular System Development and Function	1.84E-02 - 5.74E-05	16
Organismal Development	1.84E-02 - 5.74E-05	21
Tissue Development	1.84E-02 - 5.74E-05	18
Nervous System Development and Function	1.84E-02 - 1.14E-04	19
Hematological System Development and Function	1.84E-02 - 2.07E-04	15

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value range	# Molecules
Increased Levels of Potassium	7.17E-02 - 7.17E-02	1
Decreased Levels of Potassium	8.89E-02 - 8.89E-02	1

Increased Levels of Red Blood Cells

1.85E-01 - 1.85E-01

1

Cardiotoxicity

Name	p-value range	# Molecules
Cardiac Arteriopathy	4.36E-02 - 2.42E-06	9
Cardiac Infarction	2.44E-01 - 1.77E-05	7
Heart Failure	2.44E-01 - 9.90E-04	6
Cardiac Arrhythmia	2.15E-01 - 1.99E-03	4
Cardiac Inflammation	5.43E-02 - 8.71E-03	2

Hepatotoxicity

Name	p-value range	# Molecules
Liver Hyperplasia/Hyperproliferation	3.61E-01 - 1.08E-03	37
Liver Damage	2.81E-03 - 2.81E-03	3
Liver Inflammation/Hepatitis	4.07E-01 - 4.83E-03	5
Liver Steatosis	1.85E-01 - 1.14E-02	4
Liver Failure	5.43E-02 - 3.01E-02	2

Nephrotoxicity

Name	p-value range	# Molecules
Renal Damage	2.15E-01 - 1.75E-03	5

Kidney Failure	5.43E-02 - 1.96E-03	3
Renal Hypoplasia	1.22E-01 - 3.65E-02	1
Glomerular Injury	1.38E-01 - 7.17E-02	2
Renal Enlargement	1.06E-01 - 1.06E-01	1

Top Regulator Effect Networks

Top Networks

ID	Associated Network Functions	Score
1	Cardiac Infarction, Cardiovascular Disease, Organismal Injury and Abnormalities	44
2	Cell Cycle, Cardiovascular System Development and Function, Cell Morphology	33
3	Behavior, Nervous System Development and Function, DNA Replication, Recombination, and Repair	25
4	Lipid Metabolism, Small Molecule Biochemistry, Molecular Transport	17

5

Cellular Development,
Embryonic
Development,
Organismal
Development

3

Top Tox Lists

Name	p-value	Overlap
LPS/IL-1 Mediated Inhibition of RXR Function	6.33E-03	9.8 % 4/41
Long-term Renal Injury Anti-oxidative Response Panel (Rat)	6.61E-03	28.6 % 2/7
Cytochrome P450 Panel - Substrate is a Fatty Acid (Human)	1.84E-02	100.0 % 1/1
Cytochrome P450 Panel - Substrate is a Fatty Acid (Mouse)	1.84E-02	100.0 % 1/1
Cytochrome P450 Panel - Substrate is a Fatty Acid (Rat)	1.84E-02	100.0 % 1/1

Top My Lists

Top My Pathways

Top Analysis-Ready Molecules

Expr Fold Change

Molecules	Expr. Value	Chart
PIPOX	↑ 25.365	
HPGDS*	↑ 10.437	
FABP4*	↑ 7.204	
GSTO1*	↑ 5.269	
CYP2J2*	↑ 4.562	
WVOX*	↑ 4.276	
GLRA1	↑ 2.562	
PNPLA7	↑ 2.204	
KCNJ2	↑ 2.118	
PGPEP1	↑ 2.114	

Expr Fold Change

Molecules	Expr. Value	Chart
SRD5A2	↓ -5.136	
COMTD1	↓ -4.537	
SCNN1G*	↓ -3.839	
SLC20A2	↓ -3.241	
CYP3A7-CYP3A51P*	↓ -3.046	
ARL6	↓ -2.862	
CAPN15	↓ -2.673	
PLEKHD1	↓ -2.400	
NEUROD6	↓ -2.396	
RAB28	↓ -2.381	



Analysis Name: HgCl2xWater_p0.05_FC1.5_CLEAN - 2020-12-23 03:35 PM

Analysis Creation Date: 2020-12-23

Build version: exported

Content version: 60467501 (Release Date: 2020-11-19)

Experiment Metadata

Name	Value
originalColumnNames	GENEBANKACC,GEN_ID_MFR

Analysis Settings

Reference set: C. elegans (V2)

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 OR Uncategorized) AND

(confidence = Experimentally Observed) AND

(tissues/cell lines = Monocyte-derived macrophage OR Other Monocytes OR Other Breast Cancer Cell Lines OR SF-295 OR Mast cells OR

Other Granulocytes OR HS 578T OR Lung Cancer Cell Lines not otherwise specified OR Lymphoma Cell Lines not otherwise specified OR

Other NK cells OR Adipocytes OR Other Ovarian Cancer Cell Lines OR B lymphocytes not otherwise specified OR Pro-B lymphocytes OR 3T3-

L1 cells OR Adipose OR Kidney Cancer Cell Lines not otherwise specified OR Dorsal Root Ganglion OR OVCAR-3 OR Immature monocyte-derived dendritic cells OR Min6 OR Pheochromocytoma cell lines not otherwise specified OR Epithelial cells not otherwise specified OR Macrophages not otherwise specified OR Th17 cells OR Peripheral blood leukocytes not otherwise specified OR Bladder OR Other CNS Cell Lines OR OVCAR-5 OR Brain OR Heart OR Gray Matter OR Organ Systems not otherwise specified OR Smooth Muscle OR MDA-N OR RKO OR Hepatocytes OR Other Macrophages OR RAW 264.7 OR Adrenal Gland OR Hippocampus OR Microglia OR Cos-7 cells OR Granule Cell Layer OR Mammary Gland OR Spinal Cord OR SF-268 OR Ventricular Zone OR Naive B cells OR HCT-116 OR Activated Vd2 Gamma-delta T cells OR Th1 cells OR Parietal Lobe OR J774 OR OVCAR-4 OR U251 OR Thymus OR Other Mononuclear leukocytes OR HepG2 OR OVCAR-8 OR Caudate Nucleus OR HuH7 OR Lens OR Melanocytes OR NCI-H332M OR U2OS OR HOP-62 OR Jurkat OR Bone marrow-derived macrophages OR MDA-MB-361 OR Bone marrow-derived dendritic cells OR Sciatic Nerve OR Other Immune cells OR HT29 OR Other Colon Cancer Cell Lines OR Naive helper T cells OR Small Intestine OR NCI-H226 OR Astrocytes OR Blood platelets OR WEHI-231 OR Other Peripheral blood leukocytes OR Brainstem OR Kidney cell lines not otherwise specified OR Choroid Plexus OR Medulla Oblongata OR NB4 OR THP-1 OR Oocytes OR INS-1 OR K-562 OR Other Endothelial cells OR CAKI-1 OR RBL-2H3 OR Other Memory T lymphocytes OR T lymphocytes not otherwise specified OR H460 OR A375 OR Monocyte-derived dendritic cells not otherwise specified OR A549-ATCC OR PC-3 OR MALME-3M OR Beta islet cells OR HeLa OR HL-60 OR HOP-92 OR Memory B cells OR CD56bright NK cells OR SR OR Other Myeloma Cell Lines OR Cytotoxic T cells OR Cervical cancer cell line not otherwise specified OR SN12C OR Effector memory RA+ cytotoxic T cells OR BT-549 OR Purkinje cells OR Prostate Cancer Cell Lines not otherwise specified OR Other Macrophage Cancer Cell Lines OR Langerhans cells OR Osteosarcoma Cell Lines not otherwise specified OR T47-D OR Cerebellum OR Microvascular endothelial cells OR Other Cell Line OR Lymphocytes not otherwise specified OR HMC-1 OR Other Fibroblast cell lines OR PANC-1 OR Calvaria OR SW-480 OR Neutrophils OR Other Lymphocytes OR Other Lymphoma Cell Lines OR LNCaP cells OR SK-MEL-28 OR Swiss 3T3 cells OR CD4+ T-lymphocytes OR Crypt OR Other Lung Cancer Cell Lines OR J-774A.1 OR KM-12 OR Megakaryocytes OR Skin OR Kidney OR Other Melanoma Cell Lines OR Natural T-regulatory cells OR Bone marrow cells not otherwise specified OR Cartilage Tissue OR IGROV1 OR SW-620 OR Monocytes not otherwise specified OR Other Leukemia Cell Lines OR Other Teratocarcinoma Cell Lines OR Vd1 Gamma-delta T cells OR Prostate Gland OR Cortical neurons OR Other Smooth muscle cells OR UO-31 OR Trachea OR Olfactory Bulb OR Testis OR Ovarian Cancer Cell Lines not otherwise specified OR SF-539 OR Activated helper T cells OR Activated Vd1 Gamma-delta T cells OR Other Osteosarcoma Cell Lines OR Teratocarcinoma Cell Lines not otherwise specified OR Endothelial cells not otherwise specified OR U266 OR Amygdala OR Effector memory cytotoxic T cells OR Other Neurons OR Esophagus OR Peritoneal macrophages OR Salivary Gland OR SNB-75 OR CD56dim NK cells OR Keratinocytes OR Subventricular Zone OR Mesenchymal stem cells OR Cells not otherwise specified OR A498 OR ACHN OR Other Cervical cancer cell line OR Ovary OR Dendritic cells not otherwise specified OR Stomach OR HEL OR Thalamus OR Activated CD56bright NK cells OR HCC-2998 OR Other Tissues and Primary Cells OR Other Nervous System OR Pancreatic Cancer Cell Lines not otherwise specified OR Spleen

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(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 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
PXR/RXR Activation	1.04E-03	30.0 % 3/10
Calcium Transport I	1.36E-03	66.7 % 2/3
Calcium Signaling	2.07E-03	11.6 % 5/43
Sertoli Cell-Sertoli Cell Junction Signaling	7.70E-03	10.8 % 4/37
NAD Salvage Pathway II	1.18E-02	25.0 % 2/8

Top Upstream Regulators

Upstream Regulators

Name	p-value	Predicted Activation
MAFG	1.85E-04	
MAFK	1.85E-04	
SLC51A	4.61E-04	
MYT1	4.61E-04	

SLC10A1

4.61E-04

Causal Network

Name	p-value	Predicted Activation
MAFG	9.40E-05	
MAFK	1.85E-04	
MYT1	4.61E-04	
SLC10A1	4.61E-04	
bile salt	4.61E-04	

Top Diseases and Bio Functions**Diseases and Disorders**

Name	p-value range	# Molecules
Cancer	4.15E-02 - 2.30E-04	66
Organismal Injury and Abnormalities	4.28E-02 - 2.30E-04	68
Dermatological Diseases and Conditions	2.36E-02 - 4.13E-04	54
Reproductive System Disease	4.14E-02 - 4.51E-04	51
Hereditary Disorder	4.17E-02 - 4.60E-04	26

Molecular and Cellular Functions

Name	p-value range	# Molecules
Molecular Transport	4.28E-02 - 1.25E-05	28
Cellular Function and Maintenance	4.14E-02 - 2.09E-05	35
Small Molecule Biochemistry	4.28E-02 - 2.20E-04	21
Cell Death and Survival	4.28E-02 - 4.24E-04	35
Lipid Metabolism	2.16E-02 - 4.60E-04	10

Physiological System Development and Function

Name	p-value range	# Molecules
Cardiovascular System Development and Function	4.28E-02 - 1.36E-03	13
Nervous System Development and Function	4.28E-02 - 1.36E-03	16
Organ Development	4.28E-02 - 1.36E-03	9
Organ Morphology	4.28E-02 - 1.36E-03	14
Organismal Development	4.28E-02 - 1.36E-03	19

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value range	# Molecules
Decreased Levels of Hematocrit	2.16E-02 - 2.16E-02	1
Increased Levels of Potassium	1.42E-01 - 1.42E-01	1

Cardiotoxicity

Name	p-value range	# Molecules
Cardiac Stenosis	1.18E-02 - 1.18E-02	2
Heart Failure	1.07E-01 - 1.76E-02	5
Cardiac Arteriopathy	6.12E-01 - 5.53E-02	4
Cardiac Arrythmia	1.23E-01 - 6.35E-02	1
Cardiac Pulmonary Embolism	6.35E-02 - 6.35E-02	1

Hepatotoxicity

Name	p-value range	# Molecules
Hepatocellular carcinoma	4.09E-01 - 2.16E-02	10
Liver Cholestasis	3.11E-01 - 2.16E-02	2
Liver Enlargement	2.16E-02 - 2.16E-02	1
Liver Hyperbilirubinemia	2.16E-02 - 2.16E-02	1
Liver Hyperplasia/Hyperproliferation	4.09E-01 - 2.16E-02	38

Nephrotoxicity

Name	p-value range	# Molecules
Kidney Failure	1.96E-01 - 2.68E-03	4
Renal Enlargement	1.23E-01 - 9.01E-03	2

Nephrosis	1.29E-01 - 1.31E-02	4
Glomerular Injury	1.96E-01 - 2.16E-02	2
Renal Hydronephrosis	2.16E-02 - 2.16E-02	1

Top Regulator Effect Networks

Top Networks

ID	Associated Network Functions	Score
1	Cellular Function and Maintenance, Small Molecule Biochemistry, Cellular Assembly and Organization	46
2	Hereditary Disorder, Neurological Disease, Organismal Injury and Abnormalities	46
3	Inflammatory Response, Lipid Metabolism, Molecular Transport	34
4	DNA Replication, Recombination, and Repair, Cancer, Cardiovascular Disease	19
5	Hematological Disease, Hereditary Disorder, Organismal Injury and Abnormalities	6

Top Tox Lists

Name	p-value	Overlap
Genes Upregulated in Response to Chronic Renal Failure (Rat)	4.60E-04	100.0 % 2/2
PXR/RXR Activation	1.04E-03	30.0 % 3/10
CAR/RXR Activation	4.41E-03	40.0 % 2/5
Decreases Depolarization of Mitochondria and Mitochondrial Membrane	1.18E-02	25.0 % 2/8
Decreases Transmembrane Potential of Mitochondria and Mitochondrial Membrane	1.41E-02	12.5 % 3/24

Top My Lists

Top My Pathways

Top Analysis-Ready Molecules

Expr Fold Change

Molecules	Expr. Value	Chart
ABCC4	↑ 2.669	

ATP1A3	↑ 2.176
NUP93	↑ 1.951
CCT7	↑ 1.944
SNX33	↑ 1.923
PKM	↑ 1.883
SNX14	↑ 1.868
ADSS1	↑ 1.840
DHX37	↑ 1.832
ABCC3	↑ 1.766

Expr Fold Change

Molecules	Expr. Value	Chart
RASGRP3	↓ -2.811	
ASCC3	↓ -2.220	
PPP4R3A	↓ -2.201	
CAMK2D	↓ -2.015	
CAPN15	↓ -1.994	
DNAJC2	↓ -1.993	
SLC8A3	↓ -1.925	
VPS13D	↓ -1.914	
PNPLA4	↓ -1.791	
CYP3A7-CYP3A51P	↓ -1.772	



Analysis Name: meHgClxWater_p0.05_FC_1.5_CLEAN - 2020-12-23 03:34 PM

Analysis Creation Date: 2020-12-23

Build version: exported

Content version: 60467501 (Release Date: 2020-11-19)

Experiment Metadata

Name	Value
originalColumnNames	GENEBANKACC,GEN_ID_MFR

Analysis Settings

Reference set: C. elegans (V2)

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 OR Uncategorized) AND

(confidence = Experimentally Observed) AND

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(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 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
LPS/IL-1 Mediated Inhibition of RXR Function	1.08E-04	12.5 % 5/40
Basal Cell Carcinoma Signaling	5.10E-03	22.2 % 2/9
PXR/RXR Activation	6.33E-03	20.0 % 2/10
Protein Kinase A Signaling	1.24E-02	5.4 % 4/74
Regulation Of The Epithelial Mesenchymal Transition In Development Pathway	1.42E-02	13.3 % 2/15

Top Upstream Regulators

Upstream Regulators

Name	p-value	Predicted Activation
NR1I2	3.56E-05	
alitretinoin	1.04E-04	

AKR1B1	1.50E-04
glycerol	4.47E-04
galactosylceramide-alpha	4.47E-04

Causal Network

Name	p-value	Predicted Activation
St. John's wort	5.06E-06	
paraoxon	3.45E-05	
thiamine	3.45E-05	
troleandomycin	8.41E-05	
mir-210	8.41E-05	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value range	# Molecules
Connective Tissue Disorders	3.21E-02 - 8.84E-04	12
Organismal Injury and Abnormalities	3.67E-02 - 8.84E-04	36
Skeletal and Muscular Disorders	3.21E-02 - 8.84E-04	13
Gastrointestinal Disease	3.67E-02 - 1.46E-03	26
Hepatic System Disease	3.55E-02 - 1.46E-03	9

Molecular and Cellular Functions

Name	p-value range	# Molecules
Lipid Metabolism	3.67E-02 - 2.60E-04	11
Small Molecule Biochemistry	3.67E-02 - 2.60E-04	12
Cell Death and Survival	3.67E-02 - 8.84E-04	7
Molecular Transport	3.67E-02 - 1.46E-03	13
Carbohydrate Metabolism	3.67E-02 - 2.18E-03	6

Physiological System Development and Function

Name	p-value range	# Molecules
Respiratory System Development and Function	2.18E-03 - 2.18E-03	2
Digestive System Development and Function	2.46E-02 - 3.02E-03	2
Hepatic System Development and Function	2.46E-02 - 3.02E-03	2
Organ Development	3.67E-02 - 3.02E-03	7
Cardiovascular System Development and Function	3.67E-02 - 1.24E-02	4

Top Tox Functions**Assays: Clinical Chemistry and Hematology**

Name	p-value range	# Molecules
Increased Levels of Red Blood Cells	1.28E-01 - 1.28E-01	1

Increased Levels of Hematocrit

1.50E-01 - 1.50E-01

1

Cardiotoxicity

Name	p-value range	# Molecules
Cardiac Inflammation	3.67E-02 - 4.00E-03	2
Cardiac Damage	1.61E-02 - 1.61E-02	2
Cardiac Arrhythmia	3.13E-01 - 2.46E-02	2
Cardiac Dysfunction	4.87E-02 - 4.87E-02	1
Congenital Heart Anomaly	3.71E-01 - 6.05E-02	2

Hepatotoxicity

Name	p-value range	# Molecules
Liver Inflammation/Hepatitis	7.21E-02 - 3.02E-03	3
Liver Steatosis	1.49E-02 - 3.02E-03	4
Liver Hyperplasia/Hyperproliferation	4.30E-01 - 1.07E-02	20
Hepatocellular Peroxisome Proliferation	4.87E-02 - 1.24E-02	1
Liver Cholestasis	1.91E-01 - 1.24E-02	2

Nephrotoxicity

Name	p-value range	# Molecules
Kidney Failure	3.13E-01 - 1.24E-02	2

Glomerular Injury	1.81E-01 - 6.89E-02	2
Renal Inflammation	1.81E-01 - 6.89E-02	2
Renal Nephritis	1.81E-01 - 6.89E-02	2
Renal Damage	1.91E-01 - 1.50E-01	2

Top Regulator Effect Networks

Top Networks

ID	Associated Network Functions	Score
1	Lipid Metabolism, Small Molecule Biochemistry, Cancer	45
2	Cancer, Gastrointestinal Disease, Hepatic System Disease	24
3	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	19
4	Cellular Compromise, Cell Morphology, Nervous System Development and Function	3

Top Tox Lists

Name	p-value	Overlap
LPS/IL-1 Mediated Inhibition of RXR Function	1.21E-04	12.2 % 5/41
PXR/RXR Activation	6.33E-03	20.0 % 2/10
Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	2.46E-02	50.0 % 1/2
Genes Upregulated in Response to Chronic Renal Failure (Rat)	2.46E-02	50.0 % 1/2
Glutathione Depletion - Hepatocellular Hypertrophy	3.67E-02	33.3 % 1/3

Top My Lists

Top My Pathways

Top Analysis-Ready Molecules

Expr Fold Change

Molecules	Expr. Value	Chart
DST	↑ 2.892	
PGP	↑ 1.867	
TUBA1A	↑ 1.823	
ABCC3	↑ 1.772	

U2AF2	↑ 1.568
MCM7	↑ 1.547
SBNO1	↑ 1.545
KLHL8	↑ 1.541

Expr Fold Change

Molecules	Expr. Value	Chart
GBA	↓ -4.726	
HPGDS*	↓ -3.187	
RASGRP3	↓ -3.119	
SLCO4A1	↓ -2.357	
PGPEP1	↓ -2.338	
PDE8A	↓ -2.180	
FHL2	↓ -2.167	
VPS28	↓ -2.147	
SUGT1	↓ -2.089	
SLC11A2	↓ -2.077	