

Supplementary Information

Novel transcriptome assembly and comparative toxicity pathway analysis in mahi-mahi (*Coryphaena hippurus*) embryos and larvae exposed to Deepwater Horizon oil

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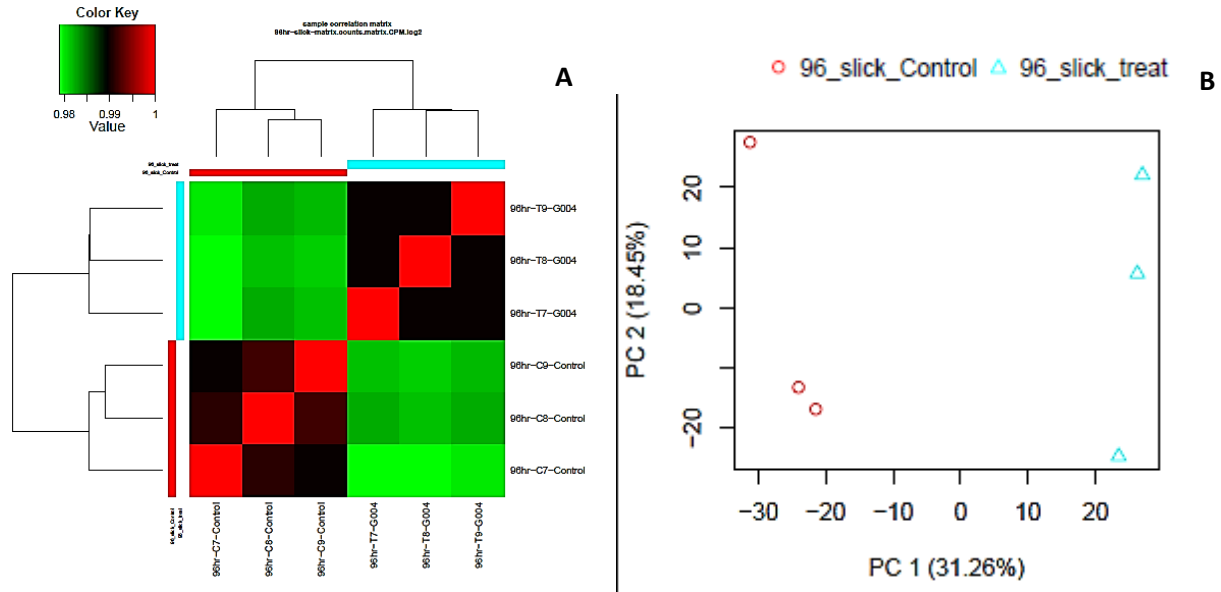
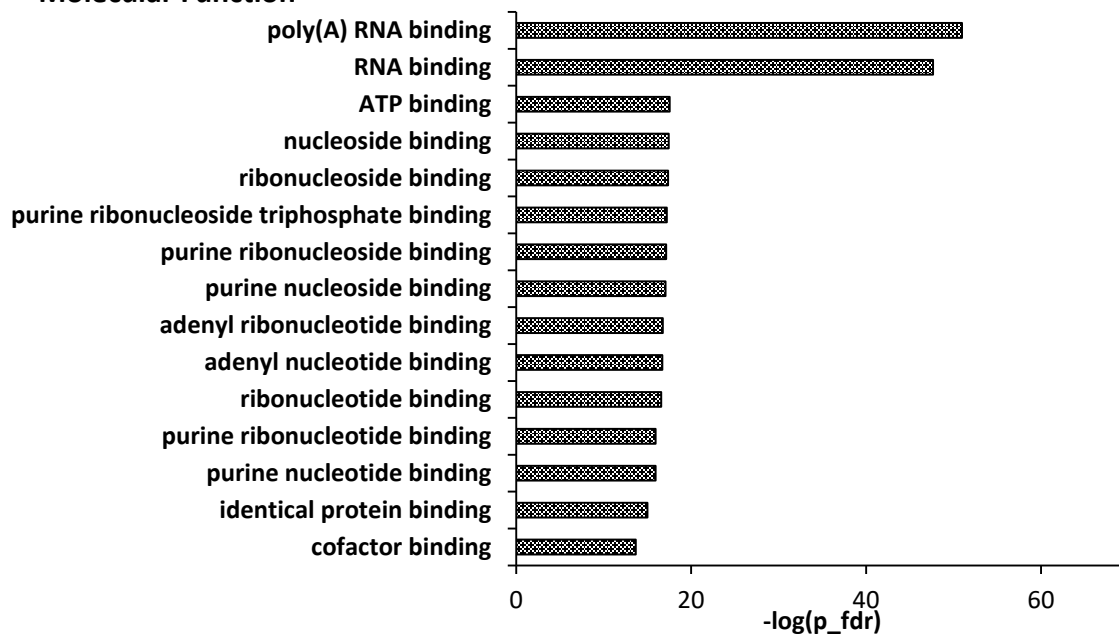
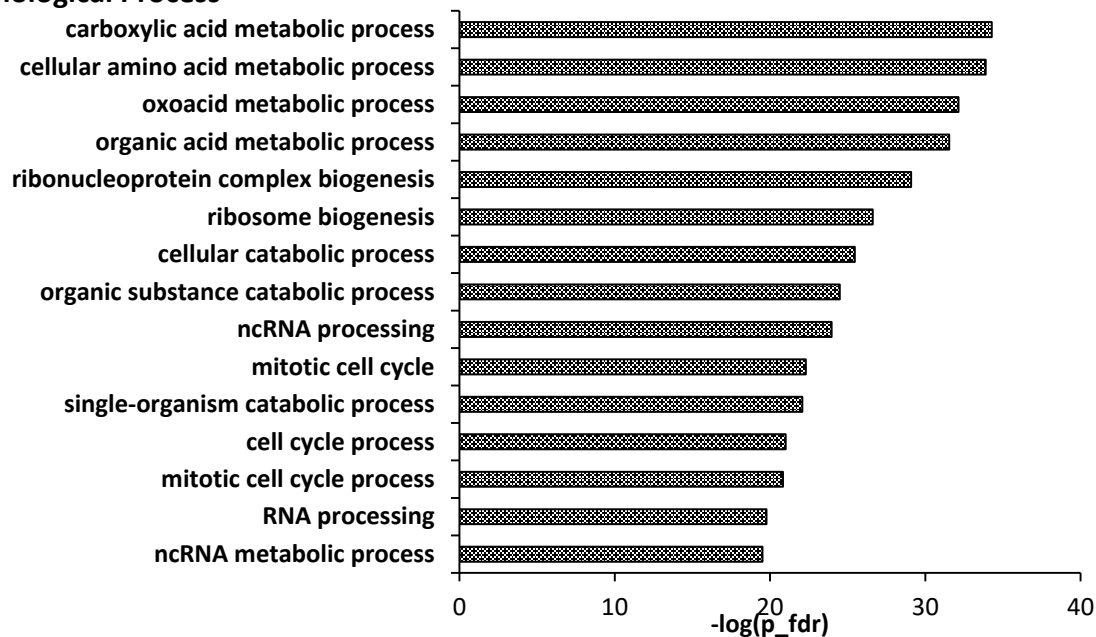


Fig. S1 Heatmap (a) showing the Euclidean distances between the samples as calculated from the DEseq2 variance stabilizing transformation of the count data. Samples are clustered by similarity. The samples from each treatment cluster together indicating global differences between the slick oil treatment and control. PCA plot (b) indicating that the first principal component (31.26%) separates the 96 hpf control and slick oil samples into the two sides of $x = 0$, indicating that the two groups are different.

Molecular Function



Biological Process



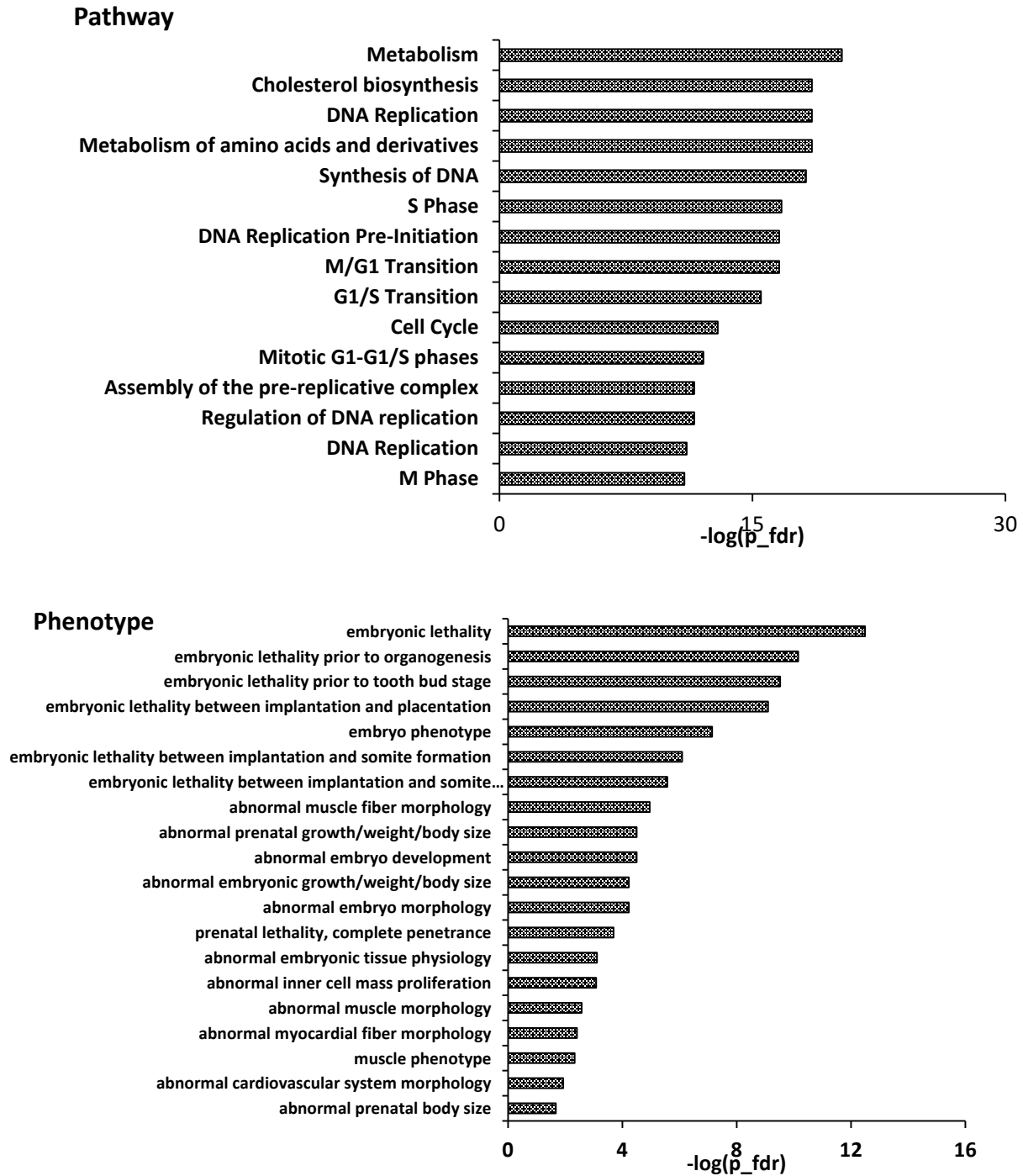


Fig. S2 Enriched molecular function, biological process, pathway and phenotype by *De novo* approach. 96 hpf mahi-mahi larvae were exposed to slick oil. The X-axis is a negative log of the adjusted p-value.

Table S1 Top enriched molecular functions, biological processes and cellular components by GOrilla.

De novo			OnRamp		
Molecular Functions	q_FDR	Gene	Molecular Functions	q_FDR	Gene
oxidoreductase activity	4.33E-07	57	oxidoreductase activity	3.46E-12	103
antioxidant activity	8.11E-06	14	cofactor binding	6.21E-09	34
lipase activity	9.64E-06	15	structural constituent of eye lens	3.36E-07	7
receptor activity	3.04E-05	48	catalytic activity	1.35E-06	120
molecular transducer activity	3.04E-05	48	coenzyme binding	1.37E-06	18
oxidoreductase activity, acting on a	5.78E-05	4	ion binding	2.18E-06	296
carboxylic ester hydrolase activity	9.07E-05	18	cation binding	4.43E-06	282
oxidoreductase activity, acting on paired donors	1.26E-04	3	metal ion binding	5.21E-06	279
tetrapyrrole binding	2.08E-04	13	iron ion binding	6.26E-06	27
heme binding	2.41E-04	9	oxidoreductase activity, acting on paired	1.03E-05	4
flavonoid 3'-monooxygenase activity	3.34E-04	1	oxidoreductase activity, acting on the CH-	1.19E-05	5
oxidoreductase activity, acting on	3.34E-04	1	aminopeptidase activity	1.51E-05	13
vitamin D 24-hydroxylase activity	3.34E-04	1	monooxygenase activity	8.79E-05	6
serine-type peptidase activity	3.35E-04	18	heme binding	9.25E-05	17
serine hydrolase activity	3.35E-04	18	oxygen binding	1.35E-04	7
transmembrane receptor activity	3.55E-04	31	oxidoreductase activity, acting on paired	1.66E-04	24
monooxygenase activity	5.08E-04	3	sulfur compound binding	1.71E-04	25
transmembrane signaling receptor	6.15E-04	29	oxidoreductase activity, acting on the	1.80E-04	6
oxidoreductase activity, acting on the	7.57E-04	3	tetrapyrrole binding	1.98E-04	17
serine-type endopeptidase activity	8.26E-04	15	oxidoreductase activity, acting on the	2.49E-04	5
Biological Processes	q_FDR	Gene	Biological Processes	q_FDR	Gene
cholesterol biosynthetic process	1.56E-18	14	small molecule metabolic process	4.00E-16	106
secondary alcohol biosynthetic process	7.82E-19	14	single-organism metabolic process	4.25E-14	226
sterol biosynthetic process	5.21E-19	14	sterol biosynthetic process	8.25E-11	20
alcohol biosynthetic process	3.88E-17	14	cholesterol biosynthetic process	8.23E-11	12
steroid biosynthetic process	1.37E-16	14	secondary alcohol biosynthetic process	6.58E-11	12
cholesterol metabolic process	2.30E-16	16	sterol metabolic process	1.47E-10	26
secondary alcohol metabolic process	3.41E-16	16	oxidation-reduction process	1.55E-10	126
sterol metabolic process	5.05E-16	16	small molecule biosynthetic process	1.63E-10	40
steroid metabolic process	7.69E-16	17	alcohol biosynthetic process	2.00E-10	12
organic hydroxy compound	2.77E-15	14	single-organism biosynthetic process	2.09E-10	61
lipid metabolic process	4.75E-13	112	steroid metabolic process	4.49E-10	29
alcohol metabolic process	5.99E-12	16	secondary alcohol metabolic process	7.07E-10	24
organic hydroxy compound metabolic	1.29E-11	16	cholesterol metabolic process	6.52E-10	24
small molecule biosynthetic process	2.65E-10	16	organic hydroxy compound metabolic	6.34E-10	36
lipid biosynthetic process	7.28E-09	15	alcohol metabolic process	6.08E-10	31
cellular lipid metabolic process	4.66E-08	87	steroid biosynthetic process	7.00E-10	12
single-organism metabolic process	1.85E-06	231	sensory perception of light stimulus	1.05E-09	26
single-organism biosynthetic process	3.61E-06	17	visual perception	9.96E-10	26

cholesterol biosynthetic process via	1.29E-05	4	organic acid metabolic process	1.79E-09	126
cholesterol biosynthetic process via lathosterol	1.23E-05	4	organic hydroxy compound biosynthetic process	1.91E-09	22
Components	q_FDR	Gene	Components	q_FDR	Gene
integral component of membrane	1.48E-13	238	extracellular region part	1.31E-10	363
intrinsic component of membrane	1.99E-13	241	extracellular region	6.16E-09	86
membrane part	1.21E-12	344	extracellular organelle	2.63E-08	288
vacuolar part	5.02E-09	101	extracellular vesicle	1.97E-08	288
vacuole	1.46E-08	79	extracellular exosome	2.82E-08	286
vacuolar lumen	5.61E-08	33	fibrillar collagen trimer	3.47E-08	10
lytic vacuole	1.50E-07	37	membrane-enclosed lumen	1.08E-07	53
lysosome	1.32E-07	37	organelle lumen	1.78E-07	51
lysosomal lumen	1.68E-07	30	extracellular space	1.91E-06	115
extracellular region part	1.72E-07	281	intracellular organelle lumen	2.60E-06	46
endoplasmic reticulum membrane	3.33E-06	22	membrane-bounded vesicle	4.24E-06	315
extracellular space	5.63E-06	71	vesicle	5.95E-06	324
plasma membrane	8.57E-05	204	collagen trimer	4.96E-04	13
extracellular exosome	2.25E-04	284	endoplasmic reticulum part	9.73E-04	47
endoplasmic reticulum	2.58E-04	37	endoplasmic reticulum membrane	2.16E-03	24
extracellular organelle	3.21E-04	284	cytoplasmic part	4.39E-03	612
extracellular vesicle	3.02E-04	284	ciliary membrane	1.12E-02	5
vacuolar membrane	2.92E-04	77	ciliary part	1.18E-02	6
plasma membrane part	3.12E-04	145	preribosome	1.44E-02	16
endoplasmic reticulum part	5.79E-04	22	extracellular matrix component	1.49E-02	22

Table S2 Top enriched molecular functions, components and biological processes by ToppGene

De novo			OnRamp		
Molecular Functions	q_FDR	Genes	Molecular Functions	q_FDR	Genes
poly(A) RNA binding	1.10E-51	404	poly(A) RNA binding	2.68E-27	338
RNA binding	2.26E-48	498	RNA binding	6.66E-24	412
ATP binding	2.86E-18	377	adenyl nucleotide binding	3.33E-16	378
nucleoside binding	3.78E-18	448	adenyl ribonucleotide binding	9.86E-16	372
ribonucleoside binding	4.38E-18	446	ATP binding	4.67E-15	361
purine ribonucleoside triphosphate	6.09E-18	442	purine nucleotide binding	1.79E-14	436
purine ribonucleoside binding	7.15E-18	444	ribonucleotide binding	3.71E-14	433
purine nucleoside binding	8.79E-18	444	purine ribonucleotide binding	9.11E-14	428
adenyl ribonucleotide binding	1.75E-17	381	nucleoside binding	1.13E-12	419
adenyl nucleotide binding	2.00E-17	383	ribonucleoside binding	1.13E-12	417
ribonucleotide binding	2.71E-17	451	purine ribonucleoside triphosphate	2.54E-12	412
purine nucleotide binding	1.17E-16	448	purine ribonucleoside binding	2.91E-12	414
purine ribonucleotide binding	1.17E-16	445	purine nucleoside binding	3.55E-12	414
identical protein binding	9.97E-16	342	protein complex binding	1.14E-11	237
cofactor binding	2.20E-14	103	structural molecule activity	2.78E-10	174

pyrophosphatase activity	1.55E-12	222	enzyme binding	1.70E-09	335
hydrolase activity, acting on acid	1.94E-12	222	cofactor binding	2.84E-09	92
hydrolase activity, acting on acid	2.12E-12	222	peptidase activity, acting on L-amino acid	9.11E-09	160
nucleoside-triphosphatase activity	3.04E-12	212	identical protein binding	9.79E-09	277
enzyme binding	7.89E-12	435	peptidase activity	3.01E-08	162
Biological Processes	q_FDR	Genes	Biological Processes	q_FDR	Genes
carboxylic acid metabolic process	5.29E-35	327	carboxylic acid metabolic process	7.20E-25	300
cellular amino acid metabolic process	1.29E-34	175	organic acid metabolic process	9.64E-24	325
oxoacid metabolic process	7.39E-33	346	oxoacid metabolic process	9.64E-24	321
organic acid metabolic process	2.91E-32	348	cellular component disassembly	4.36E-22	167
ribonucleoprotein complex	8.15E-30	184	tissue development	1.87E-20	445
ribosome biogenesis	2.46E-27	140	macromolecule catabolic process	6.93E-17	286
cellular catabolic process	3.47E-26	477	single-organism catabolic process	3.35E-16	458
organic substance catabolic process	3.26E-25	490	macromolecular complex subunit organization	1.73E-15	417
ncRNA processing	1.08E-24	156	cell development	3.49E-15	457
mitotic cell cycle	4.94E-23	297	organ morphogenesis	3.49E-15	250
single-organism catabolic process	8.28E-23	320	translational elongation	6.02E-15	64
cell cycle process	9.83E-22	371	cellular amino acid metabolic process	9.39E-15	155
mitotic cell cycle process	1.46E-21	274	mRNA metabolic process	1.45E-14	191
RNA processing	1.68E-20	267	response to endogenous stimulus	2.35E-14	348
ncRNA metabolic process	3.05E-20	187	extracellular matrix organization	4.27E-14	129
rRNA processing	6.82E-19	108	extracellular structure organization	5.09E-14	129
cell cycle	1.50E-18	436	cellular macromolecule catabolic process	6.05E-14	232
rRNA metabolic process	2.00E-18	109	translational termination	1.14E-13	51
alpha-amino acid metabolic process	3.94E-18	103	neurogenesis	1.20E-13	348
cellular amide metabolic process	4.43E-18	283	nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	1.57E-13	58
Pathways	q_FDR	Genes	Pathways	q_FDR	Genes
Metabolism	5.02E-21	439	Metabolism	5.11E-17	434
Metabolism of amino acids and derivatives	3.01E-19	95	Metabolism of amino acids and derivatives	3.34E-11	83
DNA Replication	3.01E-19	65	Extracellular matrix organization	3.34E-11	103
Cholesterol biosynthesis	3.01E-19	159	Steroid Biosynthesis	1.20E-08	19
Synthesis of DNA	6.73E-19	61	cholesterol biosynthetic	2.80E-08	17
S Phase	1.91E-17	69	Switching of origins to a post-replicative state	2.80E-08	39
M/G1 Transition	2.60E-17	54	Orc1 removal from chromatin	2.80E-08	39
DNA Replication Pre-Initiation	2.60E-17	54	Steroid biosynthesis	2.90E-08	18
G1/S Transition	3.13E-16	63	superpathway of cholesterol biosynthesis	2.90E-08	21
Cell Cycle	1.15E-13	170	Cholesterol biosynthesis	2.90E-08	19
Mitotic G1-G1/S phases	8.11E-13	67	M/G1 Transition	3.21E-08	43
Regulation of DNA replication	2.86E-12	45	DNA Replication Pre-Initiation	3.21E-08	43
Assembly of the pre-replicative	2.86E-12	42	Synthesis of DNA	4.18E-08	47
DNA Replication	7.90E-12	31	Removal of licensing factors from origins	4.42E-08	39
M Phase	1.08E-11	92	Cholesterol biosynthesis	4.99E-08	16
Removal of licensing factors from origins	1.23E-11	43	Assembly of the pre-replicative complex	6.16E-08	37

Switching of origins to a post-replicative state	1.82E-11	42	Protein digestion and absorption	1.53E-07	43
Orc1 removal from chromatin	1.82E-11	42	Regulation of DNA replication	1.53E-07	39
Ribosome biogenesis in eukaryotes	9.35E-11	46	Ubiquitin Mediated Degradation of Phosphorylated Cdc25A	1.53E-07	31
Cell Cycle Checkpoints	9.27E-10	57	p53-Independent DNA Damage Response	1.53E-07	31
Phenotypes	q_FDR	Genes	Phenotypes	q_FDR	Genes
embryonic lethality	3.25E-13	445	prenatal lethality	1.29E-08	545
embryonic lethality prior to organogenesis	7.09E-11	200	muscle phenotype	1.18E-06	337
embryonic lethality prior to tooth bud stage	3.00E-10	203	embryonic lethality	1.88E-06	425
embryonic lethality between implantation and placentation	7.97E-10	141	decreased body size	1.97E-06	516
embryo phenotype	7.28E-08	394	lethality during fetal growth through	2.07E-06	513
embryonic lethality between implantation and somite formation	8.12E-07	100	decreased total tissue mass	5.79E-05	405
embryonic lethality between implantation and somite formation, abnormal muscle fiber morphology	2.68E-06	92	decreased body weight	5.79E-05	405
abnormal embryo development	1.11E-05	114	abnormal physical strength	6.71E-05	117
abnormal prenatal growth/weight/body size	3.18E-05	246	perinatal lethality	6.82E-05	307
abnormal embryo morphology	3.18E-05	254	postnatal lethality	8.04E-05	310
abnormal embryonic growth/weight/body size	5.95E-05	294	premature death	4.41E-04	314
abnormal embryonic growth/weight/body size	5.95E-05	217	abnormal muscle physiology	4.41E-04	224
prenatal lethality, complete penetrance	2.05E-04	104	abnormal muscle morphology	5.03E-04	228
abnormal embryonic tissue physiology	7.75E-04	84	embryogenesis phenotype	5.94E-04	394
abnormal inner cell mass	8.23E-04	30	abnormal embryogenesis/ development	5.94E-04	394
abnormal muscle morphology	2.67E-03	214	abnormal cardiovascular system	7.45E-04	402
abnormal myocardial fiber morphology	3.90E-03	60	embryonic lethality prior to organogenesis	7.45E-04	168
muscle phenotype	4.69E-03	295	abnormal heart morphology	7.45E-04	291
abnormal cardiovascular system morphology	1.17E-02	381	embryonic lethality prior to tooth bud stage	8.05E-04	169
abnormal prenatal body size	2.14E-02	179	abnormal total tissue mass	1.29E-08	545

Table S3 Top enriched molecular functions, biological processes and cellular components by DAVID using zebrafish genome as background

Molecular Functions	p-value	Gene	%
RNA binding	1.50E-05	27	4.3
translation factor activity, nucleic acid binding	4.60E-04	12	1.9
translation initiation factor activity	1.30E-03	9	1.4
selenium binding	3.00E-03	6	1
tRNA binding	7.90E-03	4	0.6
oxidoreductase activity, acting on single donors with incorporation of molecular oxygen	8.70E-03	6	1

oxidoreductase activity, acting on single donors with incorporation of molecular oxygen	9.90E-03	6	1
iron ion binding	2.10E-02	18	2.9
oxidoreductase activity, acting on sulfur group of donors, disulfide as acceptor	3.70E-02	3	0.5
S-methyltransferase activity	4.60E-02	3	0.5
vascular endothelial growth factor receptor	4.60E-02	3	0.5
adenyl nucleotide binding	5.00E-02	54	8.6
acetyltransferase activity	5.10E-02	5	0.8
purine nucleoside binding	5.30E-02	54	8.6
nucleoside binding	5.70E-02	54	8.6
nucleotide binding	5.80E-02	79	12.5
ATP binding	6.60E-02	51	8.1
adenyl ribonucleotide binding	6.60E-02	51	8.1
purine nucleotide binding	6.80E-02	67	10.6
tRNA (guanine-N7-)-methyltransferase activity	7.70E-02	2	0.3
Biological Processes	p-value	Gene	%
ribonucleoprotein complex biogenesis	5.10E-09	17	2.7
mitosis	3.10E-08	16	2.5
nuclear division	4.10E-08	16	2.5
M phase of mitotic cell cycle	5.40E-08	16	2.5
M phase	7.20E-08	18	2.9
mitotic cell cycle	9.40E-08	17	2.7
cell cycle phase	1.10E-07	18	2.9
organelle fission	1.20E-07	16	2.5
transcription	1.90E-07	55	8.7
ribosome biogenesis	3.50E-07	14	2.2
cell division	1.30E-06	18	2.9
cell cycle process	2.10E-06	18	2.9
cell cycle	2.60E-06	25	4
rRNA processing	4.40E-06	11	1.7
rRNA metabolic process	5.90E-06	11	1.7
protein localization	8.00E-06	36	5.7
protein transport	1.40E-05	34	5.4
establishment of protein localization	1.40E-05	34	5.4
RNA processing	2.30E-05	15	2.4
steroid metabolic process	2.70E-05	26	4.1
Components	p-value	Gene	%
nucleolus	6.50E-14	26	4.1
membrane-enclosed lumen	7.80E-09	44	7
mitochondrion	1.90E-08	48	7.6
organelle lumen	4.70E-08	41	6.5
intracellular organelle lumen	4.70E-08	41	6.5
nuclear lumen	6.30E-07	35	5.5
chromosome, centromeric region	8.80E-07	11	1.7
condensed chromosome kinetochore	3.30E-06	8	1.3
condensed chromosome, centromeric region	3.30E-06	8	1.3
kinetochore	7.50E-06	8	1.3

endosome	9.30E-06	13	2.1
extrinsic to membrane	8.20E-05	18	2.9
condensed chromosome	8.30E-05	8	1.3
spindle	4.30E-04	8	1.3
organelle envelope	6.00E-04	29	4.6
mitochondrial part	6.30E-04	26	4.1
envelope	7.00E-04	29	4.6
mitochondrial membrane	1.00E-03	22	3.5
mitochondrial envelope	1.20E-03	23	3.6
organelle inner membrane	5.90E-03	17	2.7

Table S4 Top 50 statistically enriched canonical pathways and the list of DEGs responsible for their enrichment by IPA

De novo	-log(p-value)	Molecules
Cell Cycle Control of Chromosomal Replication	7.17E+00	MCM5,MCM6,CDC45,ORC2,CDT1,CDC7,RPA1,MCM4,RPA2,MCM3,RPA3,ORC5,ORC4,MCM7
Signaling by Rho Family GTPases	6.05E+00	PIK3R1,ARPC5,GNB5,PIKFYVE,ARHGEF1,CLIP1,STMN1,ROCK2,GNB1,PAK1,RHOG,CFL2,FGFR4,EZR,PIK3CG,MYL4,ACTA1,GNG12,ITGA4,PIK3C2B,MAPK12,KIAA1804,MYL7,CDH2,CDH1,CDH20,IRS1,GNAO1,FNBP1,ARPC1B,RHOT2,GNA14,IQGAP1,JUN,PPP1R12A,CDH3,PIK3C3,RHO,ARPC3,PI4KA,MYL12A,ITGB1,ITGA2,VIM,CDC42EP3,CDH15,GNAI3,PRKCI,Pak2,CDH17,ARPC4
Unfolded protein response	4.83E+00	PDIA2,CALR,HSPA14,ERN1,INSIG1,HSPA9,CANX,ATF6,OS9,MAP3K5,HSPA4,UBXN4,SREBF1,EDEM1,ERO1B,VCP,AMFR
Axonal Guidance Signaling	4.77E+00	DPYSL2,BMP4,ITSN1,PIK3R1,ARPC5,GNB5,MMP13,NTN1,GNB1,ROCK2,PAK1,SEMA6D,CFL2,SEMA3D,PIK3CG,FGFR4,WNT4,MYL4,GSK3B,CHMP1A,ADAMTS5,GNG12,ITGA4,PIK3C2B,COP55,TUBB2A,MM P2,HHIP,MYL7,PRKCD,IRS1,GNAO1,FZD6,EPHA2,MME,ADAM17,RND1,ARPC1B,PDGFA,GNA14,PRKA G1,WNT7A,PPP3CB,NGFR,PIK3C3,ARPC3,PRKCE,PSMD14,MMP11,SEMA3B,LNPEP,ACE,BMP1,MYL12A,ITGB1,SEMA3G,PXN,NRP2,WNT9B,CXCR4,ITGA2,EPHA3,PLXND1,BMP5,GNAI3,SEMA3A,FZD8,PR KCI,SEMA4D,FZD4,Pak2,ADAM10,SEMA3C,ADAM9,ARPC4
Mitotic Roles of Polo-Like Kinase	4.70E+00	KIF23,FZR1,ANAPC2,ESPL1,CCNB3,CDC7,PPP2R3B,PLK1,ANAPC1,SLK,PLK4,HSP90AB1,PPP2R3A,C APN1,HSP90AA1,FBXO5,PPP2R5E,KIF11,CDC25A
RhoGDI Signaling	4.67E+00	ARPC1B,ARPC5,RHOT2,PIKFYVE,GNB5,ARHGEF1,GNA14,ROCK2,GNB1,PAK1,RHOG,PPP1R12A,CFL 2,CDH3,EZR,RHO,ARPC3,MYL4,ARHGAP12,PI4KA,ACTA1,GNG12,MYL12A,ITGA4,ITGB1,ITGA2,CDH1 5,MYL7,GNAI3,CDH1,CDH2,CDH20,Pak2,GNAO1,CDH17,FNBP1,ARPC4
Integrin Signaling	4.34E+00	ARPC1B,TSPAN7,PIK3R1,RHOT2,ARPC5,PIKFYVE,PPP1CB,ITGA10,TSPAN3,PAK1,RHOG,PPP1R12A, FGFR4,PIK3CG,PIK3C3,RHO,ITGAV,ARPC3,GSK3B,ITGB4,ACTA1,MYL12A,ITGA4,ITGB1,CAPN5,PIK3 C2B,PXN,ITGA2,TNK2,GSN,TTN,MYL7,TSPAN1,IRS1,CAPN1,Pak2,CAPN9,CAPN2,ITGB6,NEDD9,FNBP 1,ARPC4
Regulation of Actin-based Motility by Rho	3.90E+00	ITGB1,ARPC1B,RHOT2,ARPC5,ITGA2,PIKFYVE,PPP1CB,GSN,MYL7,PAK1,RHOG,PPP1R12A,Pak2,RH OU,MYL4,ARPC3,FNBP1,ACTA1,ARPC4,PI4KA,ITGA4,MYL12A
Actin Cytoskeleton Signaling	3.80E+00	MYH6,ARPC1B,PDGFA,PIK3R1,ARPC5,PIKFYVE,TRIO,PPP1CB,ARHGEF1,IQGAP1,F2,ROCK2,PAK1,P PP1R12A,CFL2,FLNA,PIK3C3,FGFR4,EZR,PIK3CG,ARPC3,MYL4,ARHGAP24,GNG12,ACTA1,ITGA4,IQG AP3,MYL12A,ITGB1,VAV2,PIK3C2B,PXN,CSK,ITGA2,MYH7,GSN,TTN,MYL7,IRS1,Pak2,SSH3,ARPC4
phagosome maturation	3.79E+00	NOS1,VPS28,PRDX1,PRDX5,TCIRG1,PIKFYVE,DYNLRB2,ATP6AP1,VTI1B,DYNC1I2,PIK3C3,GOSR1,AT P6V1G1,M6PR,ATP6V0E2,CALR,VPS16,VPS41,TUBB2A,RAB7A,CANX,TSG101,ATP6V1F,DYNC1LI2,AT P6V1H,ATP6V0A2,ATP6V0E1
ILK Signaling	3.71E+00	FLNB,MYH6,PIK3R1,RHOT2,PPP2R3B,RHOG,JUN,CFL2,PPP1R12A,FLNA,PIK3CG,FGFR4,PIK3C3,RHO U,MYL4,GSK3B,ITGB4,CTNNB1,ACTA1,ITGB1,PIK3C2B,PXN,CASP3,VIM,MYH7,MAPK12,MYL7,CDH1,F LNC,PPP2R3A,IRS1,LEF1,KRT18,PTGS2,PPP2R5E,ITGB6,FNBP1
Polyamine Regulation in Colon Cancer	3.60E+00	MAX,AZIN1,PSMF1,MXD1,SAT1,SAT2,CTNNB1,PSME3,ODC1
Protein Ubiquitination Pathway	3.60E+00	FZR1,ANAPC2,UBE2A,HSPA14,PSMD9,USP2,ANAPC1,PSMC5,HSPA4,PSMD10,HSP90AB1,PSMC6,HS PE1,USP16,UCHL5,SUGT1,PSMA3,PSMD14,DNAJB1,PSMC2,AMFR,PSMB4,PSMA6,DNAJB12,UBE4B,U SP38,PSMD13,HSPA9,PSMD6,PSMA1,THOP1,PSMB6,UBE3A,DNAJB14,PSMD8,SKP2,DNAJC11,PSMD 2,PSMD12,PSMA4,HSP90AA1,PSMD1,PSMD4,DNAJC7,UBE2E1
Gα12/13 Signaling	3.56E+00	PIK3R1,ARHGEF1,MAP3K5,F2,ROCK2,IKBKB,JUN,NFKBIA,CDH3,PIK3C3,PIK3CG,FGFR4,MYL4,CTNNB 1,MYL12A,VAV2,PIK3C2B,PXN,CDH15,MAPK12,MYL7,CDH2,CDH1,CDH20,IRS1,CDH17,MEF2C
Hepatic Fibrosis / Hepatic Stellate Cell Activation	3.55E+00	MYH6,PDGFA,MMP13,COL8A1,COL6A6,COL5A1,COL1A2,COL6A1,NGFR,HGF,MYL4,ECE1,COL11A2,S TAT1,COL18A1,COL5A2,COL4A1,COL9A1,COL6A2,COL2A1,MYH7,MMP2,IGFBP5,IL1R1,MYL7,COL5A3, COL21A1,COL23A1,COL24A1,EDNRA,COL11A1,KDR,COL9A2,A2M,COL7A1
Mechanisms of Viral Exit from Host Cells	3.25E+00	SH3GL1,PRKCI,CHMP2B,VPS28,PRKCD,CHMP4B,PRKCE,PDCD6IP,TSG101,LMNB1,CHMP3,ACTA1

Assembly of RNA Polymerase I Complex	3.02E+00	POLR1D,POLR1C,POLR1A,POLR1B,TAF1C
Remodeling of Epithelial Adherens Junctions	2.97E+00	ARPC1B,TUBB2A,ARPC5,RAB7A,CTNNA1,IQGAP1,CLIP1,CDH1,HGF,ARPC3,CTNNB1,DNM1L,HGS,ARPC4,ACTA1,CTNND1
Molecular Mechanisms of Cancer	2.90E+00	BMP4,SUV39H1,PIK3R1,ARHGEF1,RBL1,PAK1,CAMK2A,RHOG,FGFR4,PIK3CG,WNT4,GSK3B,SMAD1,CDC25A,ITGA4,PIK3C2B,CCNE2,CASP3,MAPK12,RALBP1,CDH1,MAX,IRS1,PRKCD,E2F1,GNAO1,FZD6,APH1B,LEF1,FNBP1,CAMK2G,PA2G4,RHOT2,CTNNA1,GNA14,MAP3K5,E2F3,PRKAG1,NFKBIA,JUN,WNT7A,PIK3C3,RHO,PRKCE,CTNNB1,CAMK2B,BMP1,ITGB1,WNT9B,ITGA2,BMP5,GNAI3,FZD8,PRKCI,FZD4,NF1,Pak2,CTNND1
Tec Kinase Signaling	2.89E+00	PIK3R1,RHOT2,GNB5,GNA14,GNB1,PAK1,RHOG,PIK3C3,PIK3CG,FGFR4,RHO,PRKCE,STAT1,STAT5B,GN12,ACTA1,ITGA4,VAV2,ITGB1,PIK3C2B,ITGA2,STAT3,MAPK12,FRK,GNAI3,PRKCI,PRKCD,IRS1,Pak2,GNAO1,FNBP1
HGF Signaling	2.78E+00	ETS1,ITGB1,PIK3C2B,PXN,PIK3R1,ITGA2,MAP3K5,STAT3,MAPK12,ELF4,ELF2,PAK1,JUN,PRKCI,PIK3CG,FGFR4,IRS1,PRKCD,PIK3C3,HGF,PRKCE,PTGS2,ITGA4
Amyloid Processing	2.77E+00	CSNK1E,CAPN5,CSNK2A1,CAPN1,CSNK1D,PRKCE,APH1B,CAPN9,CAPN2,BACE2,GSK3B,MAPK12,PRKAG1
Semaphorin Signaling in Neurons	2.69E+00	ROCK2,ITGB1,DPYSL2,SEMA3A,PAK1,RHOG,SEMA4D,RND1,CFL2,Pak2,RHOT2,RHO,FNBP1
Rac Signaling	2.68E+00	ITGB1,PIK3C2B,RPS6KB1,ARPC1B,PIK3R1,ITGA2,ARPC5,PIKFYVE,IQGAP1,PAK1,PRKCI,JUN,CFL2,PIK3CG,FGFR4,IRS1,PIK3C3,Pak2,ARPC3,ARPC4,PI4KA,ITGA4,IQGAP3
CXCR4 Signaling	2.59E+00	PIK3R1,RHOT2,GNB5,GNA14,ROCK2,GNB1,ELMO3,PAK1,RHOG,JUN,PIK3CG,FGFR4,PIK3C3,RHO,PRKCE,MYL4,GN12,MYL12A,PIK3C2B,PXN,CXCR4,MAPK12,MYL7,GNAI3,PRKCI,PRKCD,IRS1,Pak2,GNAO1,FNBP1
NF-κB Activation by Viruses	2.59E+00	ITGB1,PIK3C2B,PIK3R1,ITGA2,TNFRSF14,IKBKB,NFKBIA,RIPK1,PRKCI,PIK3CG,IRS1,PIK3C3,FGFR4,PRKCD,ITGAV,PRKCE,IKBKAP,ITGA4
Small Cell Lung Cancer Signaling	2.59E+00	NOS1,PIK3C2B,CCNE2,FHIT,PA2G4,SUV39H1,PIK3R1,SKP2,IKBKB,NFKBIA,MAX,PIK3C3,PIK3CG,FGFR4,IRS1,TRAF4,E2F1,PTGS2
HIPPO signaling	2.59E+00	DLG1,TJP2,CSNK1D,PPP1CB,PPP2R3B,LATS2,STK3,DLG3,SKP2,CSNK1E,Ppp1cc,PPP1R10,PPP1R12A,PPP2R3A,PPP2R5E,PATJ,SMAD1,RASSF1
Virus Entry via Endocytic Pathways	2.57E+00	ITGB1,PIK3C2B,FLNB,ITSN1,PIK3R1,ITGA2,AP2A2,PRKCI,FLNC,FLNA,PIK3CG,FGFR4,IRS1,PRKCD,PIK3C3,CLTA,PRKCE,ITGB4,ITGB6,ACTA1,ITGA4
HER-2 Signaling in Breast Cancer	2.53E+00	ITGB1,TSC1,PIK3C2B,CCNE2,PIK3R1,MMP2,ERBB3,MAP3K5,PRKCI,PIK3C3,PIK3CG,PRKCD,IRS1,FGFR4,PRKCE,ITGB4,GSK3B,ITGB6
Role of p14/p19ARF in Tumor Suppression	2.50E+00	NPM1,PIK3C2B,IRS1,FGFR4,PIK3CG,PIK3R1,PIK3C3,E2F1,SEN3,SF3A1,POLR3D
Ephrin A Signaling	2.49E+00	ROCK2,VAV2,PIK3C2B,PAK1,CFL2,PIK3C3,PIK3CG,NGFR,FGFR4,IRS1,PIK3R1,ADAM10,EPHA3,EPHA2
Germ Cell-Sertoli Cell Junction Signaling	2.48E+00	PIK3R1,RHOT2,CTNNA1,MAP3K5,IQGAP1,PAK1,RHOG,CFL2,SORBS1,PIK3C3,FGFR4,PIK3CG,RHO,CTNNB1,ACTA1,ITGB1,PIK3C2B,PXN,TUBB2A,ITGA2,MAPK12,GSN,CDH2,CDH1,IRS1,Pak2,A2M,FNBP1,CTNND1,NECTIN2
PAK Signaling	2.47E+00	ITGB1,PIK3C2B,PXN,CASP3,PDGFA,PIK3R1,ITGA2,EPHA3,MAPK12,MYL7,PAK1,CFL2,PIK3CG,FGFR4,IRS1,PIK3C3,Pak2,MYL4,ITGA4,MYL12A
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	2.46E+00	ADAM17,BMP4,MMP3,PIK3R1,MMP14,MMP13,SP7,MAP3K5,IKBKB,WNT7A,JUN,NFKBIA,PPP3CB,PIK3C3,FGFR4,NGFR,PIK3CG,WNT4,GSK3B,CTNNB1,ADAMTS5,SMAD1,BMP1,ITGB1,PIK3C2B,CTSK,WNT9B,ITGA2,IL1R1,MAPK12,GSN,BMP5,FZD8,FZD4,IRS1,FZD6,LEF1,SFRP1
Actin Nucleation by ARP-WASP Complex	2.46E+00	ROCK2,ITGB1,RHOG,PPP1R12A,ARPC1B,ITGA2,ARPC5,RHOT2,RHO,ARPC3,ARPC4,FNBP1,ITGA4
Ephrin Receptor Signaling	2.44E+00	ITSN1,ARPC1B,PDGFA,ARPC5,GNB5,GNA14,GNB1,ROCK2,PAK1,CFL2,SORBS1,PIK3CG,ARPC3,GN12,ITGA4,ITGB1,GRIN1,PXN,CXCR4,ITGA2,EPHA3,STAT3,GNAI3,Pak2,GNAO1,ADAM10,DOK1,MAP4K4,EPHA2,ARPC4
Huntington's Disease Signaling	2.43E+00	POLR2F,HSPA14,SGK1,PIK3R1,GNB5,GNA14,VTI1B,AP2A2,GNB1,HSPA4,DYNC1I2,POLR2A,JUN,PIK3C3,FGFR4,PIK3CG,PRKCE,NCOR1,DNAJB1,GOSR1,GN12,CAPN5,SDHA,PIK3C2B,CASP3,PSMF1,GLS,HSPA9,HIP1,PSME3,PRKCI,CLTA,PRKCD,IRS1,CAPN1,PENK,CAPN9,CAPN2,DNM1L
NRF2-mediated Oxidative Stress Response	2.41E+00	PRDX1,PIK3R1,MAP3K5,SOD3,GSTT1,JUN,PIK3C3,ABCC1,FGFR4,PIK3CG,VCP,UBE2K,PRKCE,DNAJA3,GSK3B,DNAJB1,CBR1,ACTA1,PIK3C2B,DNAJB12,SOD1,DNAJB14,GSTO1,TXNDR1,DNAJC11,PRKCI,PRKCD,IRS1,CCT7,ENC1,DNAJC7,MGST3
IL-8 Signaling	2.40E+00	PIK3R1,RHOT2,GNB5,IQGAP1,EIF4EBP1,ROCK2,GNB1,IKBKB,RHOG,JUN,PIK3CG,FGFR4,PIK3C3,RHO,ITGAV,PRKCE,GN12,PIK3C2B,RPS6KB1,PLD3,HBEGF,MMP2,MAPK12,MYL7,GNAI3,CDH1,PRKCI,PRKCD,IRS1,PTGS2,KDR,MAP4K4,FNBP1
Type II Diabetes Mellitus Signaling	2.40E+00	PIK3C2B,PRKAB2,PRKAB1,PKLR,PIK3R1,PKM,ADIPOQ,SMPD1,MAP3K5,MAPK12,PRKAG1,KCNJ11,IKBKB,PRKCI,NFKBIA,SMPD4,PRKCD,IRS1,PIK3C3,PIK3CG,FGFR4,NGFR,ACSL5,PRKCE,SLC27A1,ACSL1
ERK/MAPK Signaling	2.34E+00	PIK3R1,PPP2R3B,PPP1CB,PRKAG1,KSR1,EIF4EBP1,ELF4,PAK1,PPP1R10,PPP1R12A,PIK3CG,FGFR4,PIK3C3,PRKCE,STAT1,PLA2G12B,ITGA4,ITGB1,ETS1,PIK3C2B,PXN,ITGA2,PLA2G3,MAPKAPK5,STAT3,ELF2,PRKCI,DUSP1,PPP2R3A,PRKCD,IRS1,Pak2,PPP2R5E
Fcy Receptor-mediated Phagocytosis in Macrophages and Monocytes	2.32E+00	VAV2,RPS6KB1,PXN,PLD3,ARPC1B,PIK3R1,ARPC5,MYO5A,PAK1,PRKCI,RAB11B,PIK3CG,EZR,PRKCD,RAB11A,PRKCE,ARPC3,ACTA1,ARPC4
nNOS Signaling in Neurons	2.29E+00	CAPN5,NOS1,GRIN1,PRKCI,CAMK2A,PPP3CB,PRKCD,CAPN1,PRKCE,CAPN9,CAPN2,PFKM
Tight Junction Signaling	2.25E+00	MYH6,CTNNA1,PPP2R3B,VTI1B,PRKAG1,CPSF4,OCN1,JUN,CLDN4,NGFR,MYL4,GOSR1,CTNNB1,ACTA1,TJP2,RAB13,MYH7,MYL7,F11R,PRKCI,CLDN23,CLDN8,PPP2R3A,CPSF3,PPP2R5E,PATJ,CLDN3,NECTIN2
AMPK Signaling	2.24E+00	TSC1,PRKAB1,PRKAB2,PIK3R1,CPT1B,CHRN1B,ADIPOQ,PPP2R3B,PFKL,PRKAG1,ELAVL1,EIF4EBP1,CCNA2,GYS1,FASN,FGFR4,PIK3CG,PIK3C3,RPTOR,HNF4A,RPS6KB1,PIK3C2B,ACACB,MAPK12,SMA
Regulation of eIF4 and p70S6K Signaling	2.19E+00	RCD3,PFKM,Ak6,PPM1B,PPP2R3A,IRS1,ACACA,PPP2R5E,HMGCR
		PABPC1,ITGB1,PIK3C2B,RPS6KB1,EIF3C,EIF4EBP2,PIK3R1,ITGA2,PPP2R3B,MAPK12,EIF2S1,EIF4G1,EIF2S2,FAU,EIF4EBP1,EIF4G2,EIF3B,PPP2R3A,IRS1,PIK3CG,FGFR4,PIK3C3,RPS27L,PPP2R5E,AGO1,

		EIF1AX,ITGA4
Ovarian Cancer Signaling	2.19E+00	PIK3C2B,RPS6KB1,PA2G4,WNT9B,SUV39H1,PIK3R1,PTGS1,MMP2,PRKAG1,FZD8,FZD4,WNT7A,MSH2,PIK3C3,PIK3CG,FGFR4,IRS1,E2F1,FZD6,WNT4,EDNRA,LEF1,PTGS2,GSK3B,CTNNB1
OnRamp	-log(p-value)	Molecules
EIF2 Signaling	2.13E+01	RPL11,RPS27,PIK3R1,SOS2,RPL39,PDPK1,RPL35A,RPS11,FGFR3,RPL13,RPS20,EIF3B,RPS13,EIF3D,PIK3CG,RPL23A,INS,EIF5,RPL21,PPP1CA,AGO1,ATM,RPL32,FGFR1,RPS8,RPL7L1,FGFR2,RPL12,EIF2S3,RPL37A,TLR9,RPL9,EIF3M,RPS6,RPL8,IRS1,RPL10,RPL6,RPS15A,INSR,RPL13A,RPSA,EIF3K,RPL36A,RPS18,PPP1CB,RPL7A,EIF4G1,EIF4E,RPL7,RPS4X,PPP1CC,RPL18A,KL,UBA52,PIK3C3,RPS9,EIF3A,RPS3,RPS17,RPL18,RPS19,EIF3H,RPL34,RPL17,PIK3C2G,RPL30,RPS10,RPL23,RPS29,RPL27,EIF3F,RPS15,RPS16,RPS26,RPS27A,RPL5,PIK3CB,RPL37,EIF3L,EIF1AX,RPS14
Superpathway of Cholesterol Biosynthesis	1.23E+01	MVD,SQLE,NSDHL,ACAT2,IDI1,MVK,HSD17B7,MSMO1,TM7SF2,SC5D,LBR,FDPS,FDFT1,EBP,DHCR7,DHCR24,ACAT1,LSS,HMGCR,HMGCS1,CYP51A1
Axonal Guidance Signaling	1.12E+01	DPYSL2,PAPPA2,ADAMTS8,ECEL1,BMP4,ITSN1,PIK3R1,SOS2,ARPC5,ADAM8,NTN1,GNB1,ECE2,PIK3CG,ABLIM3,PTCH2,ATM,EFNA2,COP5,FGFR2,MMP2,TLR9,ADAMTS6,ARPC1A,IRS1,RTN4,EPHA2,GNAL,NRP1,MME,UNC5A,ARPC1B,NOTUM,ABLIM1,EIF4E,NGG7,WNT7A,TUBA8,KL,PIK3C3,DCC,ADAM19,ARPC3,PSMD14,LNPEP,BMP1,MYL12A,SEMA3G,ADAMTS13,NRP2,MYLPF,PIK3C2G,SEMA3A,GLIS2,MAG,ADAM10,BMP7,SEMA3C,BMP6,ARPC4,NTN3,PRKCB,WNT3,RACK1,CXCL12,GNB5,MYL6B,ADAM11,TUBB,FGFR3,SEMA6D,GNB3,WNT7B,ADAM23,WNT4,ADAMTS5,FGFR1,PPP3CC,HHIP,RAC3,MYL7,CDC42,RHOA,PRKCD,FZD6,GNAT2,PRKCH,RND1,SLIT1,PDGFA,BMP3,SEMA4C,WNT2,NFATC1,CDK5,GLIS1,MKNK1,MMP11,SEMA3B,SHANK2,SEMA3F,ACE,VASP,PRKCA,PXN,WNT9B,CXCR4,TUBG1,PRKAR2A,GNAI1,PLXND1,GNAI2,PRKCI,WNT10A,LINGO1,PIK3CB,GLI1
Cholesterol Biosynthesis I	1.11E+01	SQLE,FDFT1,EBP,NSDHL,DHCR7,DHCR24,HSD17B7,MSMO1,LSS,TM7SF2,SC5D,CYP51A1,LBR
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)	1.11E+01	SQLE,FDFT1,EBP,NSDHL,DHCR7,DHCR24,HSD17B7,MSMO1,LSS,TM7SF2,SC5D,CYP51A1,LBR
Cholesterol Biosynthesis III (via Desmosterol)	1.11E+01	SQLE,FDFT1,EBP,NSDHL,DHCR7,DHCR24,HSD17B7,MSMO1,LSS,TM7SF2,SC5D,CYP51A1,LBR
Type II Diabetes Mellitus Signaling	1.01E+01	MAP2K4,RELA,SLC27A2,PRKAB2,PKLR,PIK3R1,PKM,PDPK1,SMPD1,MAP3K5,ADIPOR1,SLC27A4,FGFR3,IKBKB,NFKBIA,ACSBG1,KL,PIK3C3,PIK3CG,ACSL5,INS,ABCC8,PRKAA2,CHUK,ATM,PRKCA,PPARG,FGFR1,ACSL6,PIK3C2G,FGFR2,TLR9,TRAF2,PRKCI,PRKCD,IRS1,GCK,MAPK10,PIK3CB,SLC27A1,PRKCH,SLC27A3,INSR,ADIPOR2,SOC5,ACSL1,PRKCB
Regulation of eIF4 and p70S6K Signaling	1.01E+01	PPP2CA,RPS27,PIK3R1,SOS2,PDPK1,PPP2R3B,RPS11,FGFR3,EIF3B,RPS20,EIF3D,RPS13,PIK3CG,AGO1,ATM,RPS6KB1,FGFR1,RPS8,FGFR2,EIF2S3,TLR9,EIF3M,RPS6,IRS1,RPS15A,EIF3K,RPSA,EIF4EBP2,RPS18,EIF4G1,EIF4E,RPS4X,KL,PIK3C3,MKNK1,RPS9,EIF3A,RPS3,RPS17,RPS19,EIF3H,PIK3C2G,RPS10,RPS29,RPS15,EIF3F,RPS16,RPS26,RPS27A,PIK3CB,PPP2R5E,EIF1AX,EIF3L,RPS14
Protein Ubiquitination Pathway	9.10E+00	FZR1,UBE2A,HSPA5,PSMC5,UBE2D4,PAN2,USP8,USP10,UCHL5,USP40,PSMA2,ANAPC11,PSMC2,PSMA6,PSMB5,UBE4B,PSMC4,BIRC6,PSMD6,DNAJC2,PSMD3,THOP1,HSPA8,PSMD11,PSMB7,UBE2D2,UBE2H,RBX1,PSMD12,PSMA5,PSMA4,PSMB1,HSP90AA1,PSMD1,UBE2I,ANAPC2,PSMB3,USP24,USP14,CDC20,PSMD7,HSPB8,DNAJC10,CDC23,USP39,ANAPC1,HSPA1L,SMURF1,HSPA12B,USP13,HSP90AB1,PSMC6,USP16,USP47,PSMD14,PSMA3,DNAJB1,AMFR,PSMB4,PSMD13,MDM2,PSMA1,HSPD1,HSPA2,USP33,UBE2J1,USP4,PSMD2,DNAJB11,CDC34,UBA1,USP34,PSMC3
mTOR Signaling	8.97E+00	PRKAB2,PPP2CA,RPS27,PIK3R1,PDPK1,PPP2R3B,RPS11,FGFR3,RPS20,EIF3B,EIF3D,RPS13,PIK3CG,INS,ATM,RPS6KB1,FGFR1,RPS8,FGFR2,TLR9,EIF3M,RPS6,RHOQ,RND3,PRKCD,IRS1,RHOA,PRKCH,RPS15A,INSR,RPSA,EIF3K,RPS18,EIF4G1,RPS4X,EIF4E,KL,PIK3C3,RPS9,PRKAA2,EIF3A,RPS17,RPS3,PRKCA,RPS19,EIF3H,RPS10,PIK3C2G,RPS29,DGKZ,EIF3F,RPS15,RPS16,PRKCI,RPS26,RPS27A,PIK3CB,PPP2R5E,EIF3L,PRKCB,RPS14
Amyotrophic Lateral Sclerosis Signaling	8.31E+00	NOS1,GRIN2A,CACNA1S,PIK3R1,GRIA1,GRIN2D,GRID2,GRIA4,FGFR3,KL,PIK3C3,PIK3CG,ATM,GRIN1,GRIN2B,CAPN6,CACNA1D,CASP3,FGFR1,PIK3C2G,APAF1,FGFR2,CACNA1C,BAX,SOD1,TLR9,ALS2,CACNA1A,CCS,CAPNS1,GRIK4,IRS1,CAPN1,CAT,GLUL,PIK3CB,CAPN9,CAPN2,CAPN3,GRIA3
Protein Kinase A Signaling	7.27E+00	ENPP6,MYH10,PDE6G,BAD,RACK1,GNB5,LIPE,MYL6B,NTN1,GNB1,GYS1,CAMK2A,GNB3,RHO,RYR3,DUSP7,ANAPC11,PPP1CA,APEX1,PTCH2,GRK7,CDC25A,SMPDL3A,PTPRE,YWHAB,PDE10A,ITPR2,PD E6C,PTPN3,ITPR1,PPP3CC,PDE4B,CNGA1,CNGA3,GYS2,MYL7,PDE8A,PYGM,H3F3A/H3F3B,RHOA,PRKCD,PTPRB,ITPR3,EYA3,PTPRS,PRKCH,CAMK2G,ANAPC2,RELA,PTPN9,NOTUM,PPP1CB,CDC23,ANAPC1,NGG7,NFATC1,MPPE1,PPP1CC,NFKBIA,PPP1R10,FLNA,CREB1,DCC,SMAD4,PTPRZ1,CNGB3,CHUK,CTNNB1,PTPRT,VASP,PRKCA,CAMK2B,MYL12A,PXN,PTPRK,MYLPF,MYL7,ADCY3,GNAI1,PRKAR2A,PYGB,TCF7L1,GNAI2,PRKCI,HIST1H1E,FLNC,CDC14B,ADCY1,KDELRL3,IHH,PDE5A,PTGS2,PTPRR,PRKCB
Huntington's Disease Signaling	7.09E+00	MAP2K4,POLR2F,SGK1,PIK3R1,SOS2,RACK1,GNB5,PDPK1,HSPA5,FGFR3,GNB1,CTSD,GNB3,PIK3CG,CASQ1,TCERG1,DLG4,POLR2L,ATM,CAPN6,CASP3,FGFR1,FGFR2,DNM3,ITPR1,TLR9,RPH3A,HSPA8,CACNA1B,CAPN1,PRKCD,IRS1,PSME4,PRKCH,CAPN2,CAPN3,SDHB,HSPA1L,NGG7,TGM2,DYNC1I2,ARFIP2,CDK5,KL,PIK3C3,CREB1,DNAJB1,PRKCA,NEUROD1,SDHA,GRIN2B,HDAC1,APAF1,PIK3C2G,BAX,HIP1,HSPA2,PSMA8,PRKCI,CAPNS1,PIK3CB,CAPN9,NCOR2,DNM1L,PRKCB
Glycolysis I	6.91E+00	PKLR,ENO3,PKM,PGAM2,PFKL,PFKP,BPGM,PFKM,GPI,ALDOB,PGAM1,FBP1,ALDOA,GAPDH,GAPDHS
Hepatic Fibrosis / Hepatic Stellate Cell Activation	6.57E+00	MYH10,KLF6,COL8A1,MYL6B,MYH7B,COL11A2,COL27A1,TIMP2,COL9A1,FGFR1,COL2A1,BAMBI,FGFR2,MMP2,IGFBP5,MYL7,COL21A1,COL23A1,IGFBP3,IL1RAPL1,COL7A1,RELA,COL8A2,MYH6,COL4A5,FN1,COL4A6,PDGFA,COL10A1,MYH11,COL6A6,COL5A1,COL1A2,COL6A1,HGF,PDGFRA,COL22A1,SMAD4,ECE1,STAT1,MYH1,COL5A2,EDNRB,COL6A2,COL12A1,SMAD7,BAX,COL1A1,COL5A3,EDNRA,COL11A1,COL9A2
Thrombin Signaling	6.55E+00	PIK3R1,RACK1,GNB5,PDPK1,MYL6B,GATA2,F2,FGFR3,GNB1,IKBKB,CAMK2A,GNB3,PIK3CG,ATM,RPS6KB1,ITPR2,FGFR1,FGFR2,ITPR1,TLR9,MYL7,RHOQ,RND3,ARHGEF16,RHOA,PRKCD,IRS1,ITPR3,GNAT2,PRKCH,GNAL,CAMK2G,RELA,GATA1,NOTUM,PPP1CB,NGG7,KL,PIK3C3,CREB1,CAMK1G,GATA6,MYL12A,PRKCA,CAMK2B,MYLPF,ADCY3,PIK3C2G,GNAI1,GNAI2,PRKCI,ADCY1,PIK3CB,GATA3,GATA4,PRKCB
AMPK Signaling	6.48E+00	ADRA2B,PRKAB2,PPP2CA,PIK3R1,CPT1B,CHRN1,PPP2R3B,LIPE,PDPK1,ARID2,FGFR3,AK1,GYS1,PI

		K3CG,INS,HNF4A,ATM,PFKFB3,RPS6KB1,ACACB,SLC2A1,EEF2,FGFR1,AK3,FGFR2,TLR9,SMARCD3,GYS2,PFKM,IRS1,CPT2,ACACA,INSR,PBRM1,ARID1A,PFKL,KL,PIK3C3,CREB1,PRKAA2,EEF2K,CKM,S TRADA,PRKAR2A,PIK3C2G,PFKP,FOXO1,PPM1B,PIK3CB,CHRNE,PPP2R5E,SMARCC1,HMGCR
nNOS Signaling in Neurons	6.46E+00	NOS1,GRIN1,GRIN2B,CAPN6,GRIN2A,GRIN2D,DLG2,PPP3CC,PFKM,CAMK2A,CAPNS1,PRKCI,PRKCD,CAPN1,DLG4,CAPN9,CAPN2,PRKCH,CAPN3,PRKCA,PRKCB
fMLP Signaling in Neutrophils	6.15E+00	RELA,ARPC1B,PIK3R1,RACK1,ARPC5,GNB5,GNG7,NFATC1,FGFR3,GNB1,GNB3,NFKBIA,KL,PIK3CG,P IK3C3,CYBB,ARPC3,ATM,PRKCA,ITPR2,FGFR1,PIK3C2G,GNAI1,FGFR2,PPP3CC,ITPR1,TLR9,GNAI2,P RKCI,ARPC1A,CDC42,PRKCD,IRS1,ITPR3,PIK3CB,PRKCH,ARPC4,PRKCB
Role of NANOG in Mammalian Embryonic Stem Cell Pluripotency	6.05E+00	IL6ST,JAK1,BMP4,WNT3,AXIN1,PIK3R1,BMP3,SOS2,WNT2,FGFR3,SOX2,WNT7A,KL,WNT7B,PIK3CG,P IK3C3,GATA6,WNT4,SMAD4,CTNNB1,ATM,BMP1,SMAD9,WNT9B,FGFR1,PIK3C2G,FGFR2,TCF7L1,STA T3,TLR9,WNT10A,IRS1,FZD6,PIK3CB,BMP7,BMP6,GATA4,SALL4
Neuropathic Pain Signaling In Dorsal Horn Neurons	5.92E+00	GRIN2A,PIK3R1,GRIA1,GRIN2D,NOTUM,GRIA4,FGFR3,KCNN1,CAMK2A,KL,PIK3C3,PIK3CG,CREB1,CA MK1G,GRM6,PRKCA,CAMK2B,ATM,GRIN1,GRIN2B,ITPR2,FGFR1,PIK3C2G,PRKAR2A,FGFR2,ITPR1,TL R9,PRKCI,PRKCD,IRS1,ITPR3,PIK3CB,PRKCH,GRIA3,CAMK2G,PRKCB
CREB Signaling in Neurons	5.72E+00	GRIN2A,POLR2F,PIK3R1,RACK1,SOS2,GNB5,GRIA4,FGFR3,GNB1,GNB3,CAMK2A,PIK3CG,GRM6,POL R2L,ATM,ITPR2,FGFR1,FGFR2,ITPR1,TLR9,IRS1,PRKCD,ITPR3,GNAT2,PRKCH,GNAL,CAMK2G,GRIA1 ,GRIN2D,GRID2,NOTUM,GNG7,KL,PIK3C3,CREB1,CAMK2B,PRKCA,GRIN2B,GRIN1,ADCY3,GNAI1,PRK AR2A,PIK3C2G,GNAI2,PRKCI,GRIK4,ADCY1,PIK3CB,PRKCB,GRIA3
Leukocyte Extravasation Signaling	5.68E+00	MAP2K4,MMP20,MMP16,PIK3R1,CXCL12,CLDN7,FGFR3,PIK3CG,CYBB,ARHGAP12,ATM,TIMP2,FGFR1 ,ITGA6,FGFR2,MMP2,RAPGEF3,TLR9,MMP23B,CLDN23,CLDN8,JAM3,CDC42,RHOA,PRKCD,IRS1,MAP K10,PRKCH,CTTN,CLDN15,MMP14,MMP15,RAPGEF4,KL,PIK3C3,MMP11,CTNNB1,VASP,ACTN1,PRKC A,VAV2,CLDN10,PXN,CXCR4,ACTN2,GNAI1,PIK3C2G,GNAI2,CLDN5,PRKCI,ARHGAP9,RASGRP1,PIK3 CB,PRKCB,MSN
Maturity Onset Diabetes of Young (MODY) Signaling	5.32E+00	NEUROD1,CACNA1S,CACNA1D,PKLR,ALDOB,GCK,INS,CACNA1C,GAPDH,INSR,HNF4A,CACNA1A
eNOS Signaling	5.26E+00	PRKAB2,PIK3R1,CHRNB1,SLC7A1,PDPK1,HSPA5,HSPA1L,FGFR3,NOSIP,LPAR2,HSP90AB1,KL,PIK3C G,PIK3C3,PRKAA2,CNGB3,PRKCA,ATM,CASP3,ITPR2,FGFR1,ADCY3,PIK3C2G,PRKAR2A,FGFR2,AQP 1,ITPR1,TLR9,HSPA2,CNGA1,CNGA3,HSPA8,AQP9,PRKCI,PRKCD,IRS1,ADCY1,ITPR3,HSP90AA1,CHR NE,PIK3CB,PRKCH,PRKCB
CXCR4 Signaling	5.26E+00	MAP2K4,PIK3R1,RACK1,CXCL12,GNB5,MYL6B,GNG7,FGFR3,GNB1,ELMO3,GNB3,KL,PIK3CG,PIK3C3, MYL12A,PRKCA,ATM,PXN,ITPR2,CXCR4,EGR1,FGFR1,MYLPF,ADCY3,GNAI1,PIK3C2G,FGFR2,ITPR1, TLR9,MYL7,GNAI2,PRKCI,RHOQ,RND3,PRKCD,IRS1,RHOA,ADCY1,ITPR3,MAPK10,GNAT2,PIK3CB,PR KCH,GNAL,PRKCB
Molecular Mechanisms of Cancer	5.25E+00	MAP2K4,BMP4,JAK1,WNT3,BAD,AXIN1,PIK3R1,SOS2,MYC,FGFR3,RASGRF1,CAMK2A,WNT7B,PIK3CG ,WNT4,HIPK2,PTCH2,ATM,CDC25A,CASP3,SMAD9,FGFR1,FGFR2,RAPGEF3,TLR9,RAC3,RALBP1,RAS GRF2,CDH1,RHOQ,RND3,CDC42,ARHGEF16,RHOA,PRKCD,IRS1,FZD6,MAPK10,GNAT2,PRKCH,CDK2 ,GNAL,CAMK2G,RELA,PA2G4,BMP3,PSEN2,MAP3K5,WNT2,SYNGAP1,WNT7A,NFKBIA,CDK5,KL,PIK3C 3,SMAD4,CTNNB1,BMP1,CAMK2B,PRKCA,PRKDC,WNT9B,ADCY3,PRKAR2A,GNAI1,SMAD7,APAF1,PI K3C2G,MDM2,BAX,GNAI2,PRKCI,WNT10A,FOXO1,NF1,RASGRP1,ADCY1,IHH,PIK3CB,ATR,BMP7,BMP 6,GLI1,PRKCB
GABA Receptor Signaling	5.20E+00	AP2A1,AP2M1,ABAT,GABRA4,ADCY3,GABBR1,GPHN,ALDH9A1,GABRP,GABRB2,SLC6A11,GABRG3,K CNN1,GABRR2,GAD2,GABRG2,GABRB3,GAD1,ADCY1,GABRA6,SLC6A1,GABARAP,GABRD,GABRA1
Clathrin-mediated Endocytosis Signaling	5.16E+00	APOB,PIK3R1,ARPC5,SH3GL2,F2,FGFR3,SNX9,PIK3CG,INS,AMPH,ITGB4,SH3KBP1,ATM,MYO6,FGFR 1,FGFR2,DNM3,PPP3CC,TLR9,HSPA8,ARPC1A,PIP5K1C,CDC42,IRS1,CTTN,RBP4,APD1,AP0A1,APOA 4,ARPC1B,PDGFA,FGF13,KL,PIK3C3,ARPC3,HGS,FGF7,AP2M1,RAB7A,PIK3C2G,MDM2,HIP1,TSG101, LDLR,SYNJ1,TF,PIK3CB,DNM1L,CLU,ARPC4,HIP1R
Zymosterol Biosynthesis	5.12E+00	NSDHL,HSD17B7,MSMO1,TM7SF2,CYP51A1,LBR
Nitric Oxide Signaling in the Cardiovascular System	5.11E+00	CACNA1S,PIK3R1,SLC7A1,ARG2,ATP2A2,FGFR3,HSP90AB1,KL,PIK3C3,PIK3CG,PRKCA,ATM,CACNA1 D,GUCY2D,ITPR2,FGFR1,RYR2,PIK3C2G,PRKAR2A,ATP2A3,CACNA1C,FGFR2,ITPR1,TLR9,CACNA1A, PRKCI,PRKCD,IRS1,ITPR3,HSP90AA1,PDE5A,PIK3CB,PRKCH,PRKCB
Breast Cancer Regulation by Stathmin1	5.10E+00	PPP2CA,PIK3R1,RACK1,SOS2,GNB5,PPP2R3B,TUBB,FGFR3,GNB1,GNB3,CAMK2A,PIK3CG,PPP1CA,A TM,ITPR2,FGFR1,FGFR2,ITPR1,TLR9,CDC42,RHOA,IRS1,PRKCD,ARHGEF16,ITPR3,PRKCH,CDK2,CA MK2G,PPP1CB,GNG7,PPP1CC,PPP1R10,TUBA8,KL,PIK3C3,RB1CC1,CAMK1G,CAMK2B,PRKCA,TUBG 1,ADCY3,GNAI1,PRKAR2A,PIK3C2G,TSG101,CDK1,GNAI2,PRKCI,ADCY1,PIK3CB,PPP2R5E,PRKCB
Calcium Signaling	5.05E+00	MYH10,CHRNA1,GRIN2A,MYH6,CHRNA6,TNNT3,GRIN2D,GRIA1,CHRNB1,TNNT2,MYL6B,MYH11,ATP2 A2,GRIA4,MYH7B,NFATC1,CABIN1,CAMK2A,CASQ1,RYR3,CREB1,CAMK1G,CASQ2,MYH1,CAMK2B,G RIN2B,GRIN1,TRPC1,TP63,ITPR2,RYR2,HDAC1,SLC8A3,PRKAR2A,ATP2A3,SLC8A2,PPP3CC,TRPC6,I TPR1,MYL7,RCAN1,ATP2B3,ITPR3,CHRNE,MEF2C,GRIA3,CAMK2G
Colorectal Cancer Metastasis Signaling	5.00E+00	MAP2K4,MMP20,JAK1,WNT3,BAD,AXIN1,MMP16,PIK3R1,SOS2,RACK1,GNB5,GNB1,FGFR3,MYC,GNB3 ,WNT7B,PIK3CG,WNT4,ATM,CASP3,FGFR1,ADRBK2,FGFR2,MMP2,STAT3,TLR9,CDH1,MMP23B,RHO Q,RND3,RHOA,IRS1,FZD6,MAPK10,IL6ST,RELA,MMP14,MMP15,WNT2,GNG7,WNT7A,KL,PIK3C3,DCC, SMAD4,MMP11,CTNNB1,STAT1,PTGER4,WNT9B,ADCY3,PRKAR2A,PIK3C2G,BAX,TCF7L1,WNT10A,A DCY1,MSH6,PIK3CB,PTGS2
GM-CSF Signaling	4.99E+00	PIK3R1,RACK1,SOS2,FGFR3,CAMK2A,KL,PIK3C3,PIK3CG,CISH,HCK,STAT5B,STAT1,ATM,CAMK2B,ET S1,FGFR1,PIK3C2G,FGFR2,STAT3,PPP3CC,TLR9,IRS1,PIK3CB,PRKCB,CAMK2G
Docosahexaenoic Acid (DHA) Signaling	4.96E+00	CASP3,BAD,FGFR1,PIK3R1,PIK3C2G,APAF1,PDPK1,FGFR2,BAX,TLR9,PNPLA2,APP,FGFR3,FOXO1,KL ,PIK3CG,IRS1,PIK3C3,PIK3CB,ATM
IL-9 Signaling	4.80E+00	RELA,JAK1,PIK3R1,FGFR1,PIK3C2G,FGFR2,STAT3,TLR9,FGFR3,KL,PIK3C3,IRS1,PIK3CG,CISH,PIK3C B,STAT5B,STAT1,ATM
Role of NFAT in Cardiac Hypertrophy	4.80E+00	MAP2K4,PIK3R1,RACK1,SOS2,GNB5,CSNK1A1,HAND1,CABIN1,FGFR3,GNB1,GNB3,CAMK2A,PIK3CG, ATM,ITPR2,FGFR1,FGFR2,SLC8A2,ITPR1,PPP3CC,TLR9,IRS1,PRKCD,ITPR3,MAPK10,PRKCH,CAMK2 G,IL6ST,NOTUM,GNG7,KL,PIK3C3,CAMK1G,PRKCA,CAMK2B,HDAC1,ADCY3,SLC8A3,GNAI1,PRKAR2 A,PIK3C2G,GNAI2,RCAN1,PRKCI,ADCY1,PIK3CB,MEF2C,GATA4,PRKCB
Mitotic Roles of Polo-Like Kinase	4.78E+00	ANAPC2,KIF23,FZR1,CDC20,PLK3,PPP2CA,WEE1,PPP2R3B,CDC23,PLK1,ANAPC1,CDK1,SMC1A,SLK, PLK4,HSP90AB1,PLK2,CAPN1,HSP90AA1,PPP2R5E,ANAPC11,KIF11,CDC25A
UVB-Induced MAPK Signaling	4.78E+00	MAP2K4,RPS6KB1,BAD,FGFR1,PIK3R1,PIK3C2G,FGFR2,TLR9,EIF4E,FGFR3,H3F3A/H3F3B,PRKCI,KL, PIK3CG,IRS1,PRKCD,PIK3CB,MAPK10,PIK3CB,PRKCH,ATM,PRKCA,PRKCB

Mitochondrial L-carnitine Shuttle Pathway	4.67E+00	ACSBG1,SLC27A2,CPT1B,ACSL6,ACSL5,CPT2,SLC27A1,SLC27A3,SLC27A4,ACSL1
Aldosterone Signaling in Epithelial Cells	4.46E+00	SGK1,PIK3R1,SOS2,HSPB8,NOTUM,PDPK1,DNAJC10,PIP5K1B,HSPA5,HSPA1L,FGFR3,HSP90AB1,HS PA12B,SLC12A1,KL,PIK3CG,PIK3C3,DNAJB1,AHCY,ATM,PRKCA,ITPR2,SLC12A2,FGFR1,PIK3C2G,FG FR2,DNAJC2,ITPR1,HSPD1,TLR9,HSPA2,HSPA8,PRKCI,PIP5K1C,PRKCD,IRS1,DNAJB11,ITPR3,HSP90 AA1,PIK3CB,PRKCH,PIP4K2C,PRKCB
IGF-1 Signaling	4.45E+00	JAK1,BAD,PIK3R1,SOS2,PDPK1,FGFR3,KL,PIK3C3,PIK3CG,IGFBP1,ATM,RPS6KB1,PXN,YWHAB,FGFR 1,PIK3C2G,PRKAR2A,FGFR2,IGFBP5,STAT3,TLR9,IGFBP2,GRB10,PRKCI,NOV,FOXO1,IRS1,IGFBP3,PI K3CB,CYR61,SOC55
Insulin Receptor Signaling	4.42E+00	JAK1,BAD,SGK1,PIK3R1,SOS2,LIPE,PDPK1,PPP1CB,EIF4E,FGFR3,PPP1CC,GYS1,PPP1R10,KL,PIK3C G,INPP5B,PIK3C3,INS,PPP1CA,ATM,RPS6KB1,FGFR1,PIK3C2G,PRKAR2A,FGFR2,VAMP2,ACLY,TLR9, GRB10,GYS2,PRKCI,RHOQ,FOXO1,SYNJ1,INPP5F,IRS1,PIK3CB,INSR
Prolactin Signaling	4.39E+00	PIK3R1,SOS2,PDPK1,FGFR3,MYC,KL,PIK3C3,PIK3CG,PRLR,STAT5B,STAT1,ATM,PRKCA,FGFR1,PIK3 C2G,FGFR2,STAT3,TLR9,PRKCI,IRS1,PRKCD,PRKCH,PIK3CB,TCF7,SOC55,PRKCB
Gluconeogenesis I	4.31E+00	GPI,ALDOB,ENO3,PGAM1,FBP1,PGAM2,ALDOA,GAPDH,ME1,MDH1,GAPDHS,BPGM
Phototransduction Pathway	4.25E+00	RGS9,PDE6G,GUCY2D,GUCA1C,OPN1LW,PRKAR2A,PDE6C,GNB5,CNGA1,CNGA3,GNB1,GNB3,ARR3, RHO,PDC,RGR,GNAT2,CNGB3,OPN4

Table S5 A comprehensive list of genes in proliferation of liver cells, apoptosis of kidney cells and hypertrophy of cardiac muscle

Genes in the proliferation of liver cells	96_slick_De novo	96h_slick_OnRam p	96h-source	48h-slick	48h-source	24h-slick	24h-source
IGFBP1 (insulin like growth factor binding protein 1)	1.961031	2.042127	0.332148	0.040966	0.059637	0.125486	0.385384
FGF7 (fibroblast growth factor 7)	N/A	2.836242	0.305489	0.768168	0.187485	0.061262	0.007612
CXCL14 (C-X-C motif chemokine ligand 14)	1.108972	1.05091	0.324006	0.475926	0.171579	0.251738	0.187048
CXCR4 (C-X-C motif chemokine receptor 4)	1.637395	1.726862	0.101524	-0.01244	-0.06249	0.014399	0.035989
PTGS2 (prostaglandin-endoperoxide synthase 2)	1.021444	1.018536	0.180669	0.287539	N/A	0.225955	N/A
EDNRA (endothelin receptor type A)	0.971844	0.866202	-0.066	0.289496	0.118032	-0.04149	0.001957
HGF (hepatocyte growth factor)	0.624821	0.774913	0.221619	0.252828	0.23401	-0.0236	-0.04022
CTSB (cathepsin B)	1.041869	0.708098	0.146974	0.004254	0.004713	0.037561	0.097881
FAH (fumarylacetoacetate hydrolase)	0.462293	0.466168	0.235736	0.559404	0.115301	-0.02867	-0.04282
SMPD1 (sphingomyelin phosphodiesterase 1)	0.957336	0.92369	0.082928	-0.27571	-0.03275	0.100463	-0.02725
ADIPOQ (adiponectin, C1Q and collagen domain containing)	1.426684	N/A	N/A	N/A	N/A	N/A	N/A
IKBKB (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta)	0.521847	0.645949	0.136794	-0.06071	-0.02806	0.076825	0.117641
MMP14 (matrix metalloproteinase 14)	0.699211	0.69372	-0.02512	-0.11592	0.001382	0.061371	0.063958
PPARG (peroxisome proliferator activated receptor gamma)	N/A	1.085901	0.178374	-0.05001	N/A	0.107154	N/A
C3 (complement C3)	N/A	1.088801	0.138384	0.0148	N/A	0.018641	N/A

NFKBIA (NFKB inhibitor alpha)	0.574922	0.52987	-0.0492	0.09596	N/A	0.00674 5	N/A
F2 (coagulation factor II, thrombin)	0.419508	0.733081	0.395115	-0.49113	N/A	-0.02545	N/A
STAT1 (signal transducer and activator of transcription 1)	0.453692	0.224154	-0.0445	0.32402 4	0.09860 6	-0.02673	-0.02692
AHR (aryl hydrocarbon receptor)	N/A	0.520338	0.124935	0.15363 1	N/A	0.15499 1	N/A
PIK3IP1 (phosphoinositide-3-kinase interacting protein 1)	0.385601	0.554003	-0.00774	-0.10401	N/A	0.06434 9	N/A
S1PR2 (sphingosine-1-phosphate receptor 2)	0.226437	0.471081	0.055658	0.13762	N/A	-0.02168	N/A
IL6ST (interleukin 6 signal transducer)	0.390495	0.36916	-0.00366	-0.01143	0.01281 9	0.03775 8	0.03325 7
CREB3L3 (cAMP responsive element binding protein 3 like 3)	0.775466	N/A	N/A	N/A	N/A	N/A	N/A
HBEGF (heparin binding EGF like growth factor)	0.513463	0.130701	0.013863	0.0377	N/A	0.02959 3	N/A
ARNT (aryl hydrocarbon receptor nuclear translocator)	0.440023	0.236552	-0.0832	0.05404 1	N/A	0.07218 4	N/A
HNF4A (hepatocyte nuclear factor 4 alpha)	0.27629	0.310617	0.124767	-0.08959	-0.12738	0.10014 1	0.08716 9
XPA (XPA, DNA damage recognition and repair factor)	N/A	0.353746	0.144023	0.07268	0.04520 4	0.08226	-0.02761
FST (follistatin)	N/A	0.423069	-0.03737	0.00968 8	0.20552 8	0.01004	0.03633 4
MST1 (macrophage stimulating 1)	N/A	-0.2036	0.193857	0.20598	N/A	0.37532 5	N/A
CTNNB1 (catenin beta 1)	0.263111	0.272726	0.031348	0.02799 2	-0.12738	0.04621 3	0.01605 3
BMP4 (bone morphogenetic protein 4)	0.296213	0.422589	0.128487	-0.2303	N/A	-0.08876	N/A
STK3 (serine/threonine kinase 3)	0.302148	0.308056	0.060677	0.03678 2	-0.08194	-0.01642	-0.08116
CUL3 (cullin 3)	N/A	0.273741	0.218109	0.08552 9	N/A	-0.07556	N/A
JUN (Jun proto-oncogene, AP-1 transcription factor subunit)	0.59726	N/A	N/A	N/A	-0.01639	N/A	-0.08311
TIMP2 (TIMP metalloproteinase inhibitor 2)	N/A	0.530043	-0.0797	-0.04447	N/A	0.03465 7	N/A
ITGAV (integrin subunit alpha V)	0.140861	0.26532	-0.0517	-0.08104	0.12570 1	0.01621 6	0.00121 9
LGALS3 (galectin 3)	N/A	0.469208	0.076568	-0.03301	N/A	-0.10402	N/A
EDNRB (endothelin receptor type B)	N/A	0.222483	-0.00129	0.07461 6	-0.12209	0.12276 2	0.08335
PPARD (peroxisome proliferator activated receptor delta)	0.305502	0.071476	0.030432	-0.07811	N/A	0.01902 1	N/A
PLG (plasminogen)	N/A	0.254788	0.166508	-0.15904	N/A	0.01927	N/A
NGFR (nerve growth factor receptor)	0.288956	-0.08801	-0.07712	0.00565 3	0.00633 3	0.06735	0.07781 9
PPARA (peroxisome proliferator activated receptor alpha)	0.293066	0.044262	-0.06315	0.01003 8	-0.0274	-0.04401	0.06246 6

NCOA5 (nuclear receptor coactivator 5)	N/A	0.28125	0.020959	-0.11413	N/A	0.07582 7	N/A
ABCB4 (ATP binding cassette subfamily B member 4)	0.26331	N/A	N/A	N/A	N/A	N/A	N/A
RARA (retinoic acid receptor alpha)	N/A	0.297341	0.047655	-0.04989	-0.03711	-0.05235	-0.00391
SERPINH1 (serpin family H member 1)	-0.47336	-0.00182	-0.09607	0.39314 8	0.01261 5	0.33161 1	0.00483 2
PROX1 (prospero homeobox 1)	N/A	-0.27246	-0.11103	0.18182 4	0.11611 1	0.08118 5	0.09227 8
SMAD7 (SMAD family member 7)	N/A	0.179956	0.173863	-0.14644	0.03841 2	-0.10117	-0.09013
BMP7 (bone morphogenetic protein 7)	N/A	0.183573	-0.08836	0.03317 9	N/A	-0.11832	N/A
CTGF (connective tissue growth factor)	N/A	-0.11387	0.060619	-0.17269	-0.03436	-0.04775	0.27245 3
PTN (pleiotrophin)	0.296811	0.196468	-0.04737	-0.21857	-0.18225	-0.07255	-0.06841
ITGB1 (integrin subunit beta 1)	0.205025	0.034898	-0.06532	-0.11546	-0.17485	-0.02231	-0.03251
THBS1 (thrombospondin 1)	N/A	0.088509	-0.06684	-0.2245	0.05382 8	-0.13262	0.07745 5
TOB1 (transducer of ERBB2, 1)	-0.19469	-0.12278	0.145902	0.00890 6	-0.12483	0.02932 1	0.00244 8
INSR (insulin receptor)	N/A	-0.11754	-0.07539	-0.03759	-0.01313	0.01562 7	-0.05285
YY1AP1 (YY1 associated protein 1)	N/A	N/A	N/A	N/A	-0.16594	N/A	-0.16407
CDK2 (cyclin dependent kinase 2)	-0.39663	N/A	N/A	N/A	N/A	N/A	N/A
ODC1 (ornithine decarboxylase 1)	N/A	-0.28155	0.0594	-0.00442	-0.12315	-0.04857	-0.00551
NCOR1 (nuclear receptor corepressor 1)	-0.32895	-0.20987	-0.07655	0.04352 1	N/A	0.16135 4	N/A
FGFR2 (fibroblast growth factor receptor 2)	-0.48862	-0.13043	0.008444	0.10775	0.16865 9	-0.0812	-0.02724
CNR1 (cannabinoid receptor 1)	N/A	-0.21385	-0.13745	-0.12463	-0.08635	0.04388 6	0.04205 8
SPTBN1 (spectrin beta, non-erythrocytic 1)	N/A	-0.44559	-0.02591	-0.04315	N/A	0.00416 7	N/A
SKP2 (S-phase kinase associated protein 2)	-0.38115	-0.09559	-0.04566	-0.00748	0.02139 1	-0.01415	-0.00556
FOXM1 (forkhead box M1)	-0.53739	N/A	N/A	N/A	N/A	N/A	N/A
PIK3R1 (phosphoinositide-3-kinase regulatory subunit 1)	-0.57183	0.038126	0.051158	-0.044	-0.09909	0.06020 7	0.00787 2
GSK3B (glycogen synthase kinase 3 beta)	-0.55379	-0.22204	0.026097	-0.04947	0.0266	0.08239 2	-0.05348
MYC (v-myc avian myelocytomatosis viral oncogene homolog)	-0.30958	-0.16933	-0.15846	0.00596 2	-0.0666	-0.13777	-0.11575
SLC7A5 (solute carrier family 7 member 5)	N/A	-0.46174	-0.13969	-0.11819	-0.08632	-0.19379	N/A
XDH (xanthine dehydrogenase)	-0.43584	-0.35617	-0.24603	-0.06996	-0.01548	-0.0321	0.01030 1
E2F1 (E2F transcription factor 1)	-0.25714	-0.35064	-0.02882	-0.23558	-0.09459	-0.13179	-0.07954
RPS6KB1 (ribosomal protein S6 kinase B1)	-0.63513	-0.29687	0.020964	-0.1475	0.03577 7	-0.04839	-0.12001

COL1A1 (collagen type I alpha 1 chain)	-0.50049	-0.49173	-0.12527	0.07154 2	0.02089 6	-0.07278	-0.11117
TF (transferrin)	N/A	-0.45256	-0.23819	-0.47748	-0.2189	0.04737 1	0.02903 1
CXCL12 (C-X-C motif chemokine ligand 12)	N/A	-1.11755	0.348455	-0.44533	-0.22833	0.00569 2	0.03298 3
IGFBP1 (insulin like growth factor binding protein 1)	N/A	-0.97674	-0.18461	-0.22446	-0.05661	-0.01013	0.04233 2
Genes in the apoptosis of kidney cell lines	96_slick_De novo	96h_slick_OnRam p	96h-source	48h-slick	48h-source	24h-slick	24h-source
BCL6 (B-cell CLL/lymphoma 6)	2.294558	1.682768	0.221556	-0.1745	N/A	0.14827 5	N/A
HGF (hepatocyte growth factor)	0.624821	0.774913	0.221619	0.25282 8	0.23401	-0.0236	-0.04022
STAT3 (signal transducer and activator of transcription 3)	0.807008	0.791507	0.106058	0.05294 2	0.08308 5	0.01624 5	-0.02101
MAP3K5 (mitogen-activated protein kinase kinase kinase 5)	0.551372	0.316298	0.125268	0.18733 9	-0.00936	0.17903	0.14425 7
ECEL1 (endothelin converting enzyme like 1)	N/A	1.10889	0.169817	-0.03562	0.21095 4	0.01043 4	-0.03056
NFKBIA (NFKB inhibitor alpha)	0.574922	0.52987	-0.0492	0.09596	N/A	0.00674 5	N/A
TCF12 (transcription factor 12)	0.248445	0.404569	0.154252	0.22113 3	0.00583 3	0.03780 7	0.00181 2
F2 (coagulation factor II, thrombin)	0.419508	0.733081	0.395115	-0.49113	N/A	-0.02545	N/A
RASSF4 (Ras association domain family member 4)	0.643822	0.270413	0.055089	-0.01501	0.04111 3	-0.0209	0.02768 4
NF2 (neurofibromin 2)	N/A	0.763543	0.163365	0.06260 4	N/A	-0.0394	N/A
BAX (BCL2 associated X, apoptosis regulator)	N/A	0.702169	0.163665	0.00309 4	N/A	0.02622 8	N/A
SREBF2 (sterol regulatory element binding transcription factor 2)	N/A	0.497711	0.058523	0.09079 8	0.03234 8	0.11803 3	-0.01151
CAT (catalase)	N/A	0.605675	0.121069	0.10578 4	N/A	-0.05376	N/A
CASP3 (caspase 3)	0.437424	0.393741	-0.08941	-0.01898	N/A	0.04425 1	N/A
ATF6 (activating transcription factor 6)	0.25984	0.282648	0.042235	-0.05233	0.02775 4	0.03408 7	0.12302 1
FOXO1 (forkhead box O1)	N/A	0.691292	0.051287	-0.05764	-0.03876	-0.01499	0.08411 2
VTN (vitronectin)	N/A	0.36116	0.121318	0.06024	0.10473 1	0.04186 3	0.02397 1
PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha)	N/A	-0.01688	0.025215	0.27650 1	0.28878 1	-0.00805	0.10049 2
ABCC1 (ATP binding cassette subfamily C member 1)	0.406475	0.147779	-0.0282	0.16646 1	0.03057 6	-0.04075	-0.02012
HSPA5 (heat shock protein family A (Hsp70) member 5)	N/A	0.194962	0.198438	0.16654 1	0.02816 5	0.07241 4	-0.00284
STK26 (serine/threonine protein kinase 26)	N/A	0.469386	0.00553	0.00631 9	0.03467 8	0.03881 4	0.08489 2
CHMP5 (charged	0.592402	N/A	N/A	N/A	N/A	N/A	N/A

multivesicular body protein 5)							
DDX17 (DEAD-box helicase 17)	0.42952	0.045468	0.055024	0.01821 4	0.01527 5	0.00476 2	0.01972 8
RNF13 (ring finger protein 13)	0.245021	0.25124	-0.04917	0.06838 6	0.09126 5	-0.01357	-0.0444
UNC5C (unc-5 netrin receptor C)	N/A	0.061704	0.096947	0.16249 5	0.22422 1	-0.08336	0.07236 8
CTNNB1 (catenin beta 1)	0.263111	0.272726	0.031348	0.02799 2	-0.12738	0.04621 3	0.01605 3
TNFRSF19 (TNF receptor superfamily member 19)	0.188508	0.269331	0.00146	-0.02451	0.04719 5	-0.0635	0.10168 9
IL17RD (interleukin 17 receptor D)	0.478509	-0.07696	-0.01532	0.04957 7	0.02069 4	0.02992 4	-0.00779
RHOG (ras homolog family member G)	0.209271	0.340107	0.008911	-0.12584	N/A	0.04069 6	N/A
PSEN2 (presenilin 2)	N/A	0.396866	0.067997	-0.04658	-0.12539	0.05797 9	0.11431 1
LRP5 (LDL receptor related protein 5)	N/A	0.111777	0.052865	-0.07915	0.14101 3	0.09016 3	0.12842 4
IGFBP3 (insulin like growth factor binding protein 3)	N/A	0.426795	-0.0007	-0.02387	-0.0614	-0.01837	0.09873 4
ITGAV (integrin subunit alpha V)	0.140861	0.26532	-0.0517	-0.08104	0.12570 1	0.01621 6	0.00121 9
MAP1S (microtubule associated protein 1S)	N/A	0.267085	0.126942	0.00207 4	N/A	0.00012 2	N/A
BAD (BCL2 associated agonist of cell death)	N/A	0.374987	-0.03295	0.07483 2	N/A	-0.02608	N/A
PPARD (peroxisome proliferator activated receptor delta)	0.305502	0.071476	0.030432	-0.07811	N/A	0.01902 1	N/A
TJP2 (tight junction protein 2)	0.311715	0.049263	-0.04205	0.02055 8	-0.066	0.03767 7	0.03578 8
ZMYND11 (zinc finger MYND-type containing 11)	N/A	-0.09956	-0.04842	0.15108 7	0.16478 2	0.05406 3	0.12105
RIPK1 (receptor interacting serine/threonine kinase 1)	0.26447	0.078508	-0.00766	-0.01128	0.00453 7	-0.01384	-0.01812
ZNF512B (zinc finger protein 512B)	0.372474	-0.18363	-0.06662	0.11579 6	N/A	-0.03889	N/A
TFRC (transferrin receptor)	N/A	-0.07313	0.0198	0.10053 8	0.10796 8	-0.03595	0.03272 2
EZR (ezrin)	-0.27029	0.236371	0.062846	0.05091 3	-0.00555	-0.02651	0.07393 9
FGFR4 (fibroblast growth factor receptor 4)	0.212335	-0.05061	0.037404	-0.12988	N/A	0.00677 7	N/A
SMAD7 (SMAD family member 7)	N/A	0.179956	0.173863	-0.14644	0.03841 2	-0.10117	-0.09013
RBP4 (retinol binding protein 4)	N/A	0.51165	0.164203	-0.48076	N/A	-0.14353	N/A
GRIN2B (glutamate ionotropic receptor NMDA type subunit 2B)	N/A	-0.22009	0.005378	0.16123 2	0.17630 2	-0.01203	-0.07506
ITCH (itchy E3 ubiquitin protein ligase)	N/A	-0.16933	-0.06255	-0.03882	-0.06859	0.12823	0.23229
ILK (integrin linked kinase)	N/A	0.12497	-0.08322	-0.00554	N/A	-0.0271	N/A
PAK1 (p21 (RAC1) activated kinase 1)	-0.3029	0.19265	-0.00108	0.05228 8	0.07384	0.01718 4	-0.02556
PKD1 (polycystin 1, transient receptor potential channel interacting)	0.542496	-0.3547	-0.18674	-0.02635	0.04533 2	-0.08138	-0.09312

ELOVL4 (ELOVL fatty acid elongase 4)	-0.31604	-0.05041	0.019684	0.06946 9	0.02207 8	-0.01135	0.10571 9
ITGB1 (integrin subunit beta 1)	0.205025	0.034898	-0.06532	-0.11546	-0.17485	-0.02231	-0.03251
SLK (STE20 like kinase)	-0.25614	-0.18751	0.025097	0.05513	0.14962 8	-0.01954	-0.10988
UNC5A (unc-5 netrin receptor A)	N/A	-0.40025	-0.07986	0.07907 3	0.10061	-0.026	-0.04469
PKN2 (protein kinase N2)	N/A	-0.23533	-0.06008	-0.09494	-0.02567	0.03437 6	0.00175 5
CUL4B (cullin 4B)	N/A	-0.20992	0.006079	-0.01718	-0.07171	-0.03094	-0.07592
GLS (glutaminase)	-0.431	N/A	N/A	N/A	N/A	N/A	N/A
AATF (apoptosis antagonizing transcription factor)	-0.67618	N/A	N/A	N/A	N/A	N/A	N/A
DAP3 (death associated protein 3)	-0.30399	-0.32074	-0.02623	-0.09243	N/A	0.02244 2	N/A
GRB10 (growth factor receptor bound protein 10)	-0.63103	-0.39386	-0.12549	0.20454 5	0.19192 5	-0.01921	0.04081 3
CDK1 (cyclin dependent kinase 1)	N/A	-0.32743	0.013911	-0.1163	-0.16591	-0.05304	-0.11115
GSN (gelsolin)	-0.78665	0.134984	-0.01264	-0.07841	-0.14232	-0.00971	-0.03673
GSK3B (glycogen synthase kinase 3 beta)	-0.30958	-0.16933	-0.15846	0.00596 2	-0.0666	-0.13777	-0.11575
STRA6 (stimulated by retinoic acid 6)	N/A	-1.04227	-0.01631	0.05629 3	-0.00452	0.00326 4	0.04789 8
PRMT1 (protein arginine methyltransferase 1)	-0.39847	-0.36868	-0.07279	0.03021	N/A	-0.14869	N/A
MYC (v-myc avian myelocytomatosis viral oncogene homolog)	N/A	-0.46174	-0.13969	-0.11819	-0.08632	-0.19379	N/A
PSIP1 (PC4 and SFRS1 interacting protein 1)	-0.44666	-0.29424	-0.15178	-0.14511	0.04204 8	0.00031 2	-0.03572
IRS1 (insulin receptor substrate 1)	-0.62713	-0.74706	-0.28824	-0.24097	0.04184 2	-0.01858	0.13167 5
CA4 (carbonic anhydrase 4)	-0.89532	-0.7675	-0.15022	-0.09293	N/A	-0.00486	N/A
Genes in the hypertrophy of cardiac muscle	96_slick_De novo	96h_slick_OnRam p	96h-source	48h-slick	48h-source	24h-slick	24h-source
STAT3 (signal transducer and activator of transcription 3)	0.971844	0.866202	-0.066	0.28949 6	0.11803 2	-0.04149	0.00195 7
MAP3K5 (mitogen-activated protein kinase kinase 5)	0.624821	0.774913	0.221619	0.25282 8	0.23401	-0.0236	-0.04022
ADIPOQ (adiponectin, C1Q and collagen domain containing)	0.807008	0.791507	0.106058	0.05294 2	0.08308 5	0.01624 5	-0.02101
IKBKB (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta)	0.551372	0.316298	0.125268	0.18733 9	-0.00936	0.17903	0.14425 7
NFKBIA (NFKB inhibitor alpha)	1.426684	N/A	N/A	N/A	N/A	N/A	N/A
ECE1 (endothelin converting enzyme 1)	0.521847	0.645949	0.136794	-0.06071	-0.02806	0.07682 5	0.11764 1
IL6ST (interleukin 6 signal transducer)	0.574922	0.52987	-0.0492	0.09596	N/A	0.00674 5	N/A
HBEGF (heparin binding	0.192593	0.296006	0.070892	0.15566	N/A	0.14992	N/A

EGF like growth factor)				3		3	
BMP4 (bone morphogenetic protein 4)	0.390495	0.36916	-0.00366	-0.01143	0.01281 9	0.03775 8	0.03325 7
STK3 (serine/threonine kinase 3)	0.513463	0.130701	0.013863	0.0377	N/A	0.02959 3	N/A
IGF2R (insulin like growth factor 2 receptor)	0.296213	0.422589	0.128487	-0.2303	N/A	-0.08876	N/A
FSTL3 (follistatin like 3)	0.302148	0.308056	0.060677	0.03678 2	-0.08194	-0.01642	-0.08116
PRKCB (protein kinase C beta)	0.476799	0.451805	0.023947	-0.25316	-0.14501	0.02315 6	-0.0721
DUSP1 (dual specificity phosphatase 1)	N/A	1.029101	-0.06689	-0.4654	N/A	-0.01207	N/A
CABIN1 (calcineurin binding protein 1)	N/A	0.171513	-0.03771	-0.17017	-0.01801	0.1989	0.28493 8
MYOD1 (myogenic differentiation 1)	0.243023	0.180264	0.094669	-0.21967	N/A	0.07186	N/A
AKAP1 (A-kinase anchoring protein 1)	-0.21107	-0.2711	0.015984	0.00404	0.11463 3	0.12040 1	0.08174 9
MEF2C (myocyte enhancer factor 2C)	0.534087	-0.43205	-0.00725	-0.16206	-0.10406	-0.05443	0.01824 9
PARP1 (poly(ADP-ribose) polymerase 1)	-0.22848	-0.07043	-0.04834	0.02320 3	-0.01614	0.02305 1	-0.12955
MYBPC3 (myosin binding protein C, cardiac)	-0.20957	-0.33001	-0.18218	0.06691 9	N/A	-0.04846	N/A
PRMT5 (protein arginine methyltransferase 5)	N/A	-0.30168	0.012349	0.03489 6	-0.14089	-0.17221	-0.15675
GSK3B (glycogen synthase kinase 3 beta)	-0.43305	-0.24377	-0.04632	-0.01157	-0.05304	0.01045 7	-0.01812
FHL2 (four and a half LIM domains 2)	N/A	-0.5772	-0.13604	0.01939	-0.09413	-0.01632	-0.09266
TTN (titin)	-0.30958	-0.16933	-0.15846	0.00596 2	-0.0666	-0.13777	-0.11575
STAT3 (signal transducer and activator of transcription 3)	-0.21454	-0.23281	-0.05638	-0.42656	-0.15781	0.08281 6	0.04281 5
MAP3K5 (mitogen-activated protein kinase kinase kinase 5)	-1.12527	N/A	N/A	N/A	N/A	N/A	N/A

Table S6 A list of toxicity pathways and DEGs responsible for their enrichment by IPA-Tox

Ingenuity Toxicity Lists	-log(p-value)	Downregulated	Upregulated	Overlap with dataset	Molecules
Liver Proliferation	7.74E00	15/228 (7%)	37/228 (16%)	176/228 (77%)	PPARA,BMP4,XDH,PIK3R1,ODC1,F2,ARNT,IKBKB,CXCL14,ITGAV,SLC7A5,GSK3B,IGFBP1,HNF4A,RPS6KB1,HBEGF,SKP2,SCP2,E2F1,CTSB,MDK,IL6ST,SPTBN1,MMP14,PTN,ADIPOQ,SAT1,SMPD1,YY1AP1,JUN,NFKBIA,NGFR,HGF,RB1CC1,NCOR1,CTNBN1,STAT1,PIK3IP1,ITGB1,S1PR2,PPARD,CXCR4,CREB3L3,TOB1,STK3,FOXM1,FAH,CBS/CBSL,ABC B4,SERPINH1,EDNRA,PTGS2
Cholesterol Biosynthesis	7.5E00	1/16 (6%)	10/16 (63%)	5/16 (31%)	FDPS,FDFT1,EBP,DHCR7,PMVK,ACAT2,ACAT1,LSS,HMGCR,HMGCS1,SC5D
Cardiac Hypertrophy	6.02E00	32/435 (7%)	45/435 (10%)	358/435 (82%)	PPARA,APOB,BMP4,TCF15,RAB2A,PIK3R1,TNNT2,PBX1,CORIN,TPM1,ATP2A2,ABCA1,CABIN1,IKBKB,FHL2,FKBP1B,LCAT,PIK3CG,GSK3B,CA

					SQ2,HBEGF,MMP2,MYH7,STAT3,GSN,TTN,PFKM,ANKRD1,TRIM63,DU SP1,PRKCD,CTSB,HPRT1,IL6ST,NOS1,MYH6,ADAM17,PDGFA,ADIPO Q,MAP3K5,KCNQ1,KCNJ11,EIF4EBP1,NFKBIA,JUN,SP3,PARK7,PPP3C B,HGF,PRKCE,ECE1,CTNNB1,ACE,RASSF1,VAV2,EPAS1,SLC25A4,TRI M55,PPARD,MYOD1,XIRP1,STK3,IGF2R,PNPLA2,SEMA3A,NF1,NT5E,L AMA4,KLF5,EDNRA,MEF2C,PTGS2,CTSC,HMGCR,COL9A2,MYBPC3,A KAP1 PPARA,PIK3R1,ARNT,OCNL,IKBKB,TNIP1,ITGAV,GSK3B,IGFBP1,HNF4 A,CASP3,HBEGF,STAT3,IRF5,ADAR,E2F1,CTSB,IL6ST,MME,SIGIRR,S PTBN1,ATF7,ADIPOQ,UGCG,SMPD1,USP2,ATP2A1,ALDH2,YY1AP1,NF KBIA,JUN,FLNA,NGFR,HGF,RB1CC1,STAT1,SLC25A4,MYD88,PLK1,SO D1,STK3,SH3BP5,FAH,NFE2L1,BUB1,LDLR,NF1,ABCB4,CBS/CBSL,SE RPINH1,PTGS2,DNM1L,A2M CCNI,SUV39H1,CA4,ABCC10,BCL6,APRT,F2,NTN1,STMN1,FDFT1,RNF P13,PAK1,RHOG,EZR,ABCC1,FGFR4,ITGAV,GSK3B,HK1,ATG7,TJP2,CA SP3,DCN,HBEGF,STAT3,GSN,PFKM,DCTN2,PKD1,DUSP1,IRS1,PRKC D,RASSF4,NMNAT3,GAPDH,NEIL1,CHMP5,SFRP1,NOS1,AATF,IL17RD, ERN1,ATF6,DDX17,MAP3K5,BECN1,HNRNP,K,SIRT4,TCF12,ALKBH8,H K2,NFKBIA,ANXA5,NOP58,HGF,VCP,DAP3,PRKCE,SLC40A1,ZNF512B, CTNNB1,ATP13A2,RASSF1,DNASE1,ITGB1,HNRNP,MYD88,PPARD,G LS,ELOVL4,MAN2A1,HIP1,SOD1,PSIP1,PRMT1,GRB10,SLK,SLC7A9,RI PK1,PTGS2,ABCC3,TNFRSF19,PTGR1 PPARA,SPTBN1,MYD88,CXCR4,HMMR,NCAPG,FAM120A,STAT3,IQGA P1,FOXK1,MEN1,PSME3,VCAN,ODC1,SKP2,BUB1,IKBKB,JUN,HGF,AC SS2,E2F1,HMGCR,CTNNB1 PXN,UBE2A,COPS5,PIK3R1,CSNK1D,EIF2S1,EIF2S2,ELAVL1,ARNT,IK BKB,JUN,HSP90AB1,HIF1AN,HSP90AA1,KDR,UBE2E1,E1F1AX IL6ST,MYH6,XDH,PTN,ADIPOQ,MAP3K5,E2F3,BECN1,IQGAP1,NTN1,F STL1,IKBKB,HK2,PARK7,PHB,PPP1R10,HGF,MANF,HSPE1,GSK3B,CT NNB1,MAPKAPK2,STAT1,RASSF1,AIFM1,HK1,CALR,CASP3,UBE4B,CX CR4,TXNIP,CSK,SERPINF1,MMP2,STAT3,GSN,SH3BP5,PNPLA2,NUB1, PRKCD,E2F1,GAPDH,MDK,NECTIN2,MYBPC3 NOS1,PPARA,MYH6,TNNT2,RRM2B,CTNNA1,PPP1CB,MAP3K5,BCL6,B ECN1,ATP2A2,LPL,GSK3B,DAG1,ACE,RASSF1,VAV2,ITGB1,PTX3,ETS 1,ENTPD1,XIRP1,HBEGF,STAT3,STK3,PNPLA2,NF1,LAMA4,RERE,KLF 5,PTGS2,ACSL1,MYBPC3,NECTIN2
Liver Necrosis/Cell Death	4.79E00	18/289 (6%)	35/289 (12%)	236/289 (82%)	
Renal Necrosis/Cell Death	4.67E00	29/519 (6%)	54/519 (10%)	436/519 (84%)	
Increases Liver Hyperplasia/Hyperp roliferation	3.65E00	13/103 (13%)	10/103 (10%)	80/103 (78%)	
Hypoxia-Inducible Factor Signaling	3.29E00	8/70 (11%)	9/70 (13%)	53/70 (76%)	
Cardiac Necrosis/Cell Death	3.1E00	19/273 (7%)	26/273 (10%)	228/273 (84%)	
Cardiac Fibrosis	2.98E00	12/193 (6%)	22/193 (11%)	159/193 (82%)	
Genes Upregulated in Response to Proteinuria-induced Oxidative Stress in Renal Proximal Tubule Cells (Human)	2.75E00	1/10 (10%)	4/10 (40%)	5/10 (50%)	HSP90AA1,MAPK12,POLD1,SOD3,GSTT1
Mitochondrial Dysfunction	2.48E00	8/176 (5%)	22/176 (13%)	146/176 (83%)	PRDX5,XDH,CPT1B,ACO2,RHOT2,TRAK1,MT- CO2,NDUFA1,NDUFB9,NDUFS1,PARK7,MT-CO3,OGDH,MT- ND2,AIFM1,SDHA,NDUFV1,UCP2,CASP3,ATP5A1,MT- ND4,NDUFAF2,MAPK12,FIS1,MT-ND5,MT- ND1,NDUFV2,APH1B,BACE2,COX15 PIK3C2B,UCP2,PIK3R1,NCOA6,NCOA4,ATP2A1,KLF9,F10,LDLR,SREB F1,PIK3CG,FGFR4,IRS1,FASN,PIK3C3,ACACA,NCOR1,STRBP PPARA,PRKAB1,PRKAB2,CPT1B,TGFBR3,ADIPOQ,GNA14,AP2A2,ABC A1,PRKAG1,PLCH1,IKBKB,NFKBIA,JUN,HSP90AB1,FASN,LPL,NCOR1, STAT5B,ACOX1,NCOA6,IL1R1,CAND1,GK,IRS1,HSP90AA1,SLC27A1,M EF2C,MAP4K4 HPX,APOB,APOH,AHSG,SERPINF1,IL1R1,ABCA1,SERPINF2,FDFT1,LD LR,LCAT,SREBF1,NGFR,FASN,LPL,ACACA,NCOR1,PLTP,PTGS2,HMG CR,CYP51A1
TR/RXR Activation	2.02E00	8/98 (8%)	10/98 (10%)	80/98 (82%)	
PPARα/RXRα Activation	2E00	15/182 (8%)	14/182 (8%)	153/182 (84%)	
LXR/RXR Activation	1.91E00	9/123 (7%)	12/123 (10%)	102/123 (83%)	
Hepatic Fibrosis	1.89E00	6/101 (6%)	12/101 (12%)	83/101 (82%)	LTBP2,COL4A1,PDGFA,DCN,MMP14,MMP13,IGFBP5,MMP2,COL1A2,C OL5A1,TNC,SREBF1,HGF,ECE1,LTBP4,IGFBP1,A2M,Hspg2
Mechanism of Gene Regulation by Peroxisome Proliferators via PPARα	1.83E00	4/95 (4%)	13/95 (14%)	78/95 (82%)	PPARA,PPARD,PDGFA,CPT1B,PIK3R1,ACOX1,IL1R1,IKBKB,NFKBIA,JU N,HSP90AB1,DUSP1,LPL,HSP90AA1,NCOR1,PTGS2,STAT5B
NRF2-mediated Oxidative Stress Response	1.81E00	8/245 (3%)	28/245 (11%)	209/245 (85%)	PRDX1,PIK3R1,MAP3K5,SOD3,GSTT1,JUN,HSP90AB1,PIK3C3,PIK3CG, ABCC1,FGFR4,VCP,UBE2K,PRKCE,DNAJA3,GSK3B,DNAJB1,CBR1,AC TA1,PIK3C2B,CYP1A1,DNAJB12,SOD1,DNAJB14,TXNRD1,GSTO1,DNA JC11,PRKCI,PRKCD,IRS1,CCT7,HSP90AA1,CYP4A11,ENC1,DNAJC7,M GST3 PPARA,HPX,APOB,PKLR,APOH,FETUB,AHSG,SERPINF1,SLC22A7,MA PK12,SERPINF2,CYP8B1,ABCB4,LCAT,SREBF1,FGFR4,FASN,LPL,FBP 1,PLTP,HNF4A PRKAB1,ATP5A1,RGS16,ADIPOQ,MAP3K5,TRPV1,PSME3,ARNT,IKBKB ,SOAT2,ACOT11,DUSP1,SREBF1,PLIN2,HIF1AN,RPTOR SERPINB1,CSNK2A1,PPARD,PDGFA,IGFBP5,PSMC5,YY1,PRKCI,PRK CD,MXD1,PRKCE,NCOR1,IGFBP1,SEMA3B CSNK2A1,PIK3R1,Rdh7,MAP3K5,RBP1,PRKAG1,PSMC5,TNIP1,LBAT,J UN,PIK3CG,RDH14,PRKCE,NCOR1,NR2F6,STAT5B,MAPKAPK2,SMAD 1,RDH13,DHRS3,CSK,MAPK12,SMARCD3,PRMT1,PRKCI,DUSP1,PRKC
FXR/RXR Activation	1.8E00	10/126 (8%)	11/126 (9%)	105/126 (83%)	
Increases Liver Steatosis	1.69E00	4/91 (4%)	12/91 (13%)	75/91 (82%)	
VDR/RXR Activation	1.61E00	1/78 (1%)	13/78 (17%)	64/78 (82%)	
RAR Activation	1.54E00	6/190 (3%)	22/190 (12%)	162/190 (85%)	

					D,RDH12
Long-term Renal Injury Anti-oxidative Response Panel (Rat)	1.52E00	2/18 (11%)	3/18 (17%)	13/18 (72%)	CBS/CBSL,BLVRA,CP,SOD1,SOD3
p53 Signaling	1.47E00	8/112 (7%)	10/112 (9%)	94/112 (84%)	PIK3C2B,TP63,TOBP1,PIK3R1,RRM2B,CSNK1D,SERPINE2,JUN,PIK3C3,PIK3CG,FASN,IRS1,FGFR4,PPP1R13B,E2F1,GSK3B,TRIM29,CTNNB1
Long-term Renal Injury Pro-oxidative Response Panel (Rat)	1.44E00	2/13 (15%)	2/13 (15%)	9/13 (69%)	XDH,HIF3A,HPRT1,FMO5
Hepatic Cholestasis	1.41E00	2/162 (1%)	22/162 (14%)	138/162 (85%)	PPARA,TJP2,MYD88,SLC22A7,IL1R1,MAPK12,PRKAG1,CYP8B1,ATP8B1,SLCO1C1,IKBKB,PRKCI,JUN,NFKBIA,ABCB4,SLCO3A1,SREBF1,NGFR,FGFR4,ABCC1,PRKCD,PRKCE,HNF4A,ABCC3
Acute Renal Failure Panel (Rat)	1.33E00	5/62 (8%)	6/62 (10%)	51/62 (82%)	MYO5A,GAS2,JUN,ANXA1,TAGLN,ANXA2,IGFBP5,IGFBP1,COL18A1,A2M,EIF1AX
Genes associated with Chronic Allograft Nephropathy (Human)	1.26E00	1/21 (5%)	4/21 (19%)	16/21 (76%)	TNC,COL4A1,PDGFA,MMP2,ITGB6
Nongenotoxic Hepatocarcinogenicity Biomarker Panel	1.18E00	4/22 (18%)	1/22 (5%)	17/22 (77%)	CITED4,LOC102724788/PRODH,TRNT1,ANXA2,USP2
LPS/IL-1 Mediated Inhibition of RXR Function	1.09E00	13/253 (5%)	20/253 (8%)	220/253 (87%)	PPARA,ALDH4A1,CPT1B,FMO5,SOD3,ABCA1,GSTT1,ALDH1L1,JUN,NGFR,ACSL5,CHST3,FABP7,SULT1C3,HMGCS1,ALDH6A1,ALDH7A1,MYD88,ACOX1,IL1R1,GSTO1,HS3ST3B1,FABP2,ALDH1L2,SREBF1,SMOX,SLC27A1,PLTP,ALDH16A1,ABCC3,CYP4A11,ACSL1,MGST3
Aryl Hydrocarbon Receptor Signaling	1.07E00	11/159 (7%)	11/159 (7%)	137/159 (86%)	TRIP11,ALDH4A1,CYP1A1,CCNE2,RBL1,GSTT1,GSTO1,ARNT,CCNA2,ALDH1L1,JUN,ALDH1L2,HSP90AB1,FASN,E2F1,HSP90AA1,DHFR,ALDH16A1,ALDH6A1,MGST3,ALDH7A1,MCM7
Increases Cardiac Dysfunction	1.02E00	3/39 (8%)	4/39 (10%)	32/39 (82%)	PPARA,PTX3,ANGPTL4,PIK3CG,E2F1,SLC27A1,MAP3K5
Increases Renal Proliferation	9.49E-01	7/139 (5%)	12/139 (9%)	120/139 (86%)	ITGB1,DLGAP5,CDCP1,MMP14,TTL4,STAT3,NTN1,SKP2,CSNK1E,JUN,HGF,NOP58,E2F1,BICC1,KLF5,CHKA,LARP1,PTGS2,CTNNB1
Increases Glomerular Injury	9.36E-01	3/89 (3%)	10/89 (11%)	76/89 (85%)	SLK,ITGB1,BMP4,CASP3,PARK7,SREBF1,MYD88,TXNIP,PRKCD,PTGS2,CTNNB1,DDR1,SKP2
Oxidative Stress	9.18E-01	1/57 (2%)	8/57 (14%)	48/57 (84%)	JUN,PRDX5,DUSP1,PRDX1,XDH,STAT3,SOD1,NFE2L1,SOD3
Cell Cycle: G1/S Checkpoint Regulation	8.87E-01	10/66 (15%)	0/66 (0%)	56/66 (85%)	CCNE2,MAX,PA2G4,SUV39H1,E2F1,GSK3B,RBL1,E2F3,SKP2,CDC25A
Decreases Depolarization of Mitochondria and Mitochondrial Membrane	8.75E-01	3/27 (11%)	2/27 (7%)	22/27 (81%)	PAK1,VPS13A,ABCC1,DNM1L,ATP2A2
Renal Proximal Tubule Toxicity Biomarker Panel (Rat)	8.75E-01	2/27 (7%)	3/27 (11%)	22/27 (81%)	HSP90AA1,IGFBP1,SLC38A3,SLC15A2,OCLN
Xenobiotic Metabolism Signaling	8.08E-01	15/352 (4%)	27/352 (8%)	310/352 (88%)	ALDH4A1,LTA4H,PIK3R1,EPHX2,PPP2R3B,MAP3K5,FMO5,SOD3,GSTT1,ARNT,ALDH1L1,CAMK2A,HSP90AB1,FGFR4,PIK3CG,PIK3C3,CHST3,PRKCE,SULT1C3,CYP51A1,ALDH6A1,ALDH7A1,CAMK2B,PIK3C2B,CYP1A1,UGT8,MAPK12,GSTO1,HS3ST3B1,PRKCI,ALDH1L2,PPP2R3A,SMOX,PRKCD,IRS1,HSP90AA1,PPP2R5E,ALDH16A1,ABCC3,DNAJC7,MGST3,CAMK2G
Recovery from Ischemic Acute Renal Failure (Rat)	7.85E-01	1/14 (7%)	2/14 (14%)	11/14 (79%)	COL4A1,SGK1,RBP1
Positive Acute Phase Response Proteins	7.35E-01	2/30 (7%)	3/30 (10%)	25/30 (83%)	HPX,CP,A2M,SERPINF2,HMOX2
Swelling of Mitochondria	7.2E-01	1/15 (7%)	2/15 (13%)	12/15 (80%)	PRKCE,SOD1,AIFM1
Hormone Receptor Regulated Cholesterol Metabolism	7.17E-01	1/8 (13%)	1/8 (13%)	6/8 (75%)	LDLR,ABCA1
Negative Acute Phase Response Proteins	7.17E-01	1/8 (13%)	1/8 (13%)	6/8 (75%)	ITIH2,AHSG
Vasopressin-induced Genes in Inner Medullary Renal Collecting Duct Cells (Rat)	7.17E-01	1/8 (13%)	1/8 (13%)	6/8 (75%)	SGK1,WNK1

Fatty Acid Metabolism Increases Transmembrane Potential of Mitochondria and Mitochondrial Membrane Genes	6.81E-01	8/117 (7%)	7/117 (6%)	102/117 (87%)	ALDH4A1,CYP1A1,ACAT2,CPT1B,ACOX1,ACADSB,ALDH2,AUH,ACSL5,ACAT1,SLC27A1,CYP4A11,ACSL1,CYP51A1,ALDH7A1
Downregulated in Response to Chronic Renal Failure (Rat)	6.15E-01	3/50 (6%)	4/50 (8%)	43/50 (86%)	HSPA4,CASP3,PHB,HGF,PRKCE,DNAJB1,GSN
Renal Ischemic Resistance Panel (Rat)	5.68E-01	0/10 (0%)	2/10 (20%)	8/10 (80%)	CYP1A1,SLC22A7
Increases Renal Damage Primary	5.68E-01	2/10 (20%)	0/10 (0%)	8/10 (80%)	CCNF,FOXM1
Glomerulonephritis Biomarker Panel (Human)	5.12E-01	1/81 (1%)	9/81 (11%)	71/81 (88%)	ITGB1,BMP4,SREBF1,MYD88,TXNIP,MDK,IL1R1,ITGB6,CFP,CTNNB1
Biogenesis of Mitochondria	5.09E-01	1/11 (9%)	1/11 (9%)	9/11 (82%)	TYMS,HBEGF
Glutathione Depletion - Phase II Reactions	4.78E-01	1/20 (5%)	2/20 (10%)	17/20 (85%)	EPAS1,DNAJA3,MAN2A1
Increases Cardiac Proliferation	4.78E-01	0/20 (0%)	3/20 (15%)	17/20 (85%)	GSTO1,GSTT1,MGST3
Glutathione Depletion - CYP Induction and Reactive Metabolites	4.64E-01	1/47 (2%)	5/47 (11%)	41/47 (87%)	CASZ1,ADIPOQ,HBEGF,STAT3,STAT1,CTNNB1
Persistent Renal Ischemia-Reperfusion Injury (Mouse)	4.57E-01	0/12 (0%)	2/12 (17%)	10/12 (83%)	ABCC3,GSTT1
Increases Liver Damage	4.38E-01	1/30 (3%)	3/30 (10%)	26/30 (87%)	LTBP2,CTSS,MMP14,SOX9
Genes Upregulated in Response to Chronic Renal Failure (Rat)	3.85E-01	1/117 (1%)	12/117 (10%)	104/117 (89%)	IL6ST,PPARA,MYD88,SMPD1,STAT3,IL1R1,SH3BP5,F2,IKBKB,CTSB,PTGS2,DNM1L,STAT1
Increases Heart Failure	3.82E-01	0/5 (0%)	1/5 (20%)	4/5 (80%)	ABCC3
Cytochrome P450 Panel - Substrate is a Sterol (Human)	3.78E-01	1/23 (4%)	2/23 (9%)	20/23 (87%)	TRIM63,PIK3CG,PAX3
Cytochrome P450 Panel - Substrate is a Sterol (Mouse)	3.72E-01	1/14 (7%)	1/14 (7%)	12/14 (86%)	CYP51A1,CYP8B1
Cytochrome P450 Panel - Substrate is a Sterol (Rat)	3.72E-01	1/14 (7%)	1/14 (7%)	12/14 (86%)	CYP51A1,CYP8B1
Renal Inorganic Phosphate Homeostasis (Mouse)	3.72E-01	1/14 (7%)	1/14 (7%)	12/14 (86%)	CYP51A1,CYP8B1
Renal Glomerulus Panel (Human)	3.24E-01	1/6 (17%)	0/6 (0%)	5/6 (83%)	ATP1A2
Decreases Permeability	2.77E-01	1/17 (6%)	1/17 (6%)	15/17 (88%)	PTPRO,DAG1
Transition of Mitochondria and Mitochondrial Membrane	2.77E-01	1/7 (14%)	0/7 (0%)	6/7 (86%)	OGDH
Glutathione Depletion - Hepatocellular Hypertrophy	2.39E-01	0/8 (0%)	1/8 (13%)	7/8 (88%)	ABCC3