# Amyloidogenic light chains impair plasma cell survival

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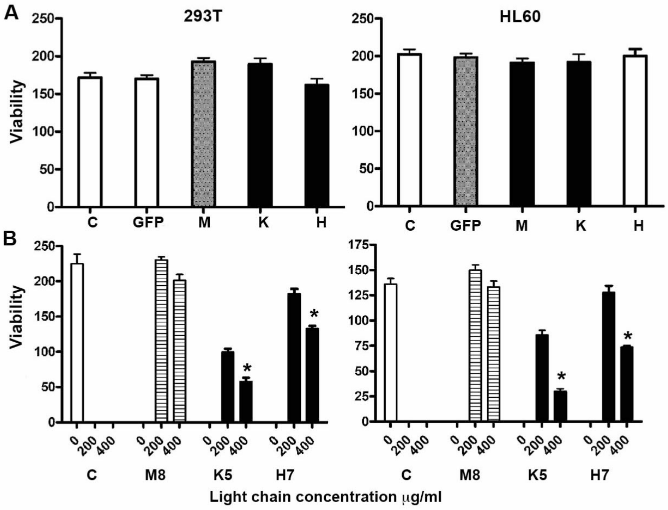
## Supplementary figures, tables and legends



C

721.221 n = 3

| | Ao | G0/G1 | S | G2M |
|---|---|---|---|---|
| Control | 9.0±0.6 | 55.8±1.4 | 19.5±0.2 | 16.8±0.7 |
| GFP | *19.5±4.4 | **49.8±4.3 | 17.4±3.3 | 13.3±3.1 |
| M | 5.4±1.1 | 58.0±2.8 | 21.7±2.3 | 16.1±2.7 |
| K | 7.1±0.7 | 57.7±0.3 | 19.0±1.2 | 17.8±1.8 |
| H | 12.2±1.6 | 54.7±2.1 | 17.0±1.3 | 17.8±2.5 |

293T n = 3

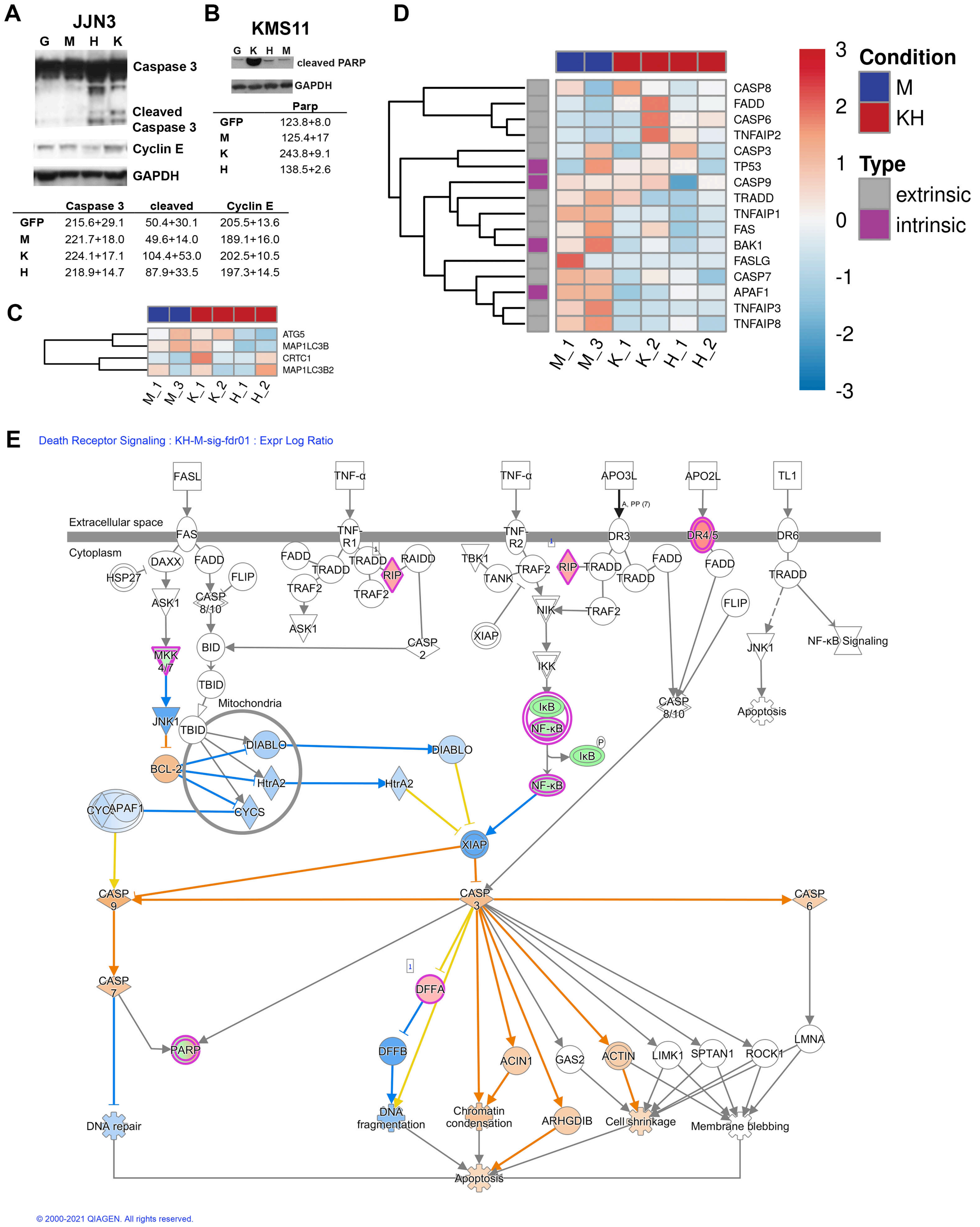
| | Ao | G0/G1 | S | G2M |
|---|---|---|---|---|
| GFP | 9.1±12.4 | 57.3±2.3 | 20.9±2.3 | 12.7±0.8 |
| M | 6.1±8.7 | 57.3±2 | 20.4±5.2 | 11.3±3.5 |
| K | 8.2±9.9 | 52.4±7.5 | 23.9±8.1 | 15.6±0.8 |
| H | 7.0±10.4 | 51.2±7.7 | 25.1±6.1 | 15.8±1.7 |

HL60 n = 2

| | Ao | G0/G1 | S | G2M |
|---|---|---|---|---|
| Contol | 13.9+0.6 | 50.3+1.3 | 19.9+0.9 | 16.2+1.3 |
| GFP | 21.5+9.1 | 49.2+2.9 | 15.9+2.8 | 13.7+3.2 |
| M | 17.1+1.1 | 55.3+0.6 | 19.4+0.5 | 8.7+1.7 |
| K | 20.9+0.4 | 52.2+1.9 | 17.7+0.7 | 9.7+2.2 |
| H | 22.9+0.5 | 50.6+1.1 | 16.6+0.3 | 10.3+13 |

**Supplementary Figure 1. Amyloidogenic light chains are not toxic when secreted by other cell types but toxic to them when supplemented exogenously in high doses.**

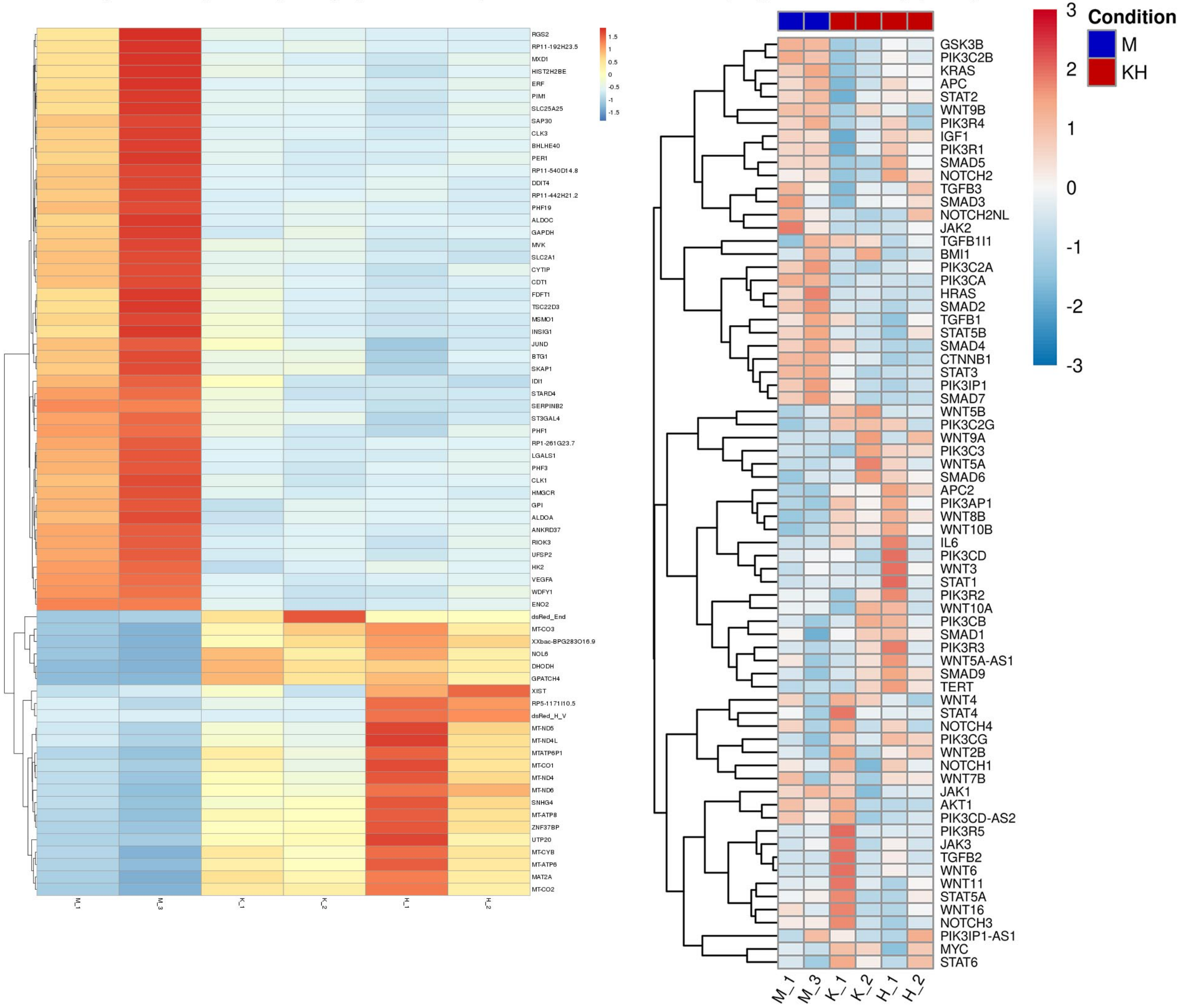
A) 293T and HL60 cell lines were infected with two different clones of each LC and with 3 separate infections with empty Lentivirus (GFP) or Lentivirus containing non-amyloidogenic (M) or nephrotoxic (K) or cardiotoxic (H), amyloidogenic light chains. Assessment of viability by ATP uptake luminescence was then measured, n=3, 5 replicates per readout, no significant differences were found. B) Purified light chains isolated from patient's urine were obtained from multiple myeloma (M8) nephrotoxic (K5) or cardiotoxic (H7) patients and supplemented to media of growing naïve 293T and HL60 cells for 5 days and viability was assessed by ATP uptake (Intensity) with CellTiter-Glo® assay. LC concentration = 0, 200 and 400 micrograms/ml, 4-5 replicates per experiment with n = 3, 4 replicates per experiment. *Significantly different from Control ($p \leq 0.02$ - 0,005). C) Cell cycle analysis of non-MM cell lines infected with lentivirus containing various LC (n=2-3 per cell line).



|  | Caspase 3 | cleaved | Cyclin E |
|---|---|---|---|
| **GFP** | 215.6+29.1 | 50.4+30.1 | 205.5+13.6 |
| **M** | 221.7+18.0 | 49.6+14.0 | 189.1+16.0 |
| **K** | 224.1+17.1 | 104.4+53.0 | 202.5+10.5 |
| **H** | 218.9+14.7 | 87.9+33.5 | 197.3+14.5 |

|  | Parp |
|---|---|
| **GFP** | 123.8+8.0 |
| **M** | 125.4+17 |
| **K** | 243.8+9.1 |
| **H** | 138.5+2.6 |

**Supplementary Figure 2. Upregulation of the apoptotic and autophagic pathways in MM cells containing cardiotoxic and nephrotoxic amyloidogenic light chains.** A) Representative western blot analysis of uncleaved and cleaved Caspase 3 and cyclin E in JJN3 cell lines infected with AL and MM LC including table measurement of intensity of bands (n=5, 2 different infections). B) Representative western blot analysis of cleaved PARP in KMS11 cell lines infected with AL and MM LC (n=5, 2 different infections) including table measurement of intensity of bands. C) Heatmap of RNA expression of genes involved in autophagy. Normalized expression values of significant genes (padj<0.1) were scaled per gene and presented according to the color code on the right. D) Heatmap of genes involved in both extrinsic (grey) and extrinsic (purple) apoptotic pathways. Normalized expression values of significant genes (padj<0.1) were scaled per gene and presented according to the color code on the right. E) IPA® Death receptor Signaling pathway generated with RNA-seq data. Its enrichment p-value in MM cells which contained cardiotoxic LC and/or nephrotoxic LC is 0.039 and but does NOT pass BH-p-value<0.05. In this figure IPA® molecular activation prediction (MAP) tool was used to predict the activation state of the unmeasured genes (upregulated (orange), downregulated (blue)), based on the expression of the experimental differentially expressed genes (DEG) (red/green, upregulated/downregulated, respectively) that participate in this pathway. The significantly differentiated expressed genes that were found in this pathway are depicted in red (upregulated) and green (downregulated). n = 3 separate infections of JJN3 cells.



A. Heatmap of TOP 50 significcant genes upregulated in M compared to K/H

B: Heatmap of genes involved in myc pathway

**Supplementary Figure 3. Heat map comparing genes expression in multiple myeloma cells that were infected with non-amyloidogenic (M) light chain as compared to cells containing cardiotoxic (H) or nephrotoxic (K) amyloidogenic light chains.** A) Top 50 genes upregulated in multiple myeloma cells that were transduced with non-amyloidogenic (M) light chain as compared to cells transduced with cardiotoxic (H) or nephrotoxic (K) amyloidogenic light chains, n=3 for each being separate infections in JJN3 cell line. B) Expression of genes that are involved in the myc pathway M compared with H/K. Normalized expression values of significant genes (padj<0.1) were scaled per gene and presented according to the color code on the right. Genes were ordered by hierarchical clustering, as indicated on the left, while samples are ordered according to their biological condition. From left to right: non-amyloidogenic (M), nephrotoxic (K), and cardiotoxic (H) light chains. Names are shown on the right for each gene. n = 3 separate infections of JJN3 cell line

## Sequence of 3 light chains cloned in –dsRED lentivirus

H3 - (Amiloidogenic light chain from a patient with heart involvement)
cagtctgtgttgactcagccaccctcaacgtctggcacccccgggcagagggtcaccatctcttgttctggaagcagct
ccaacatcgaaactaatactgtcaactggtaccagcaactcccagggacggcccccaaactcgtcatgcatactaat
aatcagcggccctcaggggtccctgaccgattctctggctccaggtctggcacctcagcctccctggccatcggtgga
ctccagtctgaggatgaggctgattatttctgtgcagcatgggatgacaacctgaatggtgtgattttcggcggcgggac
caagctgaccgtcctaggtcagcccaaggctgccccctcggtcactctgttcccaccctcctctgaggagcttcaagcc
aacaaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagca
gccccgtcaaggcgggagtggagaccaccacaccctccaaacaaagcaacaacaagtacgcggccagcagcta
cctgagcctgacgcctgagcagtggaagtcccacaaaagctacagctgccaggtcacgcatgaagggagcaccgt
ggagaagacagtggcccctacagaatgttca

K1- (Amiloidogenic light chain from a patient with kidney involvement)
cagtctgtgctgactcagccaccctcagcgtctgggacccccgggcagagggtcaccatctcttgttctggaagcagct
ccaacatcggaagtaatactgtgaactggtaccagcagctcccaggaacggcccccaaactcctcatgtacaggaa
tgatcagcggccctcaggggtccctgaccgattctctggctccaagtctggctcctcagcctccctggccatcagtggg
ctccagtctgaggatgaggctgattattactgtgcagcatgggatgacagcctgaatgtcttattcggcggagggacca
agctgaccgtcctaggtcagcccaaggctgccccctcggtcactctgttcccaccctcctctgaggagcttcaagccaa
caaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagcc
ccgtcaaggcgggagtggagaccaccacaccctccaaacaaagcaacaacaagtacgcggccagcagctacct
gagcctgacgcctgagcagtggaagtcccacaaaagctacagctgccaggtcacgcatgaagggagcaccgtgg
agaagacagtggcccctacagaatgttca

M2- (Non amiloidogenic light chain from a patient with myeloma)
Cagtctgccctgactcagcctgcctccgtgtctgggtctcctggacagtcgatcaccatctcctgcactggaaccagca
gtgatgttggaacttataatcttgtctcttggtaccagcagttcccaggcaaagcccccaaactcatgatttatgagggca
ataagcggccctcaggggtttctaatcggttctcaggctccaagtctggcaacacggcctccctgacaatctctgggctc
caggctgaggacgaggctgattatttttgctgctcatattcgggtagtggcacttccgtggtattcggcggagggaccaa
gctgaccgtcctaggtcagcccaaggctgccccctcggtcactctgttcccgccctcctctgaggagcttcaagccaac
aaggccacactggtgtgtctcataagtgacttctacccgggagccgtgacagtggcctggaaggcagatagcagccc
cgtcaaggcgggagtggagaccaccacaccctccaaacaaagcaacaacaagtacgcggccagcagctatctg
agcctgacgcctgagcagtggaagtcccacagaagctacagctgccaggtcacgcatgaagggagcaccgtgga
gaagacagtggcccctacagaatgttca

Supplementary Table 1: IPA® Diseases and Functions of the Cell death and Survival Category found in the significantly DEG (Padj<0.1) in MM cells which contained cardiotoxic LC and/or nephrotoxic LC. Excel sheet containing the experimental data that IPA® used for generating Figure 2A.

Supplementary Table 2: IPA® Diseases and Functions of the Small Molecule biochemistry Category found in the significantly DEG (Padj<0.1) in MM cells which contained cardiotoxic LC and/or nephrotoxic LC. E. Excel sheet containing the experimental data that IPA® used for generating Figure 2B.

Supplementary Table 3: Significantly DEG (Padj<0.1) in MM cells which contained cardiotoxic LC and/or nephrotoxic LC that participate in the IPA® Oxidative phosphorylation Canonical pathway. Excel sheet containing the experimental data that IPA® used for generating Figure 2C.

| **Categories** | **Diseases or Functions Annotation** | **p-value** | **B-H p-value** | **Predicted Activation State** | **Activation z-score** | **Molecules** | **# Molecules** |
|---|---|---|---|---|---|---|---|
| Cell Death and Survival | cell death of tumor cell lines | 5.41E-11 | 3.25E-08 | | 1.97 | ABCC4,ACVR1B,ADM,ADORA2A,AHSA1,AKT3,ARID3B,ARNT,ATF2,ATN1,BCL6,BHLHE40,BLNK,BNIP3L,BRAF,BRD4,BTG1,BTG3,CAMK2G,CCNG1,CDC73,CDK8,CDKN1B,CDKN1C,CDKN2D,CDT1,CHSY1,CLK3,CLPTM1L,CNPY2,CRTC2,CSNK1A1,CTTN,DDIT3,DDIT4,DFFA,DHCR7,DNAJB1,DPH2,DUSP1,DYNLL1,EGLN1,ENO1,EPHB2,FAIM,FDFT1,FLI1,FOSL1,GAPDH,GBE1,GEM,GLIPR1,GPI,HDAC5,HK2,HMGCS1,HSPA1A/HSPA1B,IGF2BP2,IL17D,ING1,ING2,IPMK,IRAK2,JUND,KDELR1,KIT,KLF6,KLF9,KMT2A,LAIR1,LGALS1,LTV1,LYN,MAP3K1,MAP3K10,MAPK7,MARCHF5,MAT2A,MCU,MIF,MLKL,MLLT3,MME,MT1X,MTFP1,MXD1,MXI1,MYBBP1A,NAMPT,NAPA,NDRG1,NEK2,NFIL3,NME1,NOL3,NQO1,NUAK1,NUP58,ODC1,OGFOD1,OXR1,PBX3,PDE4D,PHF1,PHLPP1,PIAS4,PIM1,PPP1R13L,PPP1R15A,PRDM5,PRDX1,PRKCB,PSEN2,PTK2,PTPRE,RAB32,RELA,RELB,RHOC,RICTOR,RIPK1,RIPK2,RNF2,S100A11,SAT1,SATB1,SCD,SDC1,SFPQ,SFRP2,SGMS2,SH2D4A,SMOX,SMURF1,SP1,SREBF1,SRPK2,ST3GAL1,SYK,TESK2,TFEB,TMEM123,TNFAIP3,TNFRSF10B,TP63,TSC22D2,TSC22D3,UBE2S,UIMC1,VAV3,VEGFA,WDR4,XAB2,XRCC1,ZEB1,ZFP36,ZFP82,ZNF382 | 158 |
| Cell Death and Survival | cell death | 2.91E-10 | 1.66E-07 | Increased | 2.106 | ABCC4,ACAT1,ACVR1B,ADM,ADORA2A,AGO2,AHSA1,AKT3,ALDH3B1,ALDOA,ALDOC,ALKBH5,ANGPTL4,ARID3B,ARNT,ARRB1,ATF2,ATN1,ATP7A,BAG4,BATF3,BCL6,BHLHE40,BLNK,BNIP3L,BRAF,BRD4,BTG1,BTG3,C1GALT1C1,CA9,CACNB3,CAMK2D,CAMK2G,CCNG1,CD53,CDC73,CDK8,CDKN1B,CDKN1C,CDKN2D,CDT1,CECR2,CHSY1,CLCN2,CLK3,CLPTM1L,CNPY2,CPEB4,CRTC2,CSNK1A1,CSRNP1,CTTN,CUL4B,DDAH2,DDIT3,DDIT4,DDN,DFFA,DHCR7,DHODH,DNAJB1,DNAJB2,DPH2,DUSP1,DYNLL1,EEF1E1,EFNA3,EGLN1,EGLN2,EHD3,ENO1,EPCAM,EPHB2,ERF,EYA1,F2RL3,FAIM,FDFT1,FLCN,FLI1,FNIP1,FOSL1,FOSL2,FOXI1,FUS,FXR1,FZR1,G6PC3,GAB2,GAPDH,GBA,GBE1,GEM,GLIPR1,GLIS2,GNA13,GNAQ,GPI,HDAC5,HEY1,HIPK1,HK2,HMGCR,HMGCS1,HSF2,HSPA1A/HSPA1B,HSPE1,IGF2BP2,IL17D,ING1,ING2,IPMK,IRAK2,ITPKB,ITPRIP,JMJD6,JUND,KDELR1,KDM3A,KDM4D,KDM6B,KIT,KLF10,KLF11,KLF6,KLF9,KMT2A,LAIR1,LAT,LDHA,LGALS1,LGMN,LGR4,LTV1,LYN,MAFG,MAP2K7,MAP3K1,MAP3K10,MAP3K3,MAP3K8,MAPK7,MARCHF5,MAT2A,MCU,MICA,MIF,MLKL,MLLT3,MME,MST1,MT-ND4,MT1X,MTFP1,MVK,MXD1,MXD3,MXI1,MYBBP1A,MYLK,NAMPT,NAPA,NAT8L,NCOA5,NCR3LG1,NDRG1,NEK2,NET1,NFIL3,NFKBID,NME1,NOL3,NOLC1,NPC1,NQO1,NTS,NUAK1,NUAK2,NUP58,ODC1,OGFOD1,OPTN,OXR1,PBX3,PDE3B,PDE4D,PDK1,PFKFB3,PHF1,PHLPP1,PIAS4,PIGA,PIK3AP1,PIM1,PIM3,PNO1,PNPT1,PON1,PON2,PPM1A,PPP1R13L,PPP1R15A,PPP3CC,PPP3R1,PRDM5,PRDX1,PRKCB,PSEN2,PSME3,PTK2,PTPRE,QKI,RAB32,RANBP9,RAP1A,RASSF2,RELA,RELB,RGPD3 (includes others),RGS5,RHOC,RICTOR,RIPK1,RIPK2,RNF19A,RNF2,RPRM,RUNX2,RYBP,S100A11,SAT1,SATB1,SCD,SCLY,SDC1,SELENON,SERPINB2,SFPQ,SFRP2,SGMS2,SH2D4A,SLC25A19,SLC2A1,SLC31A1,SLC46A1,SMOX,SMURF1,SP1,SREBF1,SRPK2,ST3GAL1,STEAP3,STX11,STX1A,SYK,TAB2,TBX6,TESK2,TFEB,TJP2,TMEM123,TMF1,TNFAIP3,TNFRSF10B,TNFRSF13B,TNIP1,TP53INP1,TP63,TPD52L1,TRAF3IP2,TRIP10,TSC22D2,TSC22D3,TTBK2,TXNIP,UBE2B,UBE2S,UIMC1,VASP,VAV3,VEGFA,WDR4,XAB2,XRCC1,ZEB1,ZFAND5,ZFP36,ZFP82,ZNF382 | 290 |
| Cell Death and Survival | Necrosis | 4.51E-10 | 2.44E-07 | | 1.423 | ABCC4,ACAT1,ACVR1B,ADM,ADORA2A,AHSA1,AKT3,ALDH3B1,ALDOA,ARID3B,ARNT,ARRB1,ATF2,ATN1,ATP7A,BAG4,BCL6,BHLHE40,BLNK,BNIP3L,BRAF,BRD4,BTG1,BTG3,CA9,CACNB3,CAMK2D,CAMK2G,CCNG1,CDC73,CDK8,CDKN1B,CDKN1C,CDKN2D,CDT1,CHSY1,CLK3,CLPTM1L,CNPY2,CPEB4,CRTC2,CSNK1A1,CTTN,CUL4B,DDIT3,DDIT4,DDN,DFFA,DHCR7,DNAJB1,DNAJB2,DPH2,DUSP1,DYNLL1,EFNA3,EGLN1,EGLN2,ENO1,EPHB2,F2RL3,FAIM,FDFT1,FLI1,FNIP1,FOSL1,FOXI1,FUS,G6PC3,GAB2,GAPDH,GBA,GBE1,GEM,GLIPR1,GLIS2,GNA13,GNAQ,GPI,HDAC5,HIPK1,HK2,HMGCS1,HSPA1A/HSPA1B,HSPE1,IGF2BP2,IL17D,ING1,ING2,IPMK,IRAK2,ITPKB,ITPRIP,JUND,KDELR1,KIT,KLF10,KLF6,KLF9,KMT2A,LAIR1,LAT,LDHA,LGALS1,LGMN,LTV1,LYN,MAP2K7,MAP3K1,MAP3K10,MAP3K8,MAPK7,MARCHF5,MAT2A,MCU,MIF,MLKL,MLLT3,MME,MST1,MT- | 237 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | ND4,MT1X,MTFP1,MVK,MXD1,MXD3,MXI1,MYBBP1A,MYLK,NAMPT,NAPA,NCOA5,NDRG1,NEK2,NFIL3,NFKBID,NME1,NOL3,NOLC1,NPC1,NQO1,NTS,NUAK1,NUP58,ODC1,OGFOD1,OPTN,OXR1,PBX3,PDE3B,PDE4D,PDK1,PFKFB3,PHF1,PHLPP1,PIAS4,PIK3AP1,PIM1,PIM3,PNO1,PNPT1,PON1,PON2,PPM1A,PPP1R13L,PPP1R15A,PPP3R1,PRDM5,PRDX1,PRKCB,PSEN2,PSME3,PTK2,PTPRE,QKI,RAB32,RANBP9,RELA,RELB,RGPD3 (includes others),RGS5,RHOC,RICTOR,RIPK1,RIPK2,RNF19A,RNF2,RPRM,RUNX2,S100A11,SAT1,SATB1,SCD,SDC1,SERPINB2,SFPQ,SFRP2,SGMS2,SH2D4A,SLC25A19,SLC2A1,SLC46A1,SMOX,SMURF1,SP1,SREBF1,SRPK2,ST3GAL1,STEAP3,STX1A,SYK,TESK2,TFEB,TJP2,TMEM123,TNFAIP3,TNFRSF10B,TNFRSF13B,TNIP1,TP53INP1,TP63,TRAF3IP2,TRIP10,TSC22D2,TSC22D3,TTBK2,TXNIP,UBE2S,UIMC1,VAV3,VEGFA,WDR4,XAB2,XRCC1,ZEB1,ZFP36,ZFP82,ZNF382 | |
| Cell Death and Survival | Apoptosis | 1.03E-09 | 5.31E-07 | | 1.743 | ACVR1B,ADM,ADORA2A,AGO2,AHSA1,AKT3,ALDOA,ALDOC,ALKBH5,ANGPTL4,ARID3B,ARNT,ARRB1,ATF2,ATN1,ATP7A,BAG4,BCL6,BHLHE40,BLNK,BNIP3L,BRAF,BTG1,CAMK2D,CAMK2G,CCNG1,CD53,CDC73,CDK8,CDKN1B,CDKN1C,CDKN2D,CECR2,CLCN2,CLK3,CLPTM1L,CPEB4,CRTC2,CSNK1A1,CSRNP1,CTTN,CUL4B,DDAH2,DDIT3,DDIT4,DDN,DFFA,DHODH,DNAJB1,DPH2,DUSP1,DYNLL1,EEF1E1,EGLN1,EGLN2,EHD3,ENO1,EPCAM,EPHB2,ERF,EYA1,F2RL3,FAIM,FLCN,FLI1,FNIP1,FOSL1,FOXI1,FUS,FXR1,G6PC3,GAB2,GAPDH,GEM,GLIPR1,GLIS2,GNA13,GNAQ,GPI,HDAC5,HEY1,HIPK1,HK2,HMGCR,HSF2,HSPA1A/HSPA1B,HSPE1,IGF2BP2,IL17D,ING1,ING2,IRAK2,JMJD6,JUND,KDM3A,KDM4D,KDM6B,KIT,KLF10,KLF11,KLF6,KLF9,KMT2A,LAIR1,LDHA,LGALS1,LGMN,LGR4,LTV1,LYN,MAP2K7,MAP3K1,MAP3K10,MAP3K3,MAP3K8,MAPK7,MARCHF5,MAT2A,MIF,MLKL,MLLT3,MME,MST1,MT-ND4,MTFP1,MVK,MXD1,MXI1,MYBBP1A,MYLK,NAMPT,NAPA,NCOA5,NDRG1,NET1,NFIL3,NFKBID,NME1,NOL3,NOLC1,NPC1,NQO1,NTS,NUAK1,NUAK2,ODC1,OGFOD1,OPTN,OXR1,PBX3,PDE4D,PDK1,PHF1,PHLPP1,PIAS4,PIK3AP1,PIM1,PIM3,PNPT1,PON2,PPM1A,PPP1R13L,PPP1R15A,PPP3CC,PPP3R1,PRDM5,PRDX1,PRKCB,PSEN2,PTK2,PTPRE,QKI,RAB32,RANBP9,RAP1A,RASSF2,RELA,RELB,RGS5,RHOC,RICTOR,RIPK1,RIPK2,RNF2,RPRM,RUNX2,RYBP,S100A11,SAT1,SATB1,SCD,SDC1,SELENON,SFPQ,SFRP2,SGMS2,SLC2A1,SLC46A1,SMOX,SMURF1,SP1,SREBF1,SRPK2,ST3GAL1,STEAP3,STX1A,SYK,TAB2,TESK2,TFEB,TJP2,TMEM123,TMF1,TNFAIP3,TNFRSF10B,TNFRSF13B,TNIP1,TP53INP1,TP63,TPD52L1,TRAF3IP2,TSC22D3,TXNIP,UBE2B,UIMC1,VASP,VAV3,VEGFA,XRCC1,ZEB1,ZFAND5,ZFP36,ZNF382 | 233 |
| Cell Death and Survival | apoptosis of tumor cell lines | 1.69E-09 | 7.97E-07 | | 1.208 | ACVR1B,ADM,ADORA2A,AHSA1,AKT3,ARID3B,ARNT,ATF2,ATN1,BCL6,BHLHE40,BLNK,BNIP3L,BRAF,CAMK2G,CCNG1,CDC73,CDK8,CDKN1B,CDKN1C,CDKN2D,CLK3,CLPTM1L,CRTC2,CSNK1A1,CTTN,DDIT3,DDIT4,DFFA,DNAJB1,DPH2,DUSP1,DYNLL1,ENO1,EPHB2,FAIM,FLI1,FOSL1,GAPDH,GEM,GLIPR1,HDAC5,HK2,HSPA1A/HSPA1B,IGF2BP2,IL17D,ING1,ING2,IRAK2,JUND,KIT,KLF6,KLF9,KMT2A,LAIR1,LGALS1,LTV1,LYN,MAP3K1,MAP3K10,MAPK7,MARCHF5,MAT2A,MIF,MLLT3,MME,MTFP1,MXD1,MXI1,MYBBP1A,NAPA,NDRG1,NFIL3,NME1,NOL3,NQO1,NUAK1,ODC1,OGFOD1,PBX3,PDE4D,PHF1,PHLPP1,PIM1,PPP1R13L,PPP1R15A,PRDM5,PRDX1,PRKCB,PSEN2,PTK2,PTPRE,RAB32,RELA,RELB,RHOC,RICTOR,RIPK1,RIPK2,RNF2,S100A11,SAT1,SATB1,SCD,SDC1,SFPQ,SFRP2,SGMS2,SMOX,SMURF1,SP1,SREBF1,SRPK2,ST3GAL1,SYK,TESK2,TFEB,TNFAIP3,TNFRSF10B,TP63,TSC22D3,UIMC1,VEGFA,XRCC1,ZEB1,ZFP36,ZNF382 | 127 |
| Cell Death and Survival,Organismal Injury and Abnormalities,Renal and Urological Disease | cell death of kidney cell lines | 4.41E-07 | 0.000129 | | 0.613 | ALDH3B1,ATN1,BAG4,BCL6,BNIP3L,BRAF,CUL4B,DDIT3,DDN,EPHB2,FDFT1,GAPDH,GNA13,GNAQ,HK2,HSPA1A/HSPA1B,LDHA,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,MLKL,NAMPT,NOL3,PPM1A,PPP1R15A,PPP3R1,PRKCB,PSEN2,PTK2,RELA,RIPK1,TJP2,TMEM123,TNFRSF10B,TP53INP1,VEGFA,ZEB1 | 39 |
| Cell Death and Survival,Organismal Injury and Abnormalities,Renal and Urological Disease | cell death of kidney cells | 5.84E-07 | 0.000162 | | 1.14 | ALDH3B1,ATN1,BAG4,BCL6,BNIP3L,BRAF,CDKN1B,CUL4B,DDIT3,DDN,DUSP1,EPHB2,FDFT1,GAPDH,GLIS2,GNA13,GNAQ,HK2,HSPA1A/HSPA1B,LDHA,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,MLKL,MST1,NAMPT,NOL3,PPM1A,PPP1R15A,PPP3R1,PRKCB,PSEN2,PTK2,RELA,RIPK1,TJP2,TMEM123,TNFRSF10B,TP53INP1,VEGFA,ZEB1 | 43 |
| Cell Death and Survival | cell viability | 4.57E-06 | 0.000916 | Decreased | -3.254 | ACSL5,ADORA2A,AEN,AGO2,AKT3,ALKBH8,ARNT,ARRB1,ATF2,ATP7A,BCL6,BHLHE40,BLNK,BRAF,BRD4,CA9,CACNB3,CAMK2D,CAMK2G,CCNG1,CDK8,CDKN1B,CDKN1C,CDKN2D,CLK3,COCH,CRTC2,CSNK1A1,DDIT3,DPH2,DUSP1,EFNA3,EFNA4,ENO1,EPHB2,EXO5,FLI1,FOSL1,FUS,GAB2,HDAC5,HK2,HSF2,HSPA1A/HSPA1B,HSPA6,ING1,INSIG1,ISG20L2,ITPKB,KDM4B,KIT,KLF6,LAT,LDHA,LYN,MAP3K1,MAP3K8,MAPK7,MED15,MIF,MRM1,MXD3,NA | 120 |

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|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | MPT,NDRG1,NFIL3,NME1,NOL3,NOP2,NOP58,NPC1,NUAK1,NUP58,OTUD7B,PBX3,PCGF2,PDK1,PDP1,PHLPP1,PIK3C2A,PIM1,POLR1A,PPM1A,PPP1R13L,PRKCB,PSEN2,PSME3,PTK2,PTPRE,RELA,RELB,RICTOR,RIPK1,RIPK2,RNF2,RRS1,RSF1,SAT1,SCD,SDC1,SERPINB2,SFRP2,SLC2A1,SLC31A1,STX1A,SYK,TFEB,TNFAIP3,TNFRSF10B,TNFRSF13B,TP63,TRAF3IP2,TSC22D3,TTBK2,TXNIP,U2AF1/U2AF1L5,VEGFA,XRCC1,YPEL3,ZFP36,ZNF124 |  |
| Cell Death and Survival,Organismal Injury and Abnormalities | cell death of epithelial cell lines | 1.04E-05 | 0.00185 |  | -0.617 | ALDH3B1,BAG4,BCL6,BNIP3L,BRAF,CDKN1B,CUL4B,DDIT3,DDN,DYNLL1,EPHB2,GAPDH,HK2,LDHA,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,MLKL,NAMPT,NOL3,PIM1,PPM1A,PPP1R15A,PPP3R1,PRKCB,RELA,RIPK1,TJP2,TNFRSF10B,TP53INP1,TP63,ZEB1 | 34 |
| Cell Death and Survival | cell death of melanoma cell lines | 0.000017 | 0.00278 |  | 0.221 | AKT3,ATF2,BRAF,BRD4,CDKN1B,CDT1,CNPY2,CSNK1A1,DDIT3,FAIM,IPMK,KMT2A,NME1,NOL3,NUP58,PDE4D,PIAS4,PPP1R15A,PRDM5,PRDX1,PTK2,SAT1,SH2D4A,SMOX,TNFRSF10B,TSC22D2,WDR4,XAB2,XRCC1,ZFP82 | 30 |
| Cell Death and Survival | cell death of fibroblast cell lines | 2.55E-05 | 0.00389 |  | -0.135 | ABCC4,ARNT,ATF2,ATN1,BCL6,BNIP3L,CCNG1,CDC73,CDKN1B,DDIT3,DDIT4,DFFA,DUSP1,ENO1,FLI1,FOXI1,FUS,GNA13,GNAQ,GPI,HIPK1,KLF6,MAP2K7,MAP3K1,MAP3K8,MLKL,MXD1,PIM1,PSEN2,PTK2,QKI,RELA,RGPD3 (includes others),RHOC,RIPK1,SERPINB2,STX1A,SYK,TMEM123,TNFAIP3,TNFRSF10B,TNIP1,TP53INP1,TP63,TXNIP | 45 |
| Cell Death and Survival,Embryonic Development | cell death of embryonic cell lines | 3.24E-05 | 0.00481 |  | -0.299 | ALDH3B1,BAG4,BCL6,BNIP3L,BRAF,CUL4B,DDN,EPHB2,GAPDH,GNAQ,HK2,LDHA,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,MLKL,NAMPT,NOL3,PPM1A,PPP1R15A,PPP3R1,PRKCB,RELA,RIPK1,TJP2,TNFRSF10B,TP53INP1 | 29 |
| Cell Death and Survival | cell survival | 3.46E-05 | 0.00506 | Decreased | -3.162 | ACSL5,ADORA2A,AEN,AGO2,AKT3,ALKBH8,ARNT,ARRB1,ATF2,ATP7A,BCL6,BHLHE40,BLNK,BRAF,BRD4,CA9,CACNB3,CAMK2D,CAMK2G,CCNG1,CDK8,CDKN1B,CDKN1C,CDKN2D,CLK3,COCH,CRTC2,CSNK1A1,DDIT3,DPH2,DUSP1,EFNA3,EFNA4,ENO1,EPHB2,EXO5,FLI1,FOSL1,FUS,GAB2,HDAC5,HK2,HSF2,HSPA1A/HSPA1B,HSPA6,ING1,INSIG1,ISG20L2,ITPKB,JUND,KDM4B,KIT,KLF6,LAT,LDHA,LYN,MAP3K1,MAP3K8,MAPK7,MED15,MIF,MRM1,MXD3,NAMPT,NDRG1,NFIL3,NME1,NOL3,NOP2,NOP58,NPC1,NUAK1,NUP58,ODC1,OTUD7B,PBX3,PCGF2,PDK1,PDP1,PHLPP1,PIK3C2A,PIM1,POLR1A,PPM1A,PPP1R13L,PRKCB,PSEN2,PSME3,PTK2,PTPRE,RELA,RELB,RICTOR,RIPK1,RIPK2,RNF2,RRS1,RSF1,SAT1,SCD,SDC1,SERPINB2,SFRP2,SLC2A1,SLC31A1,STX1A,SYK,TFEB,TNFAIP3,TNFRSF10B,TNFRSF13B,TP63,TRAF3IP2,TSC22D3,TTBK2,TXNIP,U2AF1/U2AF1L5,VEGFA,XRCC1,YPEL3,ZFP36,ZNF124 | 122 |
| Cell Death and Survival | cell death of blood cells | 0.000037 | 0.00534 |  | -1.259 | ABCC4,ACAT1,ADORA2A,ARNT,ARRB1,ATF2,BCL6,BLNK,BNIP3L,BTG1,CACNB3,CAMK2G,CDKN1B,CSNK1A1,DDIT3,DDIT4,DFFA,FAIM,FLI1,FNIP1,FOSL1,FUS,G6PC3,GAB2,GAPDH,ITPKB,KIT,KMT2A,LAIR1,LAT,LGALS1,LYN,MAP2K7,MAPK7,MIF,MXD1,MXD3,NAMPT,NFIL3,NFKBID,NME1,NPC1,NQO1,PDK1,PIK3AP1,PIM1,PNPT1,PON1,PPP1R13L,PRKCB,PSEN2,RELA,RICTOR,RIPK1,SATB1,SERPINB2,SLC2A1,SLC46A1,ST3GAL1,SYK,TNFAIP3,TNFRSF13B,TRAF3IP2,TSC22D3,VAV3,VEGFA | 66 |
| Cell Death and Survival | apoptosis of fibroblast cell lines | 3.79E-05 | 0.00541 |  | -0.847 | ATF2,ATN1,BCL6,BNIP3L,CCNG1,CDC73,CDKN1B,DDIT3,DDIT4,DUSP1,FLI1,FUS,GNA13,GNAQ,GPI,HIPK1,MAP2K7,MAP3K1,MAP3K8,MLKL,MXD1,PIM1,PSEN2,PTK2,QKI,RELA,RHOC,RIPK1,STX1A,SYK,TNFAIP3,TNFRSF10B,TNIP1,TP53INP1,TP63,TXNIP | 36 |
| Cell Death and Survival,Organismal Injury and Abnormalities,Renal and Urological Disease | apoptosis of kidney cell lines | 5.11E-05 | 0.00674 |  | -1.047 | ATN1,BCL6,BNIP3L,BRAF,CUL4B,DDIT3,DDN,GNA13,GNAQ,HSPA1A/HSPA1B,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,NOL3,PPM1A,PPP1R15A,PPP3R1,PSEN2,PTK2,RELA,RIPK1,TJP2,TNFRSF10B,TP53INP1,VEGFA,ZEB1 | 28 |
| Cell Death and Survival,Organismal Injury and Abnormalities | cell death of epithelial cells | 8.72E-05 | 0.00953 |  | 0.8 | ALDH3B1,ATF2,BAG4,BCL6,BNIP3L,BRAF,CDKN1B,CUL4B,DDIT3,DDN,DFFA,DYNLL1,EPHB2,FAIM,GAPDH,GLIS2,HK2,KLF10,LDHA,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,MLKL,MST1,MVK,MYLK,NAMPT,NCOA5,NDRG1,NOL3,PIAS4,PIM1,PPM1A,PPP1R15A,PPP3R1,PRKCB,PTK2,RELA,RELB,RIPK1,SCD,TJP2,TNFRSF10B,TNIP1,TP53INP1,TP63,ZEB1 | 49 |
| Cell Death and Survival,Organismal Injury and Abnormalities | necrosis of epithelial tissue | 0.000129 | 0.0131 |  | 1.388 | ADM,ALDH3B1,ATF2,BAG4,BCL6,BNIP3L,BRAF,CDKN1B,CUL4B,DDIT3,DDN,DFFA,DYNLL1,EPHB2,FAIM,GAPDH,GLIS2,HK2,KLF10,LDHA,LGALS1,LYN,MAP2K7,MAP3K1,MAP3K8,MAPK7,MIF,MLKL,MST1,MVK,MYLK,NAMPT,NCOA5,NDRG1,NOL3,PIAS4,PIM1,PPM1A,PPP1R15A,PPP3R1,PRKCB,PTK2,RELA,RELB,RGS5,RIPK1,RUNX2,SCD,TJP2,TNFAIP3,TNFRSF10B,TNIP1,TP53INP1,TP63,VEGFA,ZEB1 | 56 |
| Cell Death and Survival,Renal and Urological System | cell viability of kidney cell lines | 0.000214 | 0.0202 |  | -0.224 | ALKBH8,BCL6,EXO5,MAP3K8,NOP58,PPM1A,PSEN2,PTK2,RELA,SLC2A1,TFEB,TNFAIP3 | 12 |

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|---|---|---|---|---|---|---|---|
| Development and Function | | | | | | | |
| Cell Death and Survival | cell viability of tumor cell lines | 0.000248 | 0.0222 | Decreased | -2.952 | ACSL5,ADORA2A,AEN,AGO2,ARRB1,ATF2,BCL6,BHLHE40,BRAF,BRD4,CA9,CAMK2D,CCNG1,CDK8,CDKN1B,CDKN1C,CDKN2D,CLK3,DPH2,DUSP1,ENO1,FLI1,FOSL1,GAB2,HK2,HSF2,HSPA6,ING1,INSIG1,ISG20L2,KDM4B,KIT,KLF6,LDHA,LYN,MAP3K1,MAPK7,MED15,MRM1,NAMPT,NOL3,NOP2,NUAK1,NUP58,OTUD7B,PBX3,PCGF2,PDP1,PHLPP1,PIM1,POLR1A,PTK2,PTPRE,RELA,RELB,RICTOR,RIPK1,RNF2,RRS1,RSF1,SAT1,SCD,SDC1,SERPINB2,SLC2A1,SYK,TNFRSF10B,TP63,U2AF1/U2AF1L5,VEGFA,YPEL3,ZFP36,ZNF124 | 73 |
| Cell Death and Survival | cell death of connective tissue cells | 0.000306 | 0.0249 | | 0.741 | ABCC4,ADM,ARNT,ATF2,ATN1,BCL6,BNIP3L,CCNG1,CDC73,CDKN1B,DDIT3,DDIT4,DFFA,DUSP1,ENO1,FLI1,FOXI1,FUS,GNA13,GNAQ,GPI,HIPK1,ITPRIP,JUND,KLF6,MAP2K7,MAP3K1,MAP3K8,MLKL,MXD1,NFKBID,NPC1,PIM1,PPP1R15A,PSEN2,PTK2,QKI,RELA,RGPD3 (includes others), RHOC,RIPK1,RUNX2,SERPINB2,SFRP2,SMURF1,STX1A,SYK,TMEM123,TNFAIP3,TNFRSF10B,TNIP1,TP53INP1,TP63,TXNIP,VEGFA | 55 |
| Cell Death and Survival | cell death of immune cells | 0.000327 | 0.0262 | | -1.445 | ABCC4,ACAT1,ADORA2A,ARRB1,BCL6,BLNK,BTG1,CACNB3,CAMK2G,CDKN1B,CSNK1A1,DDIT3,DDIT4,DFFA,FAIM,FNIP1,FOSL1,FUS,G6PC3,GAB2,GAPDH,ITPKB,KIT,LAIR1,LAT,LGALS1,LYN,MAP2K7,MAPK7,MIF,MXD3,NAMPT,NFIL3,NFKBID,NME1,NPC1,NQO1,PDK1,PIK3AP1,PIM1,PNPT1,PON1,PPP1R13L,PRKCB,PSEN2,RELA,RICTOR,RIPK1,SATB1,SERPINB2,SLC2A1,ST3GAL1,SYK,TNFAIP3,TNFRSF13B,TRAF3IP2,TSC22D3,VAV3,VEGFA | 59 |
| Cell Death and Survival | cell death of hematopoietic cells | 0.00047 | 0.0331 | | 0.231 | ABCC4,ADORA2A,ARNT,ATF2,BNIP3L,DDIT4,DFFA,FAIM,FLI1,FNIP1,GAPDH,KMT2A,LGALS1,MXD1,MXD3,NFKBID,NQO1,PDK1,PIM1,RIPK1,SATB1,SLC46A1,TSC22D3,VAV3,VEGFA | 25 |
| Cell Death and Survival | cell viability of mononuclear leukocytes | 0.000508 | 0.0346 | | -1.314 | ARRB1,BCL6,BLNK,CACNB3,CAMK2G,GAB2,ITPKB,KIT,LAT,MAPK7,MIF,NFIL3,NME1,PDK1,PIM1,PRKCB,RELA,RICTOR,SYK,TNFRSF13B,TRAF3IP2,TSC22D3 | 22 |
| Cell Death and Survival,Hematological System Development and Function | cell viability of B lymphocytes | 0.000546 | 0.0363 | | -0.787 | BCL6,BLNK,ITPKB,MAPK7,MIF,NFIL3,PDK1,PRKCB,RELA,RICTOR,SYK,TNFRSF13B,TRAF3IP2,TSC22D3 | 14 |
| Cell Death and Survival | cell death of colorectal cancer cell lines | 0.000627 | 0.0392 | | 1.153 | AHSA1,BRAF,BTG3,CDKN1B,CDKN1C,CSNK1A1,DDIT3,DFFA,GLIPR1,KMT2A,MARCHF5,MIF,MLKL,MLLT3,NAPA,NDRG1,NUAK1,PHF1,PHLPP1,PPP1R15A,RELA,RICTOR,RNF2,SATB1,SFPQ,SMURF1,TNFRSF10B,VEGFA,ZNF382 | 29 |
| Cell Death and Survival | apoptosis of melanoma cell lines | 0.000657 | 0.0404 | | -0.071 | AKT3,ATF2,BRAF,CDKN1B,CSNK1A1,DDIT3,KMT2A,NME1,NOL3,PDE4D,PPP1R15A,PRDM5,PRDX1,SAT1,SMOX,TNFRSF10B | 16 |
| Cell Death and Survival,Organismal Injury and Abnormalities | apoptosis of epithelial cell lines | 0.000687 | 0.0414 | | -1.821 | BCL6,BNIP3L,BRAF,CUL4B,DDIT3,DDN,DYNLL1,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,NOL3,PIM1,PPM1A,PPP1R15A,PPP3R1,RELA,RIPK1,TJP2,TNFRSF10B,TP53INP1,TP63,ZEB1 | 24 |
| Cell Death and Survival,Embryonic Development | apoptosis of embryonic cell lines | 0.000885 | 0.0497 | | -1.867 | BCL6,BNIP3L,BRAF,CUL4B,DDN,GNAQ,LYN,MAP2K7,MAP3K1,MAP3K8,MIF,NOL3,PPM1A,PPP1R15A,PPP3R1,RELA,RIPK1,TJP2,TNFRSF10B,TP53INP1 | 20 |
| Cell Death and Survival,Neurological Disease,Organismal Injury and Abnormalities | cell death of cerebral cortex cells | 0.00102 | 0.0547 | | -0.52 | ADORA2A,CDKN1B,CDKN2D,DDIT3,DUSP1,EGLN2,FAIM,FUS,GAPDH,GBA,HK2,ITPRIP,KLF6,MAP3K1,MAPK7,MIF,NFIL3,RANBP9,RELA,SLC2A1,SP1,SRPK2,TP63,VEGFA | 24 |
| Cell Death and Survival | apoptosis of bone cancer cell lines | 0.00105 | 0.0554 | Increased | 2.39 | BCL6,BHLHE40,CDKN1B,FLI1,HDAC5,ING1,MAP3K1,MIF,NOL3,NUAK1,PPP1R13L,PRKCB,RELA,RIPK1,TNFRSF10B,TP63,UIMC1 | 17 |
| Cell Death and Survival,Hematological System Development and Function | cell viability of lymphocytes | 0.00161 | 0.0747 | | -0.935 | ARRB1,BCL6,BLNK,CACNB3,CAMK2G,ITPKB,KIT,LAT,MAPK7,MIF,NFIL3,PDK1,PIM1,PRKCB,RELA,RICTOR,SYK,TNFRSF13B,TRAF3IP2,TSC22D3 | 20 |
| Cell Death and Survival | apoptosis of colorectal cancer cell lines | 0.00163 | 0.0747 | | 0.80 | AHSA1,BRAF,CDKN1C,CSNK1A1,DDIT3,DFFA,GLIPR1,KMT2A,MARCHF5,MIF,MLLT3,NAPA,NDRG1,PHF1,PHLPP1,PPP1R15A,RELA,RICTOR,RNF2,SATB1,SFPQ,SMURF1,TNFRSF10B,ZNF382 | 24 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Cell Death and Survival | neuronal cell death | 0.00188 | 0.0774 | | -0.383 | ADORA2A,AKT3,ATF2,ATN1,ATP7A,BRAF,CDKN1B,CDKN2D,CPEB4,DDIT3,DFFA,DNAJB2,DUSP1,EFNA3,EGLN1,EGLN2,EPHB2,FAIM,FUS,GAB2,GAPDH,GBA,GPI,HDAC5,HK2,ITPRIP,KLF6,LDHA,LGALS1,LGMN,MAP2K7,MAP3K1,MAP3K10,MAPK7,MIF,MT-ND4,MXD3,NFIL3,NOL3,NPC1,NQO1,NTS,OPTN,OXR1,PDK1,PPP1R13L,PSEN2,PSME3,RANBP9,RELA,RNF19A,SLC2A1,SP1,SRPK2,STX1A,TFEB,TP63,TRIP10,VEGFA | 59 |
| Cell Death and Survival,Hair and Skin Development and Function | cell viability of epithelial cell lines | 0.00189 | 0.0774 | | -0.055 | ALKBH8,DDIT3,EXO5,MAP3K8,PCGF2,PPM1A,PSEN2,PTK2,RELA,TFEB,TNFAIP3,TP63 | 12 |
| Cell Death and Survival | cell death of bone cancer cell lines | 0.00202 | 0.0817 | Increased | 2.108 | BCL6,BHLHE40,BRD4,CDKN1B,FLI1,HDAC5,ING1,MAP3K1,MIF,NOL3,NUAK1,PPP1R13L,PRDX1,PRKCB,RELA,RIPK1,TNFRSF10B,TP63,UIMC1 | 19 |
| Cell Death and Survival | apoptosis of fibroblast-like synoviocytes | 0.00229 | 0.0859 | | 0.837 | ADM,NFKBID,RELA,TNFRSF10B,VEGFA | 5 |
| Cell Death and Survival | cell death of brain | 0.00229 | 0.0859 | | -0.884 | ADORA2A,AKT3,ATF2,CDKN1B,CDKN2D,DDIT3,DNAJB2,DUSP1,EGLN2,FAIM,FUS,GAPDH,GBA,HK2,ITPRIP,KLF6,MAP3K1,MAPK7,MIF,NFIL3,RANBP9,RELA,SLC2A1,SP1,SRPK2,TP63,TRIP10,VEGFA | 28 |
| Cell Death and Survival | cell viability of leukocytes | 0.00237 | 0.0881 | | -1.553 | ARRB1,BCL6,BLNK,CACNB3,CAMK2G,CSNK1A1,GAB2,ITPKB,KIT,LAT,LYN,MAPK7,MIF,NFIL3,NME1,PDK1,PIM1,PRKCB,RELA,RICTOR,SERPINB2,SYK,TNFRSF13B,TRAF3IP2,TSC22D3 | 25 |
| Cell Death and Survival | cell death of hematopoietic progenitor cells | 0.00281 | 0.0996 | | -0.119 | ABCC4,ADORA2A,ARNT,BNIP3L,DDIT4,DFFA,FAIM,FLI1,FNIP1,GAPDH,KMT2A,LGALS1,MXD3,NFKBID,NQO1,PDK1,RIPK1,SATB1,SLC46A1,TSC22D3,VAV3,VEGFA | 22 |
| Cell Death and Survival | apoptosis of hematopoietic cells | 0.00294 | 0.103 | | 0.043 | ADORA2A,ARNT,ATF2,BNIP3L,DFFA,FAIM,FLI1,FNIP1,KMT2A,LGALS1,MXD1,NFKBID,NQO1,PDK1,PIM1,RIPK1,SATB1,SLC46A1,TSC22D3,VAV3,VEGFA | 21 |
| Cell Death and Survival | cell death of heart | 0.0032 | 0.109 | | 0.798 | ADM,BNIP3L,CAMK2D,CDKN1B,EGLN1,FOSL1,GAPDH,GNAQ,HK2,HSPE1,JUND,MAP3K1,NAMPT,NOL3,PIM1,PPP1R15A,PRKCB,SCD,SFRP2,TNFAIP3,TXNIP,VEGFA | 22 |
| Cell Death and Survival | cell viability of blood cells | 0.00333 | 0.112 | | -1.971 | ARNT,ARRB1,BCL6,BLNK,CACNB3,CAMK2G,CSNK1A1,GAB2,ITPKB,KIT,LAT,LYN,MAPK7,MIF,NFIL3,NME1,PDK1,PIM1,PRKCB,RELA,RICTOR,SERPINB2,SYK,TNFRSF13B,TRAF3IP2,TSC22D3,VEGFA | 27 |
| Cell Death and Survival | apoptosis of sarcoma cell lines | 0.00335 | 0.113 | | 1.772 | BCL6,BHLHE40,CDKN1B,FLI1,HDAC5,ING1,ING2,MAP3K1,MIF,NOL3,NUAK1,PPP1R13L,PRKCB,RELA,RIPK1,S100A11,TNFRSF10B,TP63,UIMC1 | 19 |
| Cell Death and Survival | apoptosis of leukemia cell lines | 0.00357 | 0.116 | Increased | 2.034 | CAMK2G,CDKN1B,DDIT3,DFFA,DUSP1,HSPA1A/HSPA1B,KIT,KMT2A,LAIR1,LGALS1,LYN,MAP3K1,MLLT3,NFIL3,NQO1,PBX3,PRKCB,PTK2,PTPRE,RELA,RHOC,RIPK1,SGMS2,TNFAIP3,TNFRSF10B,TSC22D3 | 26 |
| Cell Death and Survival,Neurological Disease,Organismal Injury and Abnormalities | cell death of cortical neurons | 0.00364 | 0.116 | | -0.322 | CDKN1B,DDIT3,DUSP1,EGLN2,FAIM,FUS,GAPDH,GBA,HK2,MAP3K1,MAPK7,MIF,NFIL3,RELA,SP1,SRPK2,TP63,VEGFA | 18 |
| Cell Death and Survival | cell death of sarcoma cell lines | 0.00364 | 0.116 | | 1.785 | BCL6,BHLHE40,BRD4,CDKN1B,FLI1,HDAC5,ING1,ING2,MAP3K1,MIF,NAMPT,NOL3,NUAK1,PPP1R13L,PRDX1,PRKCB,RELA,RIPK1,S100A11,TNFRSF10B,TP63,UIMC1 | 22 |
| Cell Death and Survival | apoptosis of heart | 0.00369 | 0.116 | | 0.443 | ADM,BNIP3L,CAMK2D,CDKN1B,EGLN1,FOSL1,GAPDH,GNAQ,HSPE1,JUND,MAP3K1,NAMPT,NOL3,PIM1,SCD,SFRP2,TNFAIP3,TXNIP,VEGFA | 19 |
| Cell Death and Survival | cell death of leukemia cell lines | 0.00381 | 0.118 | | 1.903 | BTG1,CAMK2G,CDKN1B,DDIT3,DFFA,DUSP1,GAPDH,HSPA1A/HSPA1B,KIT,KMT2A,LAIR1,LGALS1,LYN,MAP3K1,MLLT3,NFIL3,NQO1,PBX3,PRKCB,PTK2,PTPRE,RELA,RHOC,RIPK1,SGMS2,TMEM123,TNFAIP3,TNFRSF10B,TSC22D3 | 29 |
| Cell Death and Survival | apoptosis of brain | 0.00401 | 0.121 | | -1.277 | AKT3,ATF2,DDIT3,DUSP1,FAIM,GAPDH,HK2,KLF6,MAP3K1,MAPK7,MIF,RANBP9,RELA,SRPK2,TP63,VEGFA | 16 |
| Cell Death and Survival,Embryonic Development | cell viability of embryonic cell lines | 0.00403 | 0.121 | | -0.446 | ALKBH8,EXO5,MAP3K8,PPM1A,PSEN2,PTK2,RELA,TFEB,TNFAIP3 | 9 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cell Death and Survival,Cell Morphology,Cellular Function and Maintenance | autophagic cell death | 0.00403 | 0.121 | | CDKN1B,CDKN2D,MAP2K7,TNFRSF10B,TP53INP1 | 5 |
| Cell Death and Survival | cell death of heart cells | 0.0042 | 0.124 | 1.159 | ADM,BNIP3L,CAMK2D,CDKN1B,EGLN1,FOSL1,GAPDH,GNAQ,HK2,HSPE1,JUND,MAP3K1,NAMPT,NOL3,PIM1,PPP1R15A,PRKCB,SFRP2,TNFAIP3,TXNIP,VEGFA | 21 |
| Cell Death and Survival | cell death of neuroblastoma cell lines | 0.00466 | 0.133 | 1.219 | ADM,AKT3,CDKN2D,DDIT3,DNAJB1,ENO1,GAPDH,HSPA1A/HSPA1B,MIF,MXI1,OXR1,PRKCB,PSEN2,PTK2,RELA,RIPK1,TNFRSF10B,UBE2S,VEGFA | 19 |
| Cell Death and Survival,Connective Tissue Disorders,Organismal Injury and Abnormalities,Skeletal and Muscular Disorders | avascular necrosis | 0.0047 | 0.133 | | ADORA2A,FDFT1,PDE3B,PDE4D | 4 |
| Cell Death and Survival,Hematological System Development and Function | survival of marginal-zone B lymphocytes | 0.00511 | 0.133 | | PDK1,TRAF3IP2 | 2 |
| Cell Death and Survival | cell death of hepatoma cell lines | 0.00614 | 0.151 | 0.573 | ACVR1B,ARNT,CCNG1,DDIT3,IGF2BP2,IRAK2,JUND,MAP3K10,MAT2A,NUAK1,PRDM5,RELA,SCD,SYK,TNFRSF10B,TP63,VEGFA | 17 |
| Cardiovascular Disease,Cell Death and Survival,Organismal Injury and Abnormalities,Skeletal and Muscular Disorders | cell death of cardiomyocytes | 0.00625 | 0.153 | 0.998 | ADM,BNIP3L,CAMK2D,CDKN1B,EGLN1,FOSL1,GAPDH,GNAQ,HK2,HSPE1,JUND,MAP3K1,NAMPT,NOL3,PIM1,PPP1R15A,PRKCB,TNFAIP3,TXNIP,VEGFA | 20 |
| Cell Death and Survival,Neurological Disease,Organismal Injury and Abnormalities | apoptosis of cerebral cortex cells | 0.00627 | 0.153 | -1.071 | DDIT3,FAIM,HK2,KLF6,MAP3K1,MAPK7,MIF,RANBP9,RELA,SRPK2,TP63,VEGFA | 12 |
| Cell Death and Survival,Neurological Disease,Organismal Injury and Abnormalities | cell death of brain cells | 0.00642 | 0.156 | -1.071 | ADORA2A,ATF2,CDKN1B,CDKN2D,DDIT3,DUSP1,EGLN2,FAIM,FUS,GAPDH,GBA,HK2,ITPRIP,KLF6,MAP3K1,MAPK7,MIF,NFIL3,RANBP9,RELA,SLC2A1,SP1,SRPK2,TP63,VEGFA | 25 |
| Cell Death and Survival | apoptosis of heart cells | 0.00702 | 0.165 | 0.74 | ADM,BNIP3L,CAMK2D,CDKN1B,EGLN1,FOSL1,GAPDH,GNAQ,HSPE1,JUND,MAP3K1,NAMPT,NOL3,PIM1,SFRP2,TNFAIP3,TXNIP,VEGFA | 18 |
| Cell Death and Survival | apoptosis of blood cells | 0.00723 | 0.168 | -0.632 | ADORA2A,ARNT,ARRB1,ATF2,BCL6,BLNK,BNIP3L,BTG1,CAMK2G,CDKN1B,DDIT3,DFFA,FAIM,FLI1,FNIP1,FOSL1,G6PC3,KMT2A,LGALS1,LYN,MIF,MXD1,NAMPT,NFKBID,NPC1,NQO1,PDK1,PIK3AP1,PIM1,PPP1R13L,PRKCB,RELA,RIPK1,SATB1,SLC46A1,ST3GAL1,TNFAIP3,TRAF3IP2,TSC22D3,VAV3,VEGFA | 41 |
| Cell Death and Survival | apoptosis of hepatoma cell lines | 0.00846 | 0.188 | 0.557 | ACVR1B,ARNT,CCNG1,DDIT3,IGF2BP2,JUND,MAP3K10,MAT2A,PRDM5,RELA,SCD,SYK,TNFRSF10B,TP63,VEGFA | 15 |
| Cell Death and Survival | cell death of pheochromocytoma cell lines | 0.00849 | 0.188 | -0.936 | ADORA2A,ATN1,DDIT4,DNAJB1,DYNLL1,FAIM,GAPDH,GEM,MAP3K1,MCU,PSEN2,SP1 | 12 |
| Cell Death and Survival,Connective Tissue Development and Function | cell viability of fibroblasts | 0.00853 | 0.189 | -1.574 | AEN,AKT3,CCNG1,COCH,MAP3K1,MIF,PTK2,RELA,SLC31A1,TP63 | 10 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cell Death and Survival | cell death of central nervous system cells | 0.0086 | 0.189 | -0.793 | ADORA2A,ATF2,CDKN1B,CDKN2D,DDIT3,DUSP1,EGLN2,FAIM,FUS,GAPDH,GBA,HK2,ITPRIP,KLF6,MAP3K1,MAPK7,MIF,NFIL3,PFKFB3,RANBP9,RELA,SLC2A1,SP1,SRPK2,TP63,VEGFA | 26 |
| Cancer,Cell Death and Survival,Organismal Injury and Abnormalities,Tumor Morphology | apoptosis of lung cancer cells | 0.00866 | 0.189 | | NDRG1,RELA,TNFRSF10B,VEGFA | 4 |

Table 1- Genes involved in cell death and survival from Figure 3A. Predictive activation decrease yellow and increase blue of pathway function.

| Categories | Diseases or Functions Annotation | p-value | B-H p-value | Predicted Activation State | Activation z-score | Molecules | # Molecules |
|---|---|---|---|---|---|---|---|
| Energy Production,Molecular Transport,Nucleic Acid Metabolism,Small Molecule Biochemistry | concentration of ATP | 0.0000407 | 0.00572 | Decreased | -2.319 | ALDOA,ATP5MC1,ENO1,FNIP1,G6PC3,GAPDH,LDHA,MCU,MTATP6,NAMPT,NQO1,NUAK1,PDK1,PIM1,PIM3,RELA,SLC25A25,SREBF1 | 18 |
| Lipid Metabolism,Small Molecule Biochemistry,Vitamin and Mineral Metabolism | synthesis of sterol | 0.0000649 | 0.00781 |  | -0.947 | ACAT1,CYP51A1,DHCR7,FDFT1,HMGCR,IDI1,INSIG1,MVK,NPC1,PON1,SCD,SREBF1,STARD4 | 13 |
| Lipid Metabolism,Small Molecule Biochemistry | synthesis of long chain fatty acid | 0.000374 | 0.0289 |  | -1.057 | ARNT,FAR2,QKI,SCD,SLC27A4,SREBF1 | 6 |
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | concentration of phospholipid | 0.000403 | 0.0297 |  | -0.774 | ARNT,BSCL2,CERT1,G6PC3,GNAQ,INSIG1,LIPG,LSR,MTMR3,NPC1,PIK3C2A,PON1,PSEN2,PTK2,SCD,SGMS2,SLC27A4,SREBF1,STARD4,SYNJ1,TXNIP,VLDLR | 22 |
| Lipid Metabolism,Small Molecule Biochemistry,Vitamin and Mineral Metabolism | synthesis of cholesterol | 0.000449 | 0.0322 |  | -1.739 | CYP51A1,DHCR7,FDFT1,HMGCR,IDI1,INSIG1,MVK,NPC1,PON1,SREBF1 | 10 |
| Small Molecule Biochemistry | metabolism of spermine | 0.000687 | 0.0414 |  |  | SAT1,SAT2,SMOX | 3 |
| Lipid Metabolism,Small Molecule Biochemistry | biosynthesis of stearic acid | 0.000687 | 0.0414 |  |  | ARNT,SCD,SREBF1 | 3 |
| Energy Production,Molecular Transport,Nucleic Acid Metabolism,Small Molecule Biochemistry | secretion of ATP | 0.000908 | 0.05 |  | -1.432 | AKT3,GNA13,LYN,NTS,PRKCB | 5 |
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | concentration of cholesterol | 0.00124 | 0.062 |  | -1.2 | ACAT1,ADM,ANGPTL4,ARNT,BSCL2,CDKN1B,DHCR7,DUSP1,FDFT1,G6PC3,HMGCR,INSIG1,KDM3A,LIPG,LSR,NAMPT,NPC1,NSUN2,PON1,PRKCB,PSEN2,RORA,SC5D,SCD,SEC24A,SREBF1,STARD4,TXNIP,VLDLR | 29 |
| Lipid Metabolism,Small Molecule Biochemistry,Vitamin and Mineral Metabolism | metabolism of cholesterol | 0.00124 | 0.062 | Decreased | -2.188 | CYP51A1,DHCR7,ENO1,FDFT1,HMGCR,IDI1,INSIG1,MVK,NPC1,PON1,SQLE,SREBF1,VLDLR | 13 |
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | quantity of saturated fatty acid | 0.00133 | 0.065 |  |  | PON1,SCD,SREBF1 | 3 |

|  |  |  |  |  |  |  |
|---|---|---|---|---|---|---|
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | concentration of sterol | 0.00136 | 0.0658 | -1.011 | ACAT1,ADM,ANGPTL4,ARNT,BSCL2,CDKN1B,DHCR7,DUSP1,FDFT1,G6PC3,HMGCR,INSIG1,KDM3A,LIPG,LSR,NAMPT,NPC1,NSUN2,PON1,PRKCB,PSEN2,RORA,SC5D,SCD,SEC24A,SLC27A4,SREBF1,STARD4,TXNIP,VLDLR | 30 |
| Small Molecule Biochemistry | regulation of spermidine | 0.00175 | 0.0747 |  | ODC1,SAT1 | 2 |
| Small Molecule Biochemistry | biosynthesis of pyrimidine | 0.00175 | 0.0747 |  | CAD,DHODH | 2 |
| Small Molecule Biochemistry | accumulation of putrescine | 0.00175 | 0.0747 |  | ODC1,SAT1 | 2 |
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | accumulation of farnesyl pyrophosphate | 0.00175 | 0.0747 |  | FDFT1,HMGCR | 2 |
| Molecular Transport,Small Molecule Biochemistry | depletion of spermidine | 0.00175 | 0.0747 |  | ODC1,SAT1 | 2 |
| Amino Acid Metabolism,Post-Translational Modification,Small Molecule Biochemistry | phosphorylation of L-amino acid | 0.00188 | 0.0774 | -1.03 | ABI1,ACVR1B,AKT3,CAMK2D,CLK1,CLK3,DUSP1,EPHB2,KIT,LYN,MAP3K10,MIF,MYLK,PPP2R5B,PRKCB,PTK2,RICTOR,RIPK2,SYK,VEGFA | 20 |
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | quantity of oleic acid | 0.00226 | 0.0859 |  | ELOVL5,SCD,SREBF1 | 3 |
| Lipid Metabolism,Molecular Transport,Nucleic Acid Metabolism,Small Molecule Biochemistry | concentration of malonyl-coenzyme A | 0.00288 | 0.101 |  | MLYCD,SAT1,SCD,SREBF1 | 4 |
| Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | quantity of steroid | 0.00302 | 0.105 | -0.577 | ABCC4,ACAT1,ADM,AKT3,ANGPTL4,ARNT,BSCL2,CDKN1B,CDKN2D,CRTC2,CRY2,DHCR7,DUSP1,FDFT1,G6PC3,GNAQ,HMGCR,INSIG1,KDM3A,KMT2C,LGR4,LIPG,LSR,MIF,NAMPT,NPC1,NSUN2,PON1,PRKCB,PSEN2,RORA,SC5D,SCD,SEC24A,SLC27A4,SREBF1,STARD4,TSC22D3,TXNIP,VAV3,VLDLR | 41 |
| Lipid Metabolism,Small Molecule Biochemistry | synthesis of monounsaturated fatty acids | 0.0035 | 0.115 |  | ARNT,SCD,SREBF1 | 3 |
| Amino Acid Metabolism,Small Molecule Biochemistry | accumulation of acidic amino acid | 0.0035 | 0.115 |  | ABCC4,GLUL,SLC17A7 | 3 |
| Small Molecule Biochemistry | metabolism of spermidine | 0.0035 | 0.115 |  | ODC1,SAT1,SAT2 | 3 |
| Carbohydrate Metabolism,Lipid | concentration of choline-phospholipid | 0.00379 | 0.117 | -1.274 | INSIG1,LIPG,PON1,PSEN2,SCD,SGMS2,SLC27A4,SREBF1 | 8 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Metabolism,Molecular Transport,Small Molecule Biochemistry | | | | | | | |
| Carbohydrate Metabolism,Molecular Transport,Small Molecule Biochemistry | concentration of D-glucose | 0.00417 | 0.124 | Decreased | -2.062 | ADM,ARNT,BSCL2,CA5B,CDKN1B,CRTC2,CRY2,CTHRC1,DDAH2,ELOVL5,HDAC5,HDAC7,IGF2BP2,KDM3A,MIF,NQO1,NUAK1,NUAK2,PDE3B,PON1,PPP1R15A,SCD,SGMS2,SLC2A1,SREBF1,STEAP3,STX1A,TXNIP,ZBED3,ZMPSTE24 | 30 |
| Amino Acid Metabolism,Small Molecule Biochemistry | metabolism of glutamine | 0.0047 | 0.133 | | | ALDH5A1,CAD,GLUL,PFAS | 4 |
| Cell Signaling,Small Molecule Biochemistry,Vitamin and Mineral Metabolism | regulation of Ca2+ | 0.0047 | 0.133 | | -1.951 | GNA13,GNAQ,NTS,VEGFA | 4 |
| Lipid Metabolism,Small Molecule Biochemistry | synthesis of palmitic acid | 0.00509 | 0.133 | | | ARNT,SLC27A4,SREBF1 | 3 |
| Carbohydrate Metabolism,Lipid Metabolism,Small Molecule Biochemistry | hydrolysis of phosphtidylinositol 5-phosphate | 0.00511 | 0.133 | | | PIP4P1,PIP4P2 | 2 |
| Carbohydrate Metabolism,Small Molecule Biochemistry | length of heparan sulfate | 0.00511 | 0.133 | | | EXT1,EXTL2 | 2 |
| Lipid Metabolism,Nucleic Acid Metabolism,Small Molecule Biochemistry | catabolism of acyl-coenzyme A | 0.00511 | 0.133 | | | ACAT1,MLYCD | 2 |
| Small Molecule Biochemistry | catabolism of spermine | 0.00511 | 0.133 | | | SAT1,SMOX | 2 |
| Amino Acid Metabolism,Post-Translational Modification,Small Molecule Biochemistry | phosphorylation of L-threonine | 0.00513 | 0.133 | | | ACVR1B,AKT3,CAMK2D,CLK1,DUSP1,MAP3K10,MYLK | 7 |
| Lipid Metabolism,Small Molecule Biochemistry | Lipolysis | 0.00522 | 0.135 | | -0.118 | ADM,ANGPTL4,ARRB1,BSCL2,EIF4EBP2,LIPG,PDE3B,PFKFB3,SLC27A4,SREBF1,TFE3 | 11 |
| Small Molecule Biochemistry | metabolism of polyamines | 0.00585 | 0.145 | | | ODC1,SAT1,SAT2,SMOX | 4 |
| Carbohydrate Metabolism,Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | quantity of lysophosphatidylcholine | 0.00585 | 0.145 | | -1.067 | LIPG,PON1,SLC27A4,SREBF1 | 4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Amino Acid Metabolism,Small Molecule Biochemistry | metabolism of glutamine family amino acid | 0.00603 | 0.149 | | ALDH5A1,CAD,DDAH2,GLUL,PFAS,SLC22A5 | 6 |
| Carbohydrate Metabolism,Lipid Metabolism,Molecular Transport,Small Molecule Biochemistry | concentration of phosphatidic acid | 0.00766 | 0.175 | -1.252 | BSCL2,G6PC3,GNAQ,INSIG1,LIPG,MTMR3,PIK3C2A,PON1,PSEN2,PTK2,SCD,SGMS2,SLC27A4,SREBF1,SYNJ1 | 15 |
| Lipid Metabolism,Small Molecule Biochemistry | fatty acid metabolism | 0.0085 | 0.188 | 0.604 | ABCC4,ACAT1,ACBD3,ACSL5,ADORA2A,ALDH5A1,ARHGEF11,ARNT,CAMK2G,CD83,CERT1,DBP,ELOVL5,FAR2,GBA,HBP1,INSIG1,KIT,KLF11,LIPG,LYN,MAP3K1,MAP3K8,MECR,MIF,MLYCD,MSMO1,NPC1,NQO1,PON1,QKI,RELA,RELB,SAMD8,SC5D,SCD,SGMS2,SLC22A5,SLC27A4,SP1,SREBF1,STARD4,STX1A,SYK,THEM4,TJP2,VEGFA,VLDLR | 48 |

Table 2. Genes involved in Small Molecule Biochemistry from Figure 3B. Predictive activation decrease yellow and increase blue of pathway function.

| **Symbol** | **Entrez Gene Name** | **Ensembl** | **Expr Intensity/ RPKM/FPKM/ Counts** | **Expr Log Ratio** | **Expr p-value** | **Expr False Discovery Rate (q-value)** | **Location** | **Type(s)** | **Entrez Gene ID for Human** | **Entrez Gene ID for Mouse** | **Entrez Gene ID for Rat** |
|---|---|---|---:|---:|---:|---:|---|---|---:|---:|---:|
| ATP5MC1 | ATP synthase membrane subunit c locus 1 | ENSG00000159199 | 1399.856 | 1.015 | 1.12E-05 | 0.00083 | Cytoplasm | transporter | 516 | 11951 | 29754 |
| MT-ATP6 | ATP synthase F0 subunit 6 | ENSG00000198899 | 45749.68 | 1.605 | 3.97E-08 | 7.62E-06 | Cytoplasm | transporter | 4508 | 17705 | 26197 |
| MT-CO1 | cytochrome c oxidase subunit I | ENSG00000198804 | 203642.6 | 1.323 | 0.000118 | 0.00466 | Cytoplasm | enzyme | 4512 | 17708 | 26195 |
| MT-CO2 | cytochrome c oxidase subunit II | ENSG00000198712 | 101738.6 | 1.561 | 5.19E-10 | 2.61E-07 | Cytoplasm | enzyme | 4513 | 17709 | 26198 |
| MT-CO3 | cytochrome c oxidase III | ENSG00000198938 | 109184.5 | 1.609 | 3.23E-11 | 2.35E-08 | Cytoplasm | enzyme | 4514 | 17710 | 26204 |
| MT-CYB | cytochrome b | ENSG00000198727 | 48355.53 | 1.317 | 4.81E-06 | 0.000415 | Cytoplasm | enzyme | 4519 | 17711 | 26192 |
| MT-ND1 | NADH dehydrogenase, subunit 1 (complex I) | ENSG00000198888 | 38078.52 | 1 | 0.00153 | 0.0327 | Cytoplasm | enzyme | 4535 | 17716 | 26193 |
| MT-ND2 | MTND2 | ENSG00000198763 | 35787.01 | 1.459 | 5.91E-09 | 1.87E-06 | Cytoplasm | enzyme | 4536 | 17717 | 26194 |
| MT-ND3 | NADH dehydrogenase, subunit 3 (complex I) | ENSG00000198840 | 13654.46 | 1.507 | 6.82E-09 | 2.07E-06 | Cytoplasm | enzyme | 4537 | 17718 | 26199 |
| MT-ND4 | NADH dehydrogenase, subunit 4 (complex I) | ENSG00000198886 | 166228.4 | 1.267 | 0.000109 | 0.00442 | Cytoplasm | enzyme | 4538 | 17719 | 26201 |
| MT-ND5 | NADH dehydrogenase, subunit 5 (complex I) | ENSG00000198786 | 68634.77 | 1.208 | 0.0018 | 0.0371 | Cytoplasm | enzyme | 4540 | 17721 | 26202 |
| MT-ND4L | NADH dehydrogenase, subunit 4L (complex I) | ENSG00000212907 | 24210.13 | 1.172 | 0.00281 | 0.0502 | Cytoplasm | enzyme | 4539 | 17720 | 26200 |

Table 3. Genes involved in the conanical pathway of oxidatible phosphorylation. Genes from Figure 4A.

|  |  | Normalized_Counts_per_Sample |  |  |  |  |  | Significant | Significant and \|lfc\|>1 |
|---|---|---|---|---|---|---|---|---|---|
| **Associated_Gene_Name** | **Description** | **M_1** | **M_3** | **K_1** | **K_2** | **H_1** | **H_2** | **KH / M** | **KH / M** |
| **No cytokine secreted** |  |  |  |  |  |  |  |  |  |
| TNFAIP1 | TNF_alpha_induced_protein_1 | 2474 | 2450 | 1722 | 1710 | 1350 | 1661 | yes | no |
| TNFAIP2 | TNF_alpha_induced_protein_2 | 201 | 153 | 184 | 464 | 273 | 230 | no | no |
| TNFAIP3 | TNF_alpha_induced_protein_3 | 13580 | 19824 | 4184 | 5441 | 6212 | 6268 | no | yes |
| TNFAIP8 | TNF_alpha_induced_protein_8 | 2272 | 2492 | 1809 | 1861 | 2028 | 1755 | yes | no |
| IL12A | interleukin_12A | 85 | 75 | 121 | 142 | 131 | 132 | yes | no |
| IL12RB1 | interleukin_12_receptor_subunit_beta_1 | 552 | 646 | 1108 | 519 | 547 | 589 | no | no |
| IL12RB2 | interleukin_12_receptor_subunit_beta_2 | 13 | 11 | 8 | 8 | 4 | 7 | no | no |
| IL1B | interleukin_1_beta | 0 | 0 | 4 | 0 | 0 | 0 | yes | no |
| IL1R2 | interleukin_1_receptor,_type_II | 0 | 0 | 1 | 0 | 0 | 1 | no | no |
| IL1RAP | interleukin_1_receptor_accessory_protein | 108 | 73 | 95 | 113 | 155 | 107 | no | no |
| IL1RAPL1 | interleukin_1_receptor_accessory_protein-like_1 | 0 | 1 | 0 | 1 | 1 | 1 | no | no |
| IL1RAPL2 | interleukin_1_receptor_accessory_protein-like_2 | 1 | 0 | 2 | 0 | 0 | 1 | no | no |
| IL1RL2 | interleukin_1_receptor-like_2 | 1 | 0 | 0 | 0 | 0 | 1 | no | no |
| **Cytokine secretion** |  |  |  |  |  |  |  |  |  |
| IL10 | interleukin_10 | 1 | 5 | 2 | 4 | 3 | 4 | no | no |
| IL10RA | interleukin_10_receptor_subunit_alpha | 329 | 355 | 796 | 262 | 291 | 434 | no | no |
| IL10RB | interleukin_10_receptor_subunit_beta | 823 | 643 | 773 | 1250 | 951 | 1234 | yes | no |
| IL6 | interleukin_6 | 0 | 0 | 1 | 0 | 2 | 0 | yes | no |
| IL6R | interleukin_6_receptor | 297 | 210 | 244 | 260 | 548 | 426 | no | no |
| IL6ST | interleukin_6_signal_transducer | 30550 | 34083 | 22126 | 20583 | 26520 | 24898 | yes | no |

Supplementary Table 4. Raw normalized counts of cytokine RNA levels involved in inflammation.