



Analysis Name: H63D and C282Y heterozygotes or H63D homozygotes vs control group

Analysis Creation Date: 2019-08-28

Build version: exported

Content version: 48207413 (Release Date: 2019-06-15)

Experiment Metadata

Name	Value
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Analysis Settings

Reference set: Ingenuity Knowledge Base (Genes Only)

Relationship to include: Direct and Indirect

Does not Include Endogenous Chemicals

Optional Analyses: My Pathways My List

Filter Summary:

Consider only molecules and/or relationships where

(species = Uncategorized OR Mouse OR Human OR Rat) AND

(tissues/cell lines = HEL OR Trigeminal Ganglion OR Lymph node OR White Matter OR 786-0 OR Skeletal Muscle OR Large Intestine OR NCI-H522 OR Cornea OR Cytotoxic T cells OR Other Kidney cell lines OR SK-MEL-5 OR Pancreatic Cancer Cell Lines not otherwise specified OR CD34+ cells OR BA/F3 OR Neuroblastoma Cell Lines not otherwise specified OR Corpus Callosum OR NCI-ADR-RES OR Placenta OR Olfactory Bulb OR Ovarian Cancer Cell Lines not otherwise specified OR Other Fibroblast cell lines OR Granule cells OR Hematopoietic

progenitor cells OR Murine NKT cells OR 293 cells OR Memory T lymphocytes not otherwise specified OR Chondrocytes OR MEF cells OR CNS Cell Lines not otherwise specified OR Other Monocyte-derived dendritic cells OR Central memory cytotoxic T cells OR MG-63 OR Granulosa cells OR NT2/D1 OR SNB-75 OR Forestomach OR Nucleus Accumbens OR Other Dendritic cells OR Other Memory T lymphocytes OR Caco2 cells OR UACC-62 OR Other Leukemia Cell Lines OR Plasma cells OR IGROV1 OR PC-3 OR Bone marrow cells not otherwise specified OR Other Cervical cancer cell line OR Nervous System not otherwise specified OR Monocytes not otherwise specified OR Splenocytes OR Other Smooth muscle cells OR Prostate Gland OR MDA-MB-468 OR Other Kidney Cancer Cell Lines OR Central memory helper T cells OR LNCaP cells OR Striatum OR Vd2 Gamma-delta T cells OR U87MG OR Other Pheochromocytoma cell lines OR Other Osteosarcoma Cell Lines OR ACHN OR NB4 OR Sertoli cells OR A549-ATCC OR Lymphocytes not otherwise specified OR Effector memory helper T cells OR Stromal cells OR Thymocytes OR T47-D OR Fibroblast cell lines not otherwise specified OR U266 OR Neutrophils OR Other Endothelial cells OR Cervical cancer cell line not otherwise specified OR Keratinocytes OR MDA-MB-435 OR NIH/3T3 cells OR Esophagus OR Embryonic stem cells OR Lung OR Ovary OR HUVEC cells OR A498 OR Peritoneal macrophages OR Hypothalamus OR Immune cell lines not otherwise specified OR Brain OR RPMI-8266 OR Hepatocytes OR Bone marrow-derived dendritic cells OR Smooth muscle cells not otherwise specified OR Other Nervous System OR Other Bone marrow cells OR Hep3B OR Other Tissues and Primary Cells OR Other Immune cell lines OR Activated CD56dim NK cells OR LOX IMVI OR Neurons not otherwise specified OR Cos-7 cells OR Activated Vd1 Gamma-delta T cells OR Hippocampus OR Intraepithelial T lymphocytes OR COLO205 OR Hepatoma Cell Lines not otherwise specified OR Peripheral blood monocytes OR PC-12 cells OR Other NK cells OR HCT-15 OR CCRF-CEM OR EKVX OR Immature monocyte-derived dendritic cells OR Pro-B lymphocytes OR MOLT-4 OR Mononuclear leukocytes not otherwise specified OR Other Pancreatic Cancer Cell Lines OR Organ Systems not otherwise specified OR U937 OR Amygdala OR Skin OR Ventricular Zone OR Spinal Cord OR Monocyte-derived dendritic cells not otherwise specified OR Lens OR P19 OR RXF-393 OR Beta islet cells OR Heart OR Macrophages not otherwise specified OR MCF7 OR UACC-257 OR Colon Cancer Cell Lines not otherwise specified OR CD56bright NK cells OR Astrocytes OR SK-N-SH OR Cardiomyocytes OR BT-474 OR BDCA-3+ dendritic cells OR A2780 OR Other Cells OR Myeloma Cell Lines not otherwise specified OR Small Intestine OR NCI-H23 OR Peripheral blood leukocytes not otherwise specified OR Activated Vd2 Gamma-delta T cells OR Th2 cells OR Tissues and Primary Cells not otherwise specified OR Choroid Plexus OR Granule Cell Layer OR Brainstem OR Salivary Gland OR T lymphocytes not otherwise specified OR MDA-MB-231 OR Pheochromocytoma cell lines not otherwise specified OR Medulla Oblongata OR Naive helper T cells OR Uterus OR B lymphocytes not otherwise specified OR Cell Line not otherwise specified OR Melanocytes OR Cartilage Tissue OR PBMCs OR Other CNS Cell Lines OR Natural T-regulatory cells OR Dermis OR Memory B cells OR Other Prostate Cancer Cell Lines OR Sciatic Nerve OR Liver OR Min6 OR HOP-62 OR Jurkat OR OVCAR-5 OR RKO OR Pyramidal neurons OR Effector memory RA+ cytotoxic T cells OR Substantia Nigra OR Other Ovarian Cancer Cell Lines OR Parietal Lobe OR HS 578T OR BDCA-1+ dendritic cells OR Myeloid dendritic cells OR Other Peripheral blood leukocytes OR Lymphoma Cell Lines not otherwise specified OR Other T lymphocytes OR HCT-116 OR Other Colon Cancer Cell Lines OR HuH7 OR

WEHI-231 OR Other Breast Cancer Cell Lines OR Mammary Gland OR 3T3-L1 cells OR Kidney Cancer Cell Lines not otherwise specified OR CD4+ T-lymphocytes OR OVCAR-3 OR Osteoblasts OR Thyroid Gland OR Lung Cancer Cell Lines not otherwise specified OR SW-620 OR TK-10 OR Vd1 Gamma-delta T cells OR MDA-N OR NCI-H226 OR Bladder OR Kidney OR Purkinje cells OR MDA-MB-361 OR Trachea OR SK-OV-3 OR HT29 OR Eosinophils OR Adrenal Gland OR Cortical neurons OR INS-1 OR Testis OR Gray Matter OR RAW 264.7 OR Breast Cancer Cell Lines not otherwise specified OR Langerhans cells OR NCI-H332M OR U2OS OR Microvascular endothelial cells OR Other B lymphocytes OR NK cells not otherwise specified OR Cerebellum OR Epithelial cells not otherwise specified OR Calvaria OR Oocytes OR Macrophage Cancer Cell Lines not otherwise specified OR Adipocytes OR Kidney cell lines not otherwise specified OR HepG2 OR Melanoma Cell Lines not otherwise specified OR Pre-B lymphocytes OR Other Lymphocytes OR J774 OR Th17 cells OR Megakaryocytes OR Stem cells not otherwise specified OR Stomach OR Dendritic cells not otherwise specified OR HL-60 OR Other Immune cells OR Crypt OR SK-MEL-2 OR HeLa OR Activated CD56bright NK cells OR Mesenchymal stem cells OR Putamen OR SN12C OR U251 OR Peripheral blood lymphocytes OR M14 OR BT-549 OR Prostate Cancer Cell Lines not otherwise specified OR Other Neurons OR Mature monocyte-derived dendritic cells OR UO-31 OR Thalamus OR SF-268 OR Leukemia Cell Lines not otherwise specified OR THP-1 OR HMC-1 OR Endothelial cells not otherwise specified OR DU-145 OR Other Melanoma Cell Lines OR Other Epithelial cells OR KM-12 OR Adipose OR OVCAR-8 OR Immune cells not otherwise specified OR Retina OR Other Granulocytes OR CAKI-1 OR Cells not otherwise specified OR Plasmacytoid dendritic cells OR Subventricular Zone OR Other Teratocarcinoma Cell Lines OR Monocyte-derived macrophage OR K-562 OR OVCAR-4 OR SF-539 OR HOP-92 OR Fibroblasts OR MALME-3M OR Cerebral Cortex OR Bone marrow-derived macrophages OR Vascular smooth muscle cells OR Other Neuroblastoma Cell Lines OR Smooth Muscle OR HCC-2998 OR Dorsal Root Ganglion OR Thymus OR Other Stem cells OR Other Organ Systems OR Other Myeloma Cell Lines OR Osteosarcoma Cell Lines not otherwise specified OR Pituitary Gland OR Other Hepatoma Cell Lines OR SK-MEL-28 OR SF-295 OR Granulocytes not otherwise specified OR Spleen OR Cerebral Ventricles OR Other Macrophages OR Activated helper T cells OR Other Monocytes OR PANC-1 OR Microglia OR Teratocarcinoma Cell Lines not otherwise specified OR Blood platelets OR Effector T cells OR Swiss 3T3 cells OR Naive B cells OR Pancreas OR SW-480 OR Other Lymphoma Cell Lines OR Other Mononuclear leukocytes OR A375 OR Epidermis OR CD56dim NK cells OR Th1 cells OR Other Cell Line OR Mast cells OR Other Macrophage Cancer Cell Lines OR Effector memory cytotoxic T cells OR J-774A.1 OR H460 OR RBL-2H3 OR SR OR Caudate Nucleus OR Other Lung Cancer Cell Lines) AND

(mol. types = biologic drug OR chemical - endogenous mammalian OR chemical - endogenous non-mammalian OR chemical - kinase inhibitor OR chemical - other OR chemical - protease inhibitor OR chemical drug OR chemical reagent OR chemical toxicant OR complex OR cytokine OR disease OR enzyme OR function OR G-protein coupled receptor OR group OR growth factor OR ion channel OR kinase OR ligand-dependent nuclear receptor OR mature microRNA OR microRNA OR other OR peptidase OR phosphatase OR transcription regulator OR translation regulator OR transmembrane receptor OR transporter) AND

(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
Gq Signaling	2,76E-04	5,7 % 9/158
G Protein Signaling Mediated by Tubby	7,29E-04	12,9 % 4/31
EIF2 Signaling	9,13E-04	4,4 % 10/225
IL-1 Signaling	1,37E-03	6,6 % 6/91
IL-8 Signaling	1,50E-03	4,5 % 9/200

Top Upstream Regulators

Name	p-value	Predicted Activation
filgrastim	2,11E-08	
miR-1250-3p (miRNAs w/seed CAUUUUC)	8,00E-06	Inhibited
miR-1468-3p (miRNAs w/seed GCAAAAU)	8,12E-06	Inhibited
camptothecin	1,80E-05	
ZC3H14	5,89E-05	

Top Diseases and Bio Functions

Diseases and Disorders

Name	p-value range	# Molecules
Infectious Diseases	1,33E-02 - 9,98E-08	67
Cancer	1,33E-02 - 1,03E-05	266
Hematological Disease	1,33E-02 - 1,03E-05	96
Immunological Disease	1,33E-02 - 1,03E-05	84
Organismal Injury and Abnormalities	1,33E-02 - 1,03E-05	273

Molecular and Cellular Functions

Name	p-value range	# Molecules
Cell Cycle	1,33E-02 - 2,01E-06	49
Cell Signaling	7,40E-03 - 2,51E-06	30
Cellular Movement	1,33E-02 - 7,60E-05	78
Cell Death and Survival	1,33E-02 - 1,12E-04	105
Cellular Function and Maintenance	1,33E-02 - 3,49E-04	71

Physiological System Development and Function

Name	p-value range	# Molecules
Tissue Morphology	1,33E-02 - 1,73E-05	50

Hematological System Development and Function	1,33E-02 - 1,17E-04	55
Organ Morphology	1,33E-02 - 1,42E-04	23
Reproductive System Development and Function	1,33E-02 - 1,42E-04	9
Organismal Development	1,33E-02 - 3,56E-04	51

Top Tox Functions

Assays: Clinical Chemistry and Hematology

Name	p-value range	# Molecules
Increased Levels of AST	1,87E-02 - 1,87E-02	2
Increased Levels of Red Blood Cells	1,71E-01 - 5,22E-02	3
Decreased Levels of Albumin	1,60E-01 - 1,60E-01	1
Increased Levels of ALT	2,75E-01 - 2,75E-01	1
Increased Levels of Creatinine	5,02E-01 - 5,02E-01	1

Cardiotoxicity

Name	p-value range	# Molecules
Cardiac Dysfunction	6,09E-01 - 4,69E-03	2
Cardiac Fibrosis	4,69E-03 - 4,69E-03	2
Congenital Heart Anomaly	2,85E-01 - 1,33E-02	2
Pulmonary Hypertension	1,33E-02 - 1,33E-02	1
Cardiac Damage	4,82E-01 - 2,64E-02	3

Hepatotoxicity

Name	p-value range	# Molecules
Hepatocellular carcinoma	4,32E-01 - 1,64E-03	19
Liver Hyperplasia/Hyperproliferation	5,02E-01 - 1,64E-03	125
Liver Steatosis	2,74E-01 - 3,95E-03	13
Degeneration of liver	3,94E-02 - 1,03E-02	3
Liver Inflammation/Hepatitis	1,00E00 - 1,10E-02	6

Nephrotoxicity

Name	p-value range	# Molecules
Renal Necrosis/Cell Death	4,96E-01 - 5,78E-03	15
Glomerular Injury	5,69E-01 - 1,33E-02	14
Renal Proliferation	2,14E-01 - 1,33E-02	2
Renal Inflammation	5,69E-01 - 7,73E-02	7
Renal Nephritis	5,69E-01 - 7,73E-02	7

Top Regulator Effect Networks

ID	Regulators	Disease & Functions	Consistency Score
1	miR-130a-3p (and other miRNAs w/seed AGUGCAA) (+8 more)	Death of embryo (+3 more)	11,759

2	CSF2,miR-136-3p (miRNAs w/seed AUCAUCG) (+8 more)	Infection by Retroviridae	6,548
3	miR-199a-3p (and other miRNAs w/seed CAGUAGU)	Organismal death	-2,333
4	miR-3585-5p (and other miRNAs w/seed UCACAAG)	Infection by Retroviridae	-6,0
5	miR-1911-5p (miRNAs w/seed GAGUACC)	Infection by Retroviridae	-7,506

Top Networks

ID	Associated Network Functions	Score
1	Protein Synthesis, RNA Damage and Repair, Cancer	52
2	Developmental Disorder, Embryonic Development, Organismal Development	45
3	Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry	37
4	Cellular Assembly and Organization, DNA Replication, Recombination, and Repair, Cancer	31
5	Immunological Disease, Inflammatory Disease, Inflammatory Response	29

Top Tox Lists

Name	p-value	Overlap
Renal Necrosis/Cell Death	9,67E-03	2,6 % 15/569
p53 Signaling	4,34E-02	4,0 % 4/99
Increases Glomerular Injury	8,41E-02	3,2 % 4/124
Decreases Permeability Transition of Mitochondria and Mitochondrial Membrane	8,96E-02	14,3 % 1/7
Increases Permeability Transition of Mitochondria and Mitochondrial Membrane	1,02E-01	12,5 % 1/8

Top My Lists

Name	p-value	Overlap
EIF 2 Heart 231018	1,59E-04	9,8 % 6/61
Eif 2 list 221018	3,58E-04	6,2 % 8/130
EIF2 Kidney 231018	2,86E-03	5,0 % 7/141
ANOVA 16 gr vs groups filt 5, fold change above 5	2,11E-02	11,8 % 2/17
101118 lungs IL-1	7,73E-02	16,7 % 1/6

Top My Pathways

Name	p-value	Overlap
231018 EIF2 Heart	1,59E-04	9,8 % 6/61
EIF2 Signaling kidney 221018	9,13E-04	4,4 % 10/225
EIF2 Signaling Heart 231018	9,13E-04	4,4 % 10/225

EIF2 Signaling 051118	9,13E-04	4,4 % 10/225
EIF2 Signaling Heart	9,13E-04	4,4 % 10/225

Top Analysis-Ready Molecules

Expr Fold Change

Molecules	Expr. Value	Chart
IGHG1*	↑ 7,497	
CEACAM8	↑ 5,144	
LTF	↑ 3,866	
MMP8	↑ 2,779	
OLFM4	↑ 2,772	
CEACAM6	↑ 2,771	
CRISP3	↑ 2,018	
GBP1	↑ 1,987	
ZNF208	↑ 1,976	
CD300C*	↑ 1,916	

Expr Fold Change

Molecules	Expr. Value	Chart
SCARNA6	↓ -1,942	
RPL18A*	↓ -1,885	
OR2L3	↓ -1,835	
RNU4ATAC	↓ -1,812	
SNORA79B	↓ -1,750	
SNHG15*	↓ -1,665	
SNORA23	↓ -1,655	
UBE2CP5	↓ -1,640	
SNORA54	↓ -1,615	
SNORA2C	↓ -1,575	